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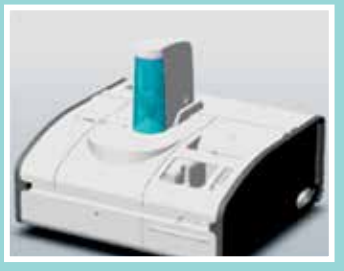

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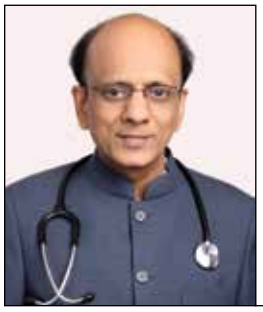

Dr KK Aggarwal
5th September 1958 - 17th May 2021

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US and Omicron Update

Speaker: Dr Monica Vasudev, *Allergist & Clinical Immunologist, Fellow of American Academy of Asthma, Allergy and Immunology, Advocate Aurora Health, Wisconsin, USA*

- There have been over 5.4 million deaths since the onset of the pandemic and the US is leading the toll with 8,37,671 deaths. There is loss not only in terms of lives, but also the quality of life.
- Variants happen because of two major factors. High number of cases increase risk of mutations. Some mutations lead to new variants. It's the changes in the spike protein that are of concern.
- It has been a year since a new variant (Omicron) was detected since Delta variant was identified in October 2020.
- The Omicron variant has over 50 mutations not seen in combination before. There are 30+ mutations in the gene for the spike protein that the coronavirus uses to attach to human cells.
- Omicron's spike protein has several mutations that are found in other variants of concern (VOC) and that are thought to make the virus more infectious, including D614G, N501Y and K417N.
- It was designated as VOC by the World Health Organization (WHO) on 26th November, 2021 and has been identified in more than 90 countries.
- Early December, a California resident who had returned from South Africa was the first identified American to be infected.
- It spreads 2 to 3 times faster than Delta and Cases double every 2 to 4 days. People are 5 times more likely to be reinfected with Omicron compared to other VOC.
- Recent research from HKUMed (Hong Kong) found that the Omicron severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) can infect faster and better than Delta in human bronchus but with less severe infection in lung. At 24 hours after infection, Omicron replicated 70 times higher than the Delta variant and the original SARS-CoV-2 virus in the bronchial tissue. But it replicated less efficiently (10 times lower) in lung tissue than the original SARS-CoV-2. This explains its high transmissibility and probably the less associated morbidity.
- Omicron is spreading rapidly in the US. It accounted for 73% of new infections last week, showing nearly a 6-fold increase within a week, as per CDC (Dec. 20, 2021).
- A study summarized the use of over-the-counter (OTC) rapid antigen tests. Seven different antigen-detecting rapid diagnostic tests (Ag-RDTs) were used (some approved/some in the process of being approved). It was found that the analytical sensitivity to detect Omicron was lower than for

the other VOCs in most of the tests evaluated. One test (Flowflex-ACON Biotech) showed the highest overall sensitivity for all SARS-CoV-2 isolates used compared to the others, and here, Omicron was detected with even slightly higher sensitivity than Delta but still lower than Alpha, Beta, Gamma and the pre-VOC SARS-CoV.

- Evaluation of coronavirus disease 2019 (COVID-19) vaccine effectiveness over time (Delta; Pre-Omicron) showed that two doses of mRNA or adenovirus vector vaccines elicit high levels of protection from symptomatic disease, but the protection waned over time at 6 months. Emerging studies show that a third dose (booster) of the same type improved effectiveness to >90%.
- In a Danish cohort study conducted at Statens Serum Institut (SSI), a third dose of either Pfizer-BioNTech or Moderna vaccine led to a "significant increase" in protection against the Omicron variant in the elderly. Among those who recently had their second vaccine dose, effectiveness against Omicron was measured at 55.2% for Pfizer-BioNTech and 36.7% for Moderna, compared to unvaccinated people. It was seen that protection quickly waned over the course of 5 months. Protection was lower and decreased faster against Omicron than against the Delta variant after a primary vaccination course. The third dose of Pfizer-BioNTech's vaccine restored protection to 54.6% in people aged 60 or more who had been inoculated 14 to 44 days earlier, compared to those with only two doses.
- Another study from Hong Kong showed that a third dose of the Pfizer vaccine given to those who received two doses of either the Pfizer or CoronaVac provides protective levels of protective antibody against the Omicron variant. Whereas the third dose of CoronaVac given to those who received two previous doses of CoronaVac does not provide adequate levels of protective antibody.
- The Novavax (NVX-CoV2373) vaccine is a promising vaccine. It uses a novel platform where a different virus (a baculovirus) is combined with the genetic information needed to make a spike protein, a key fragment of SARS-CoV-2. When moth cells are infected with this virus, they manufacture the spike protein. Scientists then harvest and fuse those proteins with a nanoparticle, which combine with spike proteins are what is injected in the Novavax vaccine.
- The first study with Novavax was done in Mexico and US, which showed 90.4% reduction in symptomatic cases from 7 days after second dose compared with people given placebo. The second study conducted in the UK found 89.7% efficacy in reducing symptomatic cases.
- Two dose primary regimen of the Novavax demonstrated cross-reactive immune responses against Omicron and other variants. The third dose increased immune responses with a 9.3-fold rise in anti-spike IgG and 19.9-fold increase in angiotensin-converting enzyme 2 (ACE2) inhibition. Immune responses in adolescents were 2- to 4-fold higher than adults against broad array of variants of interests (VOIs) and VOCs. After two doses, Omicron wild-type neutralization was <4-fold lower than prototype, suggesting that both a booster dose as well as an Omicron-specific vaccine may be beneficial.
- The monoclonal antibodies and antiviral pills are intended to keep people newly diagnosed with COVID from being hospitalized.
- The two commonly used monoclonal antibody treatments are casirivimab/indevimab and baml-anivimab/etesevimab. These have reduced activity against the Omicron variant of SARS-CoV-2 and may have little to no effectiveness in patients infected with the Omicron variant. Their use has been suspended until further notice (as of 23rd December) since the Omicron is spreading very rapidly.
- Sotrovimab appears to retain effectiveness against Omicron.
- There is a new long-acting monoclonal antibody combination (tixagevimab co-packaged with cilgavimab), which has been granted emergency use authorization (EUA) by the US Food and Drug Administration (FDA) for use as pre-exposure prophylaxis for patients at high risk of severe COVID-19.
- Omicron has escaped neutralization from the family of monoclonal antibodies and their combinations that are available with the possible exception of sotrovimab.
- On December 22, the FDA authorized the first easy to use pill "Paxlovid" (Pfizer) to treat COVID-19 in the US with the surge in Omicron cases. An 89% reduction in the number of hospitalizations or deaths was seen compared with placebo; 6.3% (placebo) vs. 0.8% (Paxlovid). A 94% reduction in

people aged 65 years and older was seen with 10-fold decline in viral load. Fewer adverse events and lab data showed potent anti-Omicron activity.

- Molnupiravir (Merck) was granted EUA on 23rd December. It is indicated for the treatment of mild-to-moderate COVID-19 in adults with positive results of direct SARS-CoV-2 viral testing, and who are at high-risk for progression to severe COVID-19, including hospitalization or death, and for whom alternative COVID-19 treatment options authorized by the FDA are not accessible or clinically appropriate. It's not recommended for use during pregnancy because of potential fetal harm (animal studies).
- We have to use the Swiss Cheese model, which means that its not just one thing which will help. The pandemic has to be addressed in as many different ways as we can.
- Patients hospitalized in the US are mainly Delta. Its only in the last week that there has been a surge of Omicron.
- There is no antibody response with J&J vaccine against Omicron as per a study from South Africa.
- It is likely that the Omicron will leave some residual effect on the body even if it is a mild disease.
- The two new oral pills will probably be complementary to the monoclonal antibodies in the long-term. Their distribution will be based on need and geographical location and access to healthcare. Monoclonal antibodies will be available in big hospitals, whereas in the periphery, the oral pills will be necessary.
- There has been a 10-15% decline in hospitalization rate in the last week. Its too soon to know how many of the 73% cases are symptomatic as the country is witnessing a rise right now and the picture is likely to become clearer in the coming weeks. The information is emerging and rapidly changing.
- The chances of getting long COVID from Omicron are not known yet.
- We have to be vigilant to understand the pattern of the local infection.
- We should not assume that Omicron is mild; every patient has the potential to become sick.
- New protocol in South Africa: Asymptomatic positive cases do not need to isolate. Only the mild and symptomatic patients need to isolate for 8 days. Moderately ill patients are isolated for 10 days regardless of vaccination status. No quarantine required for contacts/family. Also, no need of contact tracing/testing of asymptomatic patients.

Participants – Member National Medical Associations:

Dr Yeh Woei Chong, Singapore, Chair-CMAAO; Dr Ravi Naidu, Malaysia, Immediate Past President-CMAAO; Dr Marthanda Pillai, India Member-World Medical Council, Advisor-CMAAO; Dr Angelique Coetzee, South Africa; Dr Akhtar Hussain, South Africa; Dr Md Jamaluddin Chowdhury, Bangladesh; Dr Qaiser Sajjad, Pakistan; Dr Prakash Budhakoti, Nepal

Invitees: Dr Monica Vasudev, USA; Dr SK Aggarwal; Dr Nidhi Dhawan; Dr Anita Dhar; Dr Shashank Joshi; Dr Darakhshan Khan; Dr HE Randere; Dr Patricia La'Brooyi; Dr Chee Kheong Chan; Dr Tang Kim Lian; Ms Nina Gupta; Dr S Sharma, Editor-IJCP Group

Moderator: Mr Saurabh Aggarwal

Source: *Minutes of an International Weekly Meeting on COVID-19 held by HCFI Dr KK Aggarwal Research Fund (25th December, 2021, Saturday 9.30 am-11 am)*

■■■■

People with HIV have a Higher Risk for Heart Failure

A study, published in *Mayo Clinic Proceedings*, has noted that people with HIV have a higher risk of developing heart failure compared to those without HIV. Researchers identified 38,868 people with HIV who were members of Kaiser Permanente from 2000 to 2016 in Northern California, Southern California and the Mid-Atlantic States. Every person was matched with up to 10 Kaiser Permanente members from the corresponding region who did not have HIV, but were the same age, sex and race (n = 386,586). People in both the groups who developed heart failure during follow-up were identified. People with HIV had a 68% higher likelihood of developing heart failure compared to those without HIV. Additionally, people aged 40 years or below, females or those of Asian or Pacific Islander descent had the highest risk… (*Source: HT – ANI*)

ORIGINAL RESEARCH

Effectiveness of Self-Instructional Module on Knowledge Regarding Effect of Outdoor Games in Stress and Anxiety Reduction among Adolescents

B RAJESH

ABSTRACT

This study was aimed at finding the effectiveness of self-instructional module on knowledge regarding the effect of outdoor games in stress and anxiety reduction among adolescents at a selected junior college in Bhadrachalam, Telangana. Purposive nonprobability simple random sampling technique was adopted to select 60 participants. Self-structured tool was used to collect the data. The results revealed that in the pre-test, majority of the respondents (66.7%) had inadequate knowledge, 33.3% had moderate knowledge and nobody had the adequate knowledge regarding the effect of outdoor games on stress and anxiety reduction, and the percentage mean and the standard deviation was 49.7 and 5.83. The self-instructional module on the effect of outdoor games on stress and anxiety reduction was distributed after pre-testing on the same day. In the post-test, majority of the respondents (86.7%) had adequate knowledge, and 13.33% had moderate knowledge while nobody had inadequate knowledge regarding the effect of outdoor games on stress and anxiety reduction, and the percentage mean and the standard deviation was 81.2 and 6.33. The paired 't' test value was 27.51. The calculated 't' value was greater than table value (0.05, 59df) = 2.00. Hence, the null hypothesis (H_0) was rejected and research hypothesis (H_1) was accepted. This indicates that there is a significant difference between mean pre-test and post-test knowledge scores of adolescents. It was concluded that the self-instructional module has been effective in increasing knowledge of adolescents regarding effect of outdoor games on stress and anxiety reduction.

Keywords: Knowledge, self-instructional module, stress, anxiety, outdoor games

Most of the people and students experience stress and anxiety in their daily busy schedule. Stress refers to a demand that the brain or physical body is exposed to. Students can report feeling stressed when they face several demands. The feeling of being stressed can be incited by an event that has the potential to make someone feel frustrated or nervous. Anxiety can be a reaction to stress. The level of the anxiety of each student is due to various factors, such as gender, age, level of education, etc.

The term stress has now become so infused into our thoughts that sometimes it feels that it has always been there. Stress can occur in students. From the large number of stresses faced by students and young adults, academic stress emerges as a significant health problem. In recent years, it has been estimated that 10% to 30% of students experience academic-related stress. Academic burden, unrealistic ambitions, lack of opportunities, and competitiveness are some of the sources of stress which give rise to fear and anxiety.

Stress is an individual's physical, mental and emotional reaction to a condition that disturbs the normal equilibrium. If stress is intense, continuous or repeated, if the person is unable to cope or if support is lacking, then it becomes a negative phenomenon leading to physical illness and psychological disorders. Stress is nothing but a state of mental and emotional strain. Playing stress relief games is a good way to get rid of anxiety and depression. Games relieve stress a lot faster than traditional relaxation techniques or methods. Games can give effective and instant stress relief solutions.

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Anxiety is a natural response to a perceived or imagined threat. It is as natural as many of the emotions that we go through in everyday situations. Anxiety acts like our body's alarm system, warning us of possible dangers or difficulties. Anxiety refers to apprehension or uneasiness that develops from expectation of danger, whose source is not known. College students require significantly more effort than students of high school. College students are expected to become more independent and instructors are usually more demanding and work is more difficult. As a result of increased demands, college students to experience greater levels of stress related to academics.

A study of over 1,00,000 students by Penn's Center for Collegiate Mental Health noted that more than half of the students visiting campus health clinics had anxiety as a concern. The finding was substantiated by the American College Health Association (ACHA) 2015 National College Health Assessment survey, reporting that around 15.8% of college students had been diagnosed with, or treated for, anxiety. The survey noted that 21.9% of students stated that within the last 1 year, anxiety had impacted their academic performance, characterized by getting a lower grade on an exam or a major project, receiving an incomplete or dropping a course. That increased from 18.2% in the ACHA's 2008 survey.

Outdoor games/activities may be followed to find peace in nature, enjoy life and relax and can also be used as a medium in education and team building. The outdoors may meet the needs of physical health, risk-taking, building social ties and may also fulfil the needs of achievement. The outdoors can serve as an environment where people show what they can do.

The average age of onset for many mental health conditions seems to be the usual college age range of 18 to 24 years. In fact, according to the National Institute of Mental Health, 75% of all individuals with an anxiety disorder will experience symptoms before age 22. Other students, who might not have clinical anxiety, stress or depression, still suffer. According to the 2006 ACHA survey, 45% of women and 36% of men felt so depressed that it was difficult to function.

The goals of this study are to promote health, to preserve health, and to minimize suffering from stress and anxiety of the students. The goals are embodied in the outdoor games. Successful reduction of stress and anxiety can be achieved through the cost-effective and joyful method of playing outdoor games. From all the findings, we came to the conclusion that stress and anxiety are the major problems experienced by students. So, a self-instructional module on knowledge regarding effect of outdoor games on stress and anxiety reduction will help to improve the knowledge of college students.

MATERIAL AND METHODS

The quantitative research approach with one group research design was adopted in this study. Non-probability simple random sampling technique was used to select the participants (n = 60). The tool used for the study was organized as Section I- Sociodemographic data, and Section II- Structured questionnaire, to assess the knowledge regarding the effect of outdoor games on stress and anxiety reduction. The self-instructional module on the effect of outdoor games on stress and anxiety reduction was distributed after pre-testing on the same day. All the items in the questionnaire were prepared based on the reviews, previous studies, journals, magazines, research articles and studies related to stress and anxiety reduction. Ten experts constituting 3 psychiatrists, 2 psychologists and 5 mental health nursing personnel validated the tool. The reliability of the tool was computed by using split half technique. The Karl Pearson's coefficient correlation method was used to check reliability. The calculated 'r' value was 0.90. It indicates that the tool which is taken by the researcher is reliable, valid and predictable of the desired objectives. The data was analyzed by using descriptive and inferential statistics.

RESULTS

Figure 1 shows the classification of respondents according to their knowledge level in the pre-test. The data showed that majority of the respondents (66.7%) had inadequate knowledge, 33.3% had moderate knowledge and none had adequate knowledge regarding stress and anxiety reduction by outdoor games.

Figure 2 shows the classification of respondents according to their knowledge level in the post-test. The data showed that majority of the respondents (86.7%) had adequate knowledge, 13.33% had moderate knowledge and nobody had inadequate knowledge regarding stress and anxiety reduction by outdoor games.

Table 1 and Figure 3 show that in pre-test, majority (66.7%) of the respondents had inadequate knowledge, 33.3% of them had moderate knowledge but none of them had adequate knowledge regarding stress and anxiety reduction by outdoor games. In the post-test, majority (86.7%) of the respondents had adequate knowledge, 13.3% had moderate knowledge and none of them had inadequate knowledge level regarding stress and anxiety reduction by outdoor games.

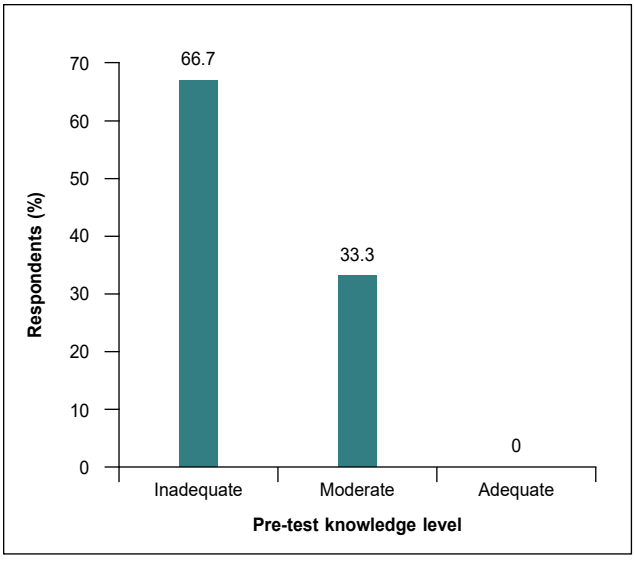

Figure 1. Classification of respondents on pre-test knowledge level of stress and anxiety reduction by outdoor games.

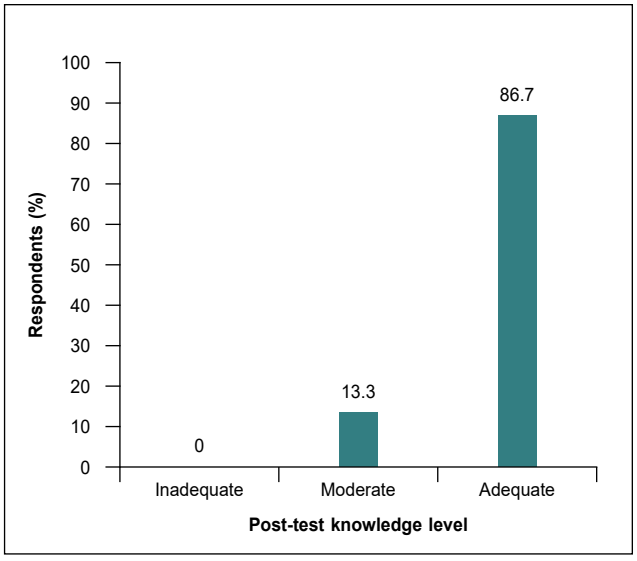

Figure 2. Classification of respondents on post-test knowledge of stress and anxiety reduction by outdoor games.

Table 1. Classification of Respondents on Pre-test and Post-test Knowledge Level of Stress and Anxiety Reduction by Outdoor Games (n = 60)

Knowledge level	Category	Classification of respondents			
		Pre-test		Post-test	
		Number	Percentage (%)	Number	Percentage (%)
Inadequate	≤50% score	40	66.7	0	0.0
Moderate	51-75% score	20	33.3	8	13.3
Adequate	>75% score	0	0.0	52	86.7
Total		**60**	**100.0**	**60**	**100.0**

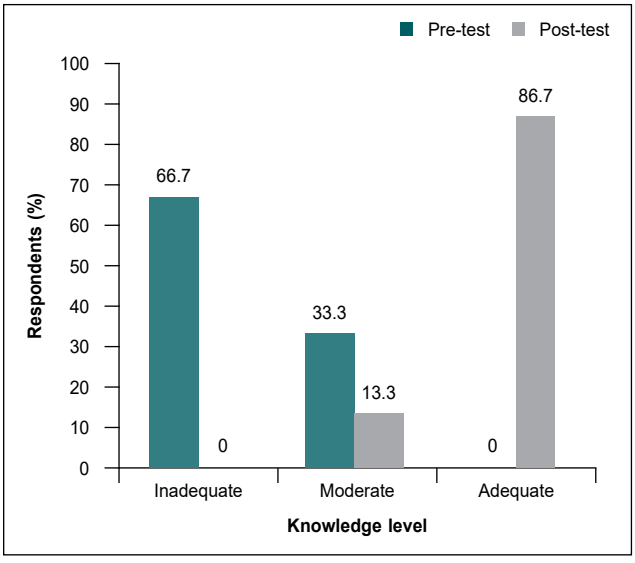

Figure 3. Classification of respondents on pre-test and post-test knowledge.

Table 2 and Figure 4 depict mean, mean%, standard deviation (SD), SD% of pre-test and post-test knowledge scores, enhancement in post-test knowledge score and paired 't' test value. The mean percentage of pre-test was 49.7% and post-test was 81.2% with the enhancement of 31.36%. The paired 't' test value was 27.51. The calculated 't' value is greater than table value (0.05, 59df) = 2.00. Hence, the null hypothesis (H_0) is rejected and research hypothesis (H_1) is accepted. This indicates that there is a significant difference between mean pre-test and post-test knowledge scores of respondents. It was concluded that the self-instructional module has been effective in increasing knowledge of adolescents regarding effect of outdoor games on stress and anxiety reduction.

The Chi-square analysis was carried out to determine the association of post-test knowledge regarding effect of outdoor games on stress and anxiety reduction

Table 2. Overall Pre-test and Post-test Mean Knowledge Scores on Effect of Outdoor Games on Stress and Anxiety Reduction among Adolescents

Aspects	Max. score	Respondents knowledge				Paired 't' test
		Mean	SD	Mean (%)	SD (%)	
Pre-test	30	14.9	1.75	49.7	5.83	27.51*
Post-test	30	24.30	1.9	81.2	6.33	
Enhancement	30	9.41	2.52	31.36	8.36	

*Significant at 5% level; t (0.05, 59df) = 2.009.

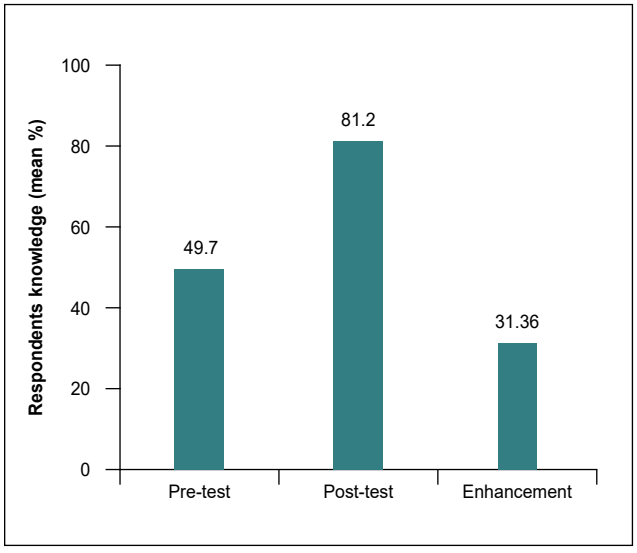

Figure 4. Overall pre-test and post-test knowledge level on stress and anxiety reduction by outdoor games.

among adolescents with their selected demographic variables such as age, gender, religion, type of family, family income, dietary pattern, residential area, type of recreation, source of stress and anxiety and source of information regarding effect of outdoor games on stress and anxiety reduction. Out of these, the knowledge was significantly associated with type of family (10.61, df = 3), residential area (6.65, df = 2) and source of information (9.16, df = 3) at 5% level ($p < 0.05$).

The results of Chi-square analysis indicated that there was significant association between pre-test knowledge with their selected demographic variables such as type of family, residential area and source of information regarding effect of outdoor games on stress and anxiety reduction among students. Hence, null hypotheses (H_{02}) was rejected and research hypotheses (H_2) was accepted. It indicates that there was a significant association between the pre-test knowledge regarding effect of outdoor games on stress and anxiety reduction among respondents with their selected demographic variables.

DISCUSSION

The present study assessed the knowledge level regarding the effect of outdoor games on stress and anxiety reduction among adolescents and found that majority (66.7%) of the subjects had inadequate knowledge in the pre-test and maximum (86.7%) number of subjects had adequate knowledge in the post-test and concluded that there was a significant improvement in subjects' knowledge in the post-test after administration of self-instructional module. Thus, the self-instructional module was found to be effective in improving the knowledge regarding effect of outdoor games on stress and anxiety reduction among adolescents.

Provision of self-instructional module will improve students' knowledge regarding stress and anxiety and steps to be followed to reduce stress and anxiety by outdoor games. The students had expressed that they were able to gain more knowledge regarding effect of outdoor games on stress and anxiety reduction and the teaching enabled them to reflect on their own performance and skills, and they had actively participated in the learning process. Significant perceived learning among students had taken place in all aspects of self-instructional module regarding effect of outdoor games on stress and anxiety reduction.

Hence, the developed self-instructional module was instructionally effective, appropriate and feasible and can be used to motivate and help the adolescents.

It emphasizes that adequate knowledge owned by the nurses might help them to update themselves on the recent advancements, which in turn helps them to give health education to the students on stress and anxiety reduction, to follow precautions in early identification and prevention of complications and also to improve abilities.

Student nurses should be made aware on various aspects of stress and anxiety complications, which arise

due to lack of care. The student nurses from school and college of nursing should be encouraged to attend specialized courses and seminars regarding stress and anxiety reduction.

Staff development program in any organization is the prime responsibility of the nurse administrator. In the era of technological advancement, the demand for quality and competent care poses a challenge to nurse administrators to demonstrate their efficiency in providing care to students with stress and anxiety complications and reduction at the earliest.

The nurse administrator should formulate policies, protocols, and guidelines and systems of emphasis on nursing research or clinical studies are needed to improve the quality of the nursing care.

CONCLUSION

The present study was done to evaluate the effectiveness of self-instructional module on knowledge regarding effect of outdoor games on stress and anxiety reduction among adolescents. There was a substantial increase in the level of knowledge among students after intervention of self-instructional module. Hence, the self-instructional module proved to be effective in increasing the knowledge and improving correct practices regarding effect of outdoor games on stress and anxiety reduction among adolescent students.

SUGGESTED READING

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REVIEW ARTICLE

Dapagliflozin in the Landscape of Type 2 Diabetes Management

SANJAY KALRA*, PRABHU N KASTURE†, MOHAN T SHENOY‡, RAJESH M TRIMUKHE#

ABSTRACT

As per current statistics, India accounts for more than 74 million individuals living with diabetes. Many of these individuals have associated cardiovascular disease (CVD) and chronic kidney disease (CKD) comorbidities. Optimal glycemic management is important because uncontrolled glycemia may accelerate the macrovascular and microvascular complications, further aggravating the comorbid conditions. Metformin is used as the first-line therapy in most persons. However, there are some who do not tolerate metformin, are unable to achieve required glycemic targets or require greater efforts for cardiovascular (CV) risk reduction. These patients require an alternative hypoglycemic agent to be used as either monotherapy or as combination treatment with metformin, respectively. Sodium-glucose cotransporter-2 (SGLT2) inhibitors are one such novel class of drugs that can be used as either monotherapy or as part of two drug (dual) or three drug (triple) combinations with other oral hypoglycemic agents or insulin. Dapagliflozin is a promising option for managing type 2 diabetes with CV and renal benefits, weight and blood pressure reducing properties. A low risk of hypoglycemia and drug-drug interactions are the added advantages. In this article, the authors have reviewed the existing clinical evidences on dapagliflozin and highlighted its place in the diabetes management landscape.

Keywords: Type 2 diabetes mellitus, CVD, dapagliflozin

THE CURRENT LANDSCAPE OF DIABETES MANAGEMENT

Globally, 1 in 10 adults are living with diabetes, out of which half are undiagnosed. While worldwide, 537 million people live with diabetes, India accounts for a staggering 74 million plus adults living with diabetes. A significant proportion of those with diabetes have associated microvascular and macrovascular complications.[1]

Conventionally, treatment has focused on controlling hyperglycemia and preventing the devastating consequences of uncontrolled blood glucose on the body. Early and effective intervention to optimize blood glucose levels is a fundamental principle of diabetes. The current armamentarium of diabetes treatment includes several oral hypoglycemic agents including biguanides, sulfonylureas, meglitinides, dipeptidyl peptidase-4 (DPP-4) inhibitors, glucagon-like peptide 1 (GLP-1) receptor agonists, sodium-glucose cotransporter-2 (SGLT-2) inhibitors, thiazolidinediones and alpha-glucosidase inhibitors.[2]

The management of diabetes is flexible, individualized, and all treatment strategies are underlined by lifestyle modification, especially diet and exercise through diabetes education and self-management.[2] However, many patients do not achieve the targeted glycemic goal or manage blood glucose effectively, thereby requiring the need for multiple therapies and even insulin. Despite improved risk factor control with the currently available therapies, improved glycemic control is not always associated with robust macrovascular benefits. In these cases, antihyperglycemic agents which can solve the dual purpose of glycemic control and risk management are needed.[3]

Various factors must be considered when first-line therapy is personalized in individuals with type 2 diabetes mellitus (T2DM). Some of these factors are age, weight, pregnancy, renal or hepatic dysfunction, ease of use, polypharmacy, occupation, costs and side effects.

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Tolerability and side effects play an important role in noncompliance and therapy failure in individuals with T2DM. Besides, treatment for T2DM is a progressive therapy which frequently requires insulin replacement therapy. Obesity seen in most type 2 diabetes patients is associated with insulin resistance and it is important to target it in diabetes management.[4]

In this article, we have reviewed and integrated clinical trial data and the management approach of T2DM to demonstrate the place of SGLT2 inhibitors, particularly dapagliflozin, in the therapy of diabetes.

SODIUM-GLUCOSE COTRANSPORTER-2 INHIBITORS

The current guidelines recommend metformin as the preferred initial pharmacological therapy for T2DM. However, for patients who do not tolerate metformin, SGLT2 inhibitors may be given as monotherapy. Additionally, patients who do not achieve adequate glycemic targets may require addition of a second oral hypoglycemic agent for achieving better glycemic control. SGLT2 inhibitors are a novel class of drugs approved for the management of T2DM, with a unique mechanism of action which is also insulin independent.[5] They can also be used to reduce the risk of cardiovascular (CV) and renal disease progression.

SGLT2 inhibitors have a glucose-lowering effect through a specific renal action. They lower the threshold for renal glucose reabsorption by competitively inhibiting the SGLT2-mediated glucose reabsorption, which in persons with diabetes, is observed to get enhanced as a maladaptive response. By removing glucose, SGLT2 inhibitors facilitate weight loss (caloric loss), and a related mild osmotic diuresis due to sodium co-excretion, which leads to volume depletion and therefore reduction in blood pressure.[2]

It has been seen that in persistent hyperglycemic conditions like diabetes, the renal threshold for renal reabsorption increases because of the upregulated SGLT2 inhibitors and thereby its enhanced activity, bringing about increased reabsorption of both glucose and salt, worsening hyperglycemia. SGLT2 inhibitors have demonstrated effectiveness in lowering glucose levels and also safety in preventing hypoglycemia as their glucose-lowering effect is dependent on ambient glycemia.[3]

Currently, there are seven identified SGLT2 inhibitors, including canagliflozin, dapagliflozin, empagliflozin, ipragliflozin, luseogliflozin, tofogliflozin and remogliflozin.[6] Out of the seven identified SGLT2 inhibitors, empagliflozin has the greatest selectivity for SGLT2 receptor compared to SGLT1, while canagliflozin is the least selective. Empagliflozin and dapagliflozin have shown efficacy in lowering combined risk of CV death or hospitalization for heart failure and favorable influence on renal functions in patients with diabetes.[7,8]

Dapagliflozin

Dapagliflozin is a selective inhibitor of SGLT2 and improves glycemic control.[9] It is rapidly absorbed following oral administration and reaches peak plasma concentration in 2 hours. Dapagliflozin exhibits oral bioavailability of 78% and gets metabolized by the uridine diphosphate-glucuronosyltransferase enzyme in liver and kidneys. Studies have shown that dapagliflozin is extensively metabolized, with 73.7% recovered in excretions (72.0% in urine and 1.65% in feces). The predominant metabolite in humans is dapagliflozin 3-O-glucuronide, that accounts for 60.7% of the dose being completely recovered in urine. The metabolite is formed in both kidney and the liver. It is suggested that both the liver and the kidney are involved in the metabolic clearance of dapagliflozin.[10]

Dapagliflozin has proven efficacy in managing uncontrolled T2DM. It is known to improve glycemic control and stabilize insulin dosing, with additional property of weight reduction and without any increment in hypoglycemic episodes in people with T2DM.[9,11] Studies have also demonstrated the long-term benefits of dapagliflozin when used with insulin.[11]

While SGLT2 inhibitors are widely accepted as second-line agents after metformin in the management of T2DM, there have been some inconsistent findings about their association with urinary tract infection (UTI) and genital mycotic infections. This also prompted Food and Drug Administration (FDA) to issue a warning in 2015 regarding the link between SGLT2 inhibitors and UTIs. However, most recent systemic review and meta-analytical data does not report any link between SGLT2 inhibitors and UTIs. The results from a real-world study in 2019 have shown that there is no associated increased risk of UTI, while there may be an associated increased risk of genital mycotic infections within 30 days in older women and men.[12]

In pediatric patients with T2DM, there are limited treatment options. It has been proven clinically that a single oral dose of dapagliflozin shows similar results in adults and pediatric patients.[13] However, its use is not approved in this patient population.

Place of dapagliflozin in T2DM management

Dapagliflozin is the first novel SGLT2 inhibitor with proven efficacy in improving glycemic parameters when used alone or in combination with metformin or other oral hypoglycemic agents.[6] It is also a reliable option as add on with insulin therapy in suboptimally controlled T2DM.[14] It effectively reduces glycemic levels and body weight in treatment-naïve patients including early type 2 diabetes patients.[15,16]

As monotherapy

Clinical studies in Asian population have evidenced the efficacy of dapagliflozin in controlling hyperglycemia in patients with T2DM who have experienced metformin failure. Dapagliflozin was proven to be efficacious and well-tolerated in these patients.[17,18] In a real-world, prospective study in Indian patients (n = 1,941), dapagliflozin significantly reduced glycated hemoglobin (HbA1c) and body weight in T2DM patients. It was well-tolerated, and no safety signals were detected in Indian population.[19]

Combination therapy of dapagliflozin with other agents

As dual therapy

Dapagliflozin has been studied with various oral hypoglycemic agents including metformin,[20] glimepiride,[21] pioglitazone,[22] sitagliptin[23] and exenatide.[24-26] The highest reduction in HbA1c was observed with metformin, while the weight benefit is greater when used with sulfonylureas. So far, no studies of dual therapy of dapagliflozin with GLP-1 analog therapy have been conducted.[4]

As triple therapy

Dapagliflozin has been used with metformin and sitagliptin, metformin and saxagliptin, and metformin and a sulfonylurea in triple combinations. In these studies, improved glycemic reduction and body weight reductions have been seen.[4]

Combination therapy showed benefits in patients with type 2 diabetes who could not be managed with metformin alone. In studies where saxagliptin and dapagliflozin have been added to background metformin therapy, an improved glycemic control without any significant occurrence of hypoglycemia was seen. Triple therapy with dapagliflozin, saxagliptin and metformin was effective over long-term and was well-tolerated.[27-31] When compared against glimepiride and metformin, the triple therapy showed comparable efficacy in glycemic control but reduced body weight and systolic blood pressure with reduced occurrence of hypoglycemic incidence.[32,33]

It has been observed that early intensification to triple therapy with dapagliflozin and saxagliptin led to better, more durable glycemic management compared with addition of sitagliptin only (dual therapy) in patients with high HbA1c level not managed with metformin monotherapy.[34] Many studies have been conducted to assess the benefits of triple therapy with metformin, saxagliptin and dapagliflozin and all showed better glucose-lowering compared to dual therapy when either agent was added to metformin background therapy in patients with uncontrolled type 2 diabetes.[35] Several other studies have demonstrated benefits of the triple therapy in glycemic control, decreasing HbA1c and lower risk of hypoglycemia, and clinically relevant body weight difference. These results were similar in insulin naïve patients and in those on insulin therapy.[36-38]

Table 1 shows the effect of dapagliflozin in combination with other oral hypoglycemic agents.

Table 1. Effect of Dapagliflozin Combined with Other Oral Hypoglycemic Agents in Individuals with T2DM

Dapagliflozin in combination with	Effect on glycemic control	HbA1c	Weight reduction	Hypoglycemia	Other effects	Tolerability
Dual combination						
Metformin[20]	Decrease glycemic levels in poorly managed patients	-	-	-	-	Well-tolerated
Pioglitazone[22]	-	Further lowering of HbA1c	Alleviated side effects of weight gain	Rare occurrence of hypoglycemia	Reduced edema, Rare occurrence of CHF and fracture	Well-tolerated
Glimepiride[21]	-	Significant reduction in HbA1c	Reduced weight	-	-	Well-tolerated

Table 1. Effect of Dapagliflozin Combined with Other Oral Hypoglycemic Agents in Individuals with T2DM

Dapagliflozin in combination with	Effect on glycemic control	HbA1c	Weight reduction	Hypoglycemia	Other effects	Tolerability
Dual combination						
Sitagliptin[23]	-	Reduction in HbA1c	Reduced weight	-	Additional clinical benefit	Well-tolerated
Exenatide[24-26]	Improved glycemic parameter		Weight reduction		Improved CV safety profile Reduction in systolic blood pressure	Well-tolerated
Triple combination						
Saxagliptin + Metformin[27,28,30-34]	Improved glycemic control	Significant reduction	Reduced body weight	Rare occurrence of hypoglycemia	Reduced systolic blood pressure	Well-tolerated
Metformin + Sulfonylurea[39]	Sustained glycemic control	HbA1c reduced	Reduced body weight	-	Reduction in systolic blood pressure	Well-tolerated

In combination with insulin

With insulin, dapagliflozin increases insulin-mediated tissue glucose disposal and causes an endogenous glucose production.[6] Studies have shown that dapagliflozin can improve the sensitivity to insulin, thereby improving glycemic management.[40] It is also known that individuals with T2DM may not have adequately controlled blood glucose, thus requiring increase in insulin dose. Increased insulin dosage may result in troubling or dangerous side effects. In such patients, dapagliflozin given along with insulin inhibits the renal absorption of glucose and thus improves glycemic control. In fact, the use of dapagliflozin, in patients who are on insulin therapy, helps in stabilizing insulin to be given in lower dose thus alleviating the side effects due to high insulin dose.[9,41] The DAISY (Dapagliflozin Added to patients under InSulin therapY) trial has further strengthened the evidence suggesting that adding dapagliflozin to insulin has several clinical benefits, and is well-tolerated in patients with T2DM.[42] Long-term studies (3-4 years) have demonstrated a positive long-term benefit in glycemic control and reductions in body weight and systolic blood pressure with general well-tolerance.[43,44]

Pleiotropic Benefits of Dapagliflozin: Benefits Beyond Glucose Control

Weight reduction

Compared to metformin, dapagliflozin has a significant effect in reducing weight, either as monotherapy or given in combination.[39] When used in combination with metformin, dapagliflozin has a better positive and synergistic effect on body weight, waist circumference, glycemic, CV and metabolic parameters versus exclusive metformin therapy in overweight or obese at-risk women population with a recent history of gestational diabetes mellitus.[45] Studies have clearly suggested that a combination therapy of dapagliflozin and saxagliptin had a favorable metabolic profile and can reduce liver fat and adipose tissue.[46] These results make dapagliflozin a good choice in patients with high body mass index (BMI) or those who are obese or overweight.

Lipid-lowering

A study has shown that there is a modest but statistically significant increase in both high-density lipoprotein (HDL) and low-density lipoprotein (LDL) cholesterol with no effect on triglycerides or the LDL/HDL ratio.[47] Dapagliflozin is also known to suppress potent atherogenic small dense LDL cholesterol (sdLDL-C) and increase HDL_2-C, a favorable cardiometabolic marker.[48]

Lowering of blood pressure

Dapagliflozin has a beneficial effect of lowering systolic blood pressure. It acts synergistically with drugs like β-blockers and calcium channel blockers to effectively lower blood pressure.[49] Studies have demonstrated dapagliflozin to be an important adjunct to insulin in managing hyperglycemia, reducing weight and blood pressure in Asian population.[50]

Benefits in CVD

Dapagliflozin is effective when added to usual regimen in patients with T2DM and pre-existing cardiovascular disease (CVD), a history of hypertension or chronic kidney disease (CKD). It significantly improved HbA1c

reduction, reduced systolic blood pressure, body weight without adversely affecting CV safety. Similar results were observed in elderly patients also.[51,52] The CVD-REAL 2 study conducted in patients from the Asia Pacific, the Middle East, and the North America, favored SGLT2 inhibitors over other glucose-lowering drugs for lower risk of death, hospitalization for heart failure, myocardial infarction and stroke.[53] These results suggested that the results of CVD-REAL 2 study can be juxtaposed in the high CVD risk Indian population who require more aggressive treatment for diabetes than other patient groups.

Benefits in heart failure

DECLARE-TIMI 58 trial showed that dapagliflozin lowered the incidence of CV death or hospitalization for heart failure in high-risk atherosclerotic cardiovascular disease (ASCVD). The results were equally pronounced irrespective of the patient's age and clear-cut benefits were shown in elderly patients as well.[54,55] In DECLARE-TIMI 58 study, dapagliflozin also reduced the risk of major CV events in patients with prior myocardial infarction.[56] The DIVERSITY-CVR study has highlighted dapagliflozin to be a better choice compared to DPP-4 inhibitors (sitagliptin) in alleviating cardiometabolic risk factors in patients with early-stage but insufficiently controlled T2DM.[57]

Currently, DAPA-MI trial is underway to assess the effect of dapagliflozin when given in addition to standard of care therapies for patients with myocardial infarction to prevent hospitalization for heart failure or CV death.[58] DAPA-AF trial is also ongoing to estimate the effectiveness of dapagliflozin in reducing the burden of atrial fibrillation (AF) in patients undergoing catheter ablation of symptomatic AF.[59]

Benefits in chronic kidney disease

Various landmark trials have enumerated the benefits of personalizing dapagliflozin in treatment of patients with diabetic kidney disease, CVD or at-risk of CVD or CKD. The results of DERIVE study evidenced the positive benefit of dapagliflozin in treating T2DM patients with concomitant CKD.[60]

The more recent DAPA-HF and DAPA-CKD trials have been much talked about in terms of dapagliflozin's benefit in T2DM patients with underlying CVD or CKD or those at high-risk. DAPA-HF trial has demonstrated that dapagliflozin consistently reduced the risk of death and worsening heart failure and improved symptoms in patients of all age groups.[61,62] The results were irrespective of whether the patients were given sacubitril/valsartan/mineralocorticoid receptor antagonist or not, but when used together, the combination further reduced the morbidity and mortality in patients with heart failure with reduced ejection fraction (HFrEF).[63,64] DAPA-HF trial has also shown that dapagliflozin reduced the risk of worsening heart failure and death, improved results with similar efficacy, safety and tolerability in ischemic and nonischemic patients.[65] DAPA-CKD trial has shown that dapagliflozin reduced the risk of sustained decline in the estimated glomerular filtration rate (eGFR) of at least 50%,[66] reduced the risk of main adverse kidney and CV events and all-cause mortality, end in patients with diabetic and nondiabetic kidney disease.[67]

Sleep apnea

Dapagliflozin has significant effect in reducing apnea-hypopnea index, and improved hypoxemia during sleep and excessive daytime sleepiness. Clinical studies have proven its benefits in T2DM patients with obstructive sleep apnea hypopnea syndrome.[68]

Liver disease

Dapagliflozin has significant benefits on liver diseases. Studies have shown that it improves liver steatosis in patients with T2DM and nonalcoholic fatty liver disease (NAFLD), and attenuates liver fibrosis, particularly in patients with significant liver fibrosis.[69,70]

Table 2 enumerates indications for dapagliflozin use in individuals with type 2 diabetes.

Table 2. Indications for Dapagliflozin use in Individuals with Type 2 Diabetes

Glycemic control	Extraglycemic benefits	Safety and tolerability
As monotherapy if metformin is contraindicated or not tolerated	To reduce risk of ASCVD in persons with established/ high-risk factors for ASCVD	To minimize risk of hypoglycemia
Dual therapy if monotherapy is not sufficient	To reduce risk of hospitalization for heart failure	To minimize risk of weight gain/promote weight loss
Triple therapy if dual therapy is insufficicent	To reduce rate of progression of CKD	To minimize risk of drug-drug interactions
With insulin, to reduce the dose of insulin		

TYPE 2 DIABETES MANAGEMENT GUIDELINES AND DAPAGLIFLOZIN

Research Society for the Study of Diabetes in India (RSSDI) Guidelines on the Pharmacotherapy of Type 2 Diabetes

SGLT2 inhibitors, such as dapagliflozin, are advised to be used in individuals where metformin is contraindicated or not tolerated. Dual therapy is recommended to be prescribed initially if it is thought that initial monotherapy may not achieve required glycemic targets.[71]

Dual therapy with metformin and SGLT2 inhibitors (dapagliflozin) is recommended if monotherapy fails. If dual therapy fails, triple therapy with dapagliflozin may be initiated. Dapagliflozin is favored as the second-line agent of choice in T2DM patients with a history of CVD.[71]

ADA Guidelines on the Pharmacotherapy of Type 2 Diabetes

American Diabetes Association (ADA) guidelines on type 2 diabetes pharmacotherapy recommendations are:[72]

- *Other medications including SGLT2 inhibitors, with or without metformin based on glycemic requirements are appropriate initial therapy for individuals with T2DM with or at high risk for ASCVD, heart failure and/or CKD.*
- *Among individuals with T2DM who have established ASCVD or indicators of high CV risk, established CKD or heart failure, and SGLT2-inhibitor and/or GLP-1 receptor agonist with demonstrated CVD benefit is recommended as part of the glucose-lowering regimen and comprehensive CV risk reduction, independent of A1c and in consideration of patient-specific factors.*
- *In patients with T2DM and established ASCVD, multiple ASCVD risk factors or diabetic kidney disease, and SGLT2-inhibitor with demonstrated CV benefit is recommended to reduce the risk of major adverse cardiovascular events (MACE) and/or heart failure hospitalization.*
- *In patients with type 2 diabetes and established ASCVD or multiple risk factors for ASCVD, combined therapy with an SGLT2 inhibitors with demonstrated CV benefit and a GLP-1 receptor agonist with demonstrated CV benefit may be considered for additive reduction in the risk of adverse CV and kidney events.*
- *In patients with T2DM and established HFrEF, SGLT2 inhibitor with proven benefit in this patient population is recommended to reduce risk of worsening heart failure and CV death.*
- *SGLT2 inhibitors should be given to all patients with stage 3 CKD or higher and type 2 diabetes, irrespective of glycemic control.*
- *In patients with T2DM and diabetic kidney disease, use of an SGLT2 inhibitor in patients with an eGFR ≥25 mL/min/1.73 m^2 and urinary albumin ≥300 mg/g creatinine is recommended to reduce CKD progression and CV events.*
- *In patients with CKD who are at increased risk for CV events or CKD progression or are unable to use an SGLT2 inhibitor, a nonsteroidal mineralocorticoid receptor antagonist (MRA) is recommended to reduce CKD progression and CV events.*

DAPAGLIFLOZIN IN TYPE 1 DIABETES MELLITUS

When compared with patients with T2DM, diabetic ketoacidosis is relatively frequent in patients with type 1 diabetes mellitus (T1DM) who are unable to produce sufficient insulin. In the DEPICT-1 and DEPICT-2 studies, frequent events of diabetic ketoacidosis were reported with dapagliflozin. The factors attributing to the increased frequency were missed insulin doses or failure of insulin pump. Though dapagliflozin safety and tolerability has been proven in T1DM with insulin, it is still important to judiciously select patients, given the risk of the occurrence diabetic ketoacidosis events.[73] Hence, it is not recommended for T1DM patients, however, in advanced conditions, it may be considered as beneficial, based upon the supportive evidence.

CONCLUSION

In T2DM patients, dapagliflozin can be effectively given as monotherapy, and in those who are already on metformin therapy but do not have adequate blood glucose control, dapagliflozin can be given safely as an adjunct to metformin therapy. In patients requiring aggressive therapy to manage blood glucose levels, dapagliflozin is a crucial component of combination therapy with other oral hypoglycemic agents (both two drug combinations and three drug combinations) and even insulin, as it reduces the chances of hypoglycemic events and lowers body weight. Dapagliflozin has a significant benefit in optimizing insulin doses to a lower value so that the side effects due to high insulin dose can be avoided. Based upon the evidence, dapagliflozin may be a worthwhile consideration for prescription even in T1DM cases in near future. It has various pleiotropic benefits including lowering of weight, small dense lipids, and systolic blood pressure, benefitting

patients with CVD and CKD. In conclusion, review of all the studies indicates that dapagliflozin is safe, effective, well-tolerated in all patient subgroups and offers multiple benefits making it particularly useful in elderly diabetics, obese diabetics, pregnant women with a recent history of gestational diabetes, lean patients with uncontrolled blood glucose, CVD or CKD comorbid patients or those at high risk of CVD or CKD.

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CASE REPORT

Scrub Typhus with Multiple Cranial Nerve Palsy: A Rare Case Presentation

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ABSTRACT

Scrub typhus, a rickettsial disease endemic in several parts of India, usually presents with acute symptoms. It is caused by small intracellular Gram-negative bacteria belonging to the Rickettsiaceae family. Optic neuritis and lateral rectus palsy may be associated with a range of autoimmune disorders, infectious diseases and raised intracranial tension. In this case, we report optic neuritis and lateral rectus palsy induced by *Orientia tsutsugamushi.* We report a case of a 23-year-old woman presenting with complaints of high-grade fever, vomiting and generalized swelling since 5 days. During this febrile period, on 4/10/2021, she complained of difficulty in vision and double vision. She was found to be positive for scrub typhus on 5/10/2021. Optic neuritis was diagnosed on the basis of ophthalmologic examination and magnetic resonance imaging (MRI) brain. Investigation was done to rule out autoimmune disorders (vasculitis and connective tissue diseases). Rickettsial optic neuritis was confirmed by detection of specific antibodies in serum and the negativity of other serologic tests. Fever, eschar, history of tick exposure and supportive diagnostic tests usually lead to the diagnosis. This case aims to raise awareness among the healthcare providers for this type of association. Scrub typhus should be included in the differential diagnosis when a patient presents with fever with or without eschar and isolated or multiple cranial nerve palsy.

Keywords: Eschar, *Orientia tsutsugamushi,* rickettsial disease

Scrub typhus, a rickettsial disease endemic in several parts of India, usually presents with acute symptoms. Scrub typhus is caused by small intracellular Gram-negative bacteria belonging to the Rickettsiaceae family. They are transmitted by transovarial and transstadial route in trombiculid mites.[1] Infected larval mites (chiggers) inoculate organism into the skin. The clinical presentation of scrub typhus infections varies from mild and self-limiting to fatal. Disseminated vasculitis is the basic pathogenic mechanism of this infection and it may subsequently lead to multiple-organ involvement.[2] Violations [involvement of] eye during scrub typhus infection are uncommon. We report a case of optic neuritis and lateral rectus palsy revealing *Orientia tsutsugamushi* infection in a 23-year-old woman.

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CASE REPORT

A 23-year-old woman hailing from Western Rajasthan presented with a 5 days' history of high-grade fever, vomiting and generalized swelling. She also developed yellowish discoloration of sclera. After 2 days of admission, she developed difficulty in vision. On examination, the patient was febrile; pulse rate was 98/min, regular; blood pressure (BP) was 120/70 mmHg and respiratory rate was 18/min. The patient had a dark black, pigmented, raised patch on left arm suggestive of an eschar (Fig. 1). On neurological examination, cranial nerve examination revealed left lateral rectus palsy (Fig. 2). Then, the patient underwent an ophthalmologic consultation, which showed low visual acuity. Her visual acuity was 6/10. Fundoscopy revealed that the left eye optic disc was pale and there were no retinal vessel abnormalities (Fig. 3).

There were no other significant findings on physical examination.

Other blood results indicated moderate anemia, and peripheral blood smear showed normocytic normochromic anemia with relative lymphocytosis. Malaria parasite slide and dual antigen were negative, there was increased white cell count and platelet count was normal. Aspartate aminotransferase - 424 IU/L,

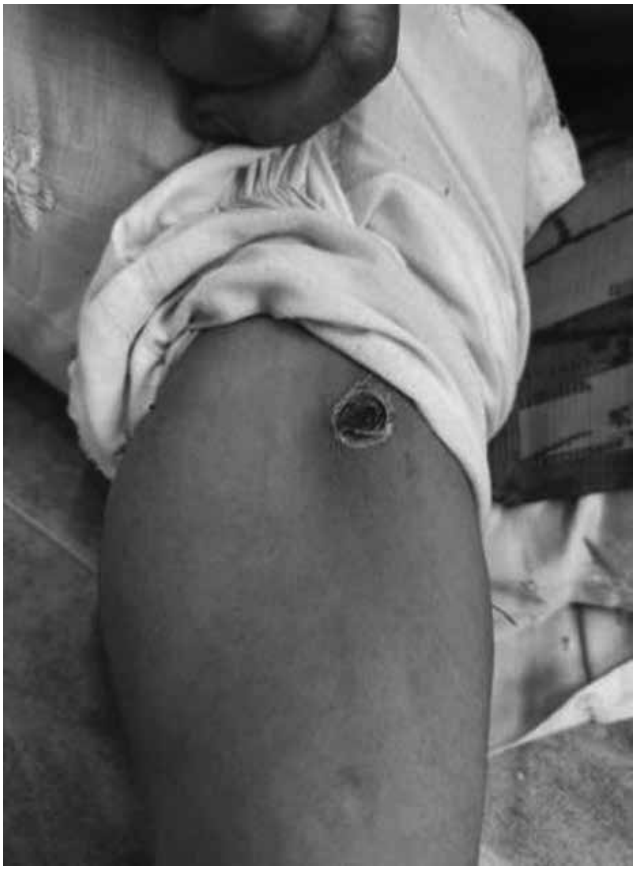

Figure 1. Eschar

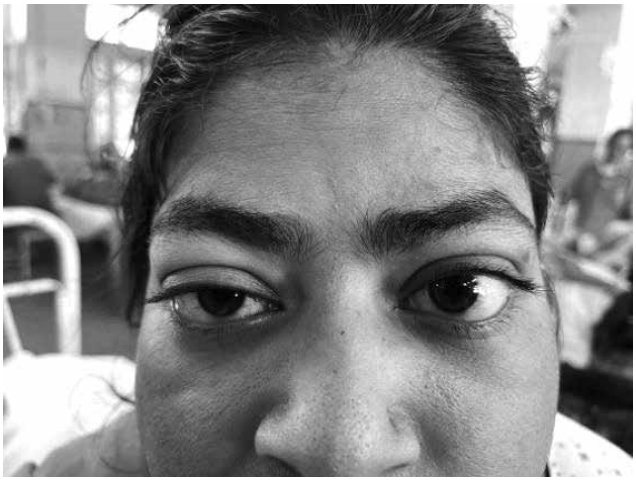

Figure 2. Left lateral rectus palsy

alanine aminotransferase - 345 IU/L, total bilirubin - 2.5 mg/dL (direct bilirubin - 2.173), alkaline phosphatase - 594 IU/L, erythrocyte sedimentation rate - 20 mm/hr. Serum C-reactive protein was within normal range, serum calcium - 8.7 mg/day, serum albumin - 2 g/dL. Urine microscopy showed no cells or casts. Proteinuria was negative and renal function test revealed urea - 56 mg/dL, creatinine - 1.72 mg/dL.

Figure 3. Pale optic disc

Immunological exams, including complement fractions C3 and C4, rheumatoid factor, antinuclear antibodies, antineutrophil cytoplasmic antibodies, antiphospholipid antibodies were negative. Cerebrospinal fluid (CSF) examination was done which was clear in color, glucose level - 75 mg/dL, protein level - 112 mg/dL, cells -130/µL, in which 70% were lymphocytes and 30% neutrophils; adenosine deaminase (ADA) - 8 IU/µL. Culture sensitivity report showed sterile sample; cartridge-based nucleic acid amplification test (CBNAAT) sample was negative for tuberculosis.

Blood for hepatitis B surface antigen (HBsAg), anti-hepatitis C virus (HCV), venereal disease research laboratory (VDRL), human immunodeficiency virus (HIV)-1 and HIV-2 antibody, dengue NS-1 antigen and IgM, IgG anti-dengue antibody by enzyme-linked immunosorbent assay (ELISA), Widal test were negative.

Considering the patient's area of living, clinical presentation of fever and skin lesion, blood test to confirm scrub typhus (IgM) was sent which came out positive on ELISA. Chest X-ray was normal. Brain magnetic resonance imaging (MRI) with intravenous contrast showed left optic nerve appearing mildly thickened (Fig. 4) and abnormal post-contrast

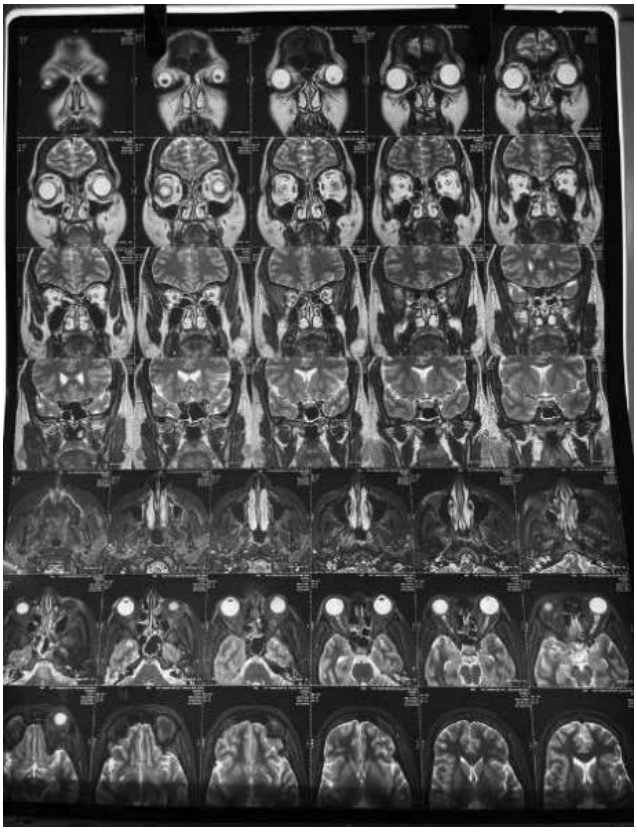

Figure 4. MRI brain showing left optic.

enhancement; rest of white matter and grey matter interpreted as nonspecific abnormalities.

A diagnosis of left eye optic neuritis and 6th cranial nerve palsy related to rickettsial infection was made on the basis of clinical, immunological, serological and imaging findings, and the patient also had an eschar on the left arm. The patient received corticosteroid therapy - intravenous methylprednisolone pulse for 5 days followed by 1 mg/kg/day tapering dose of oral steroid for 2 weeks and doxycycline 200 mg/day for 15 days. After the initiation of treatment, the patient reported a marked improvement in vision which was confirmed by ophthalmological examination (Visual acuity 8/10 in the left eye).

DISCUSSION

Scrub typhus is a tropical illness caused by *O. tsutsugamushi*, transmitted to human beings by an arthropod belonging to the family Trombiculidae. It is associated with multisystem involvement. *O. tsutsugamushi* is an obligate intracellular Gram-negative bacterium. It is prevalent in some parts of India including North eastern region.[3] Rickettsial organisms are transmitted to people by insects (ticks and mites) and cause diseases such as typhus, the spotted fevers and scrub typhus.[1] Rickettsiae are small, nonflagellated, Gram-negative coccobacilli.[4]

Optic neuritis is closely associated with multiple sclerosis and neuromyelitis optica. However, it may also be associated with an array of autoimmune or infectious diseases. Optic neuritis due to infections is rare. Neuroretinitis is the most common ocular manifestation in eye infections.[5] After entering humans, these microorganisms invade the vascular endothelium and reticuloendothelial cells, causing vasculitis. This leads to skin rash, swelling, microvascular leakage, tissue hypoperfusion and end-organ ischemic injury. Thrombus formation results in tissue infarction and hemorrhagic necrosis.[4]

The common organ system complications seen in scrub typhus are hepatitis, acalculous cholecystitis, pancreatitis, acute renal failure, acute respiratory distress syndrome, hilar lymphadenopathy, pleural effusion, meningoencephalitis, seizures, vasculitic cerebral infarct, cardiac rhythm abnormalities, myocarditis, etc.[6] Fever, neurological disturbances and skin rash are the major symptoms of rickettsial infection.[1] Ocular involvement in rickettsial disease is uncommon and usually underdiagnosed.

The rickettsial infection may involve any part of the eye. Retinitis with or without mild or moderate vitreitis is a common clinical finding. It presents as white retinal lesions adjacent to retinal vessels and are variable in number, size and location.[7] Cystoid macular edema, serous retinal detachment, hypofluorescent choroidal spots, conjunctival hemorrhage and uveitis have also been noted.

Optic nerve involvement has been noted, including optic disc edema, optic disc staining on fluorescein angiography and optic neuritis with or without visual loss.[8]

Diagnosis of rickettsial infection is usually based on serology along with the clinical presentation and history of exposure to ticks, travel in endemic area, symptoms during summer months, etc. Doxycycline is the antibiotic of choice in rickettsial diseases.[8] Along with doxycycline, systemic steroids should be prescribed in case of ocular involvement, including severe retinitis, vitreitis, retinal vascular occlusion or optic nerve involvement.[7]

Our case report illustrates the difficulties in diagnosing the exact cause of optic neuritis and left rectus palsy when it is associated with multiple clinical and immunological disorders.

CONCLUSION

Rickettsial fever is endemic in some states of India and its diagnosis requires a high index of suspicion as its initial clinical features resemble many diseases. However, focal neurologic signs with classic clinical features, like fever, maculopapular rash, eschar, in an endemic area, should alert the physician to consider scrub typhus as one of the possible differentials. The positive rickettsial serology, CSF finding, and the epidemiologic context and the negativity of all other investigations established the diagnosis of rickettsial infection in this case. Corticosteroids and doxycycline were prescribed with a partial improvement of visual acuity.

Rickettsioses should be considered in the differential diagnosis of acute optic neuritis with 6th cranial nerve palsy in areas where scrub typhus fever is endemic. Diagnosis must be early in order to have a better response to treatment, combining doxycycline and corticosteroids.

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Antibodies Weak Against Omicron Variant, Suggests More Evidence

Additional evidence from laboratory experiments points to the weaknesses of COVID-19 vaccines and antibody drugs against the Omicron variant.

A study posted on bioRxiv, conducted by researchers at Columbia University, noted that Omicron variant was considerably resistant to neutralization by antibodies in blood from individuals who had received Pfizer/BioNTech, Moderna, J&J or Oxford/AstraZeneca COVID-19 vaccines, or from COVID survivors.

The researchers also tested 9 approved monoclonal antibodies and 10 that are still in the experimental stage. Neutralizing potential of 18 out of the 19 antibodies was either nullified or impaired.

In a separate study, posted on bioRxiv, researchers from Europe also stated that Omicron variant was either completely or partially resistant to neutralization by 9 monoclonal antibodies that were tested in the study, and also by antibodies in blood samples obtained from vaccine recipients and COVID survivors.

The European researchers stated that neutralizing antibody levels were 5- to 31-fold lower against Omicron compared to the Delta variant… (*Source: Reuters*)

No Major Side Effect with India's First mRNA Vaccine, Say Experts

Investigators involved in Phase 3 trials for HGCO19, India's first mRNA vaccine, being developed by Gennova Biopharmaceuticals Limited, have stated that nearly 90% of trial volunteers have not experienced any side effect after receiving either one or two doses of the vaccine thus far.

Dr Ashish Bavdekar, one of the principal investigators, who is leading the trials at Pune's KEM Hospital Research Center, said that the data from the Phase 1 trial on vaccine immunogenicity was also encouraging, adding that the side effects, reported in a minority of participants, were very mild and not significant. He stated that some volunteers did not report any side effects. Dr Bavdekar said that the minor side effects included mild fever or headache. He added that the picture will be clear after the Phase 3 trials as the sample size was much larger for this phase… (*Source: ET Healthworld – TNN*)

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CASE REPORT

Multi-organ Injuries Due to a Lightning Strike: A Rare Case

RAGHAVENDRA G*, DEVENDER SUKHWAL*, HEMANT MATHUR†, NAVEEN HM*, DP SINGH†, ABHISHEK NYATI*

ABSTRACT

Injuries due to a lightning strike are uncommon presentations in the emergency department. Common injuries caused by lightning include burns, muscle pains, cardiac arrest, hearing loss, seizures, behavioral changes and ocular cataracts. We report a case of a 26-year-old primigravida with history of 3 months of amenorrhea who was struck by lightning as she was standing beside a tree. It left her unconscious, immediately after which she was taken to the emergency department of Maharana Bhupal Govt Hospital (MBGH Hospital), Udaipur, Rajasthan. Entry wound was from right ear and the exit wound was on abdomen. Examination confirmed linear first- and superficial second-degree burns. The electrocardiogram (ECG) showed deep and symmetrical T-wave inversion in precordial and lateral leads. There was an associated elevation of troponin T levels (peak: 432 ng/L), suggestive of myocarditis. On otoscopic examination, she was found to have rupture of tympanic membrane bilaterally. A transthoracic echocardiography revealed reduced ejection fraction of the left ventricle to 25% with global left ventricle hypokinesia, moderate mitral regurgitation and tricuspid regurgitation. This case aims to raise awareness among the healthcare providers regarding multiple organ involvement in lightning injury.

Keywords: Lightning, seizures, myocarditis, echocardiography

Lightning injuries are injuries caused by a lightning strike. An interdisciplinary approach towards patients with muti-organ injuries following lightning strike is significant. Lightning strike is a common cause of sudden cardiac death and is also associated with injuries to several organ systems.[1,2] Lightning injuries are divided into direct strikes, side splash, contact injury and ground current.[3]

Presented here is the case of a 26-year-old woman who was struck by lightning and developed multi-organ injuries.

CASE REPORT

A 26-year-old primigravida with history of 3 months of amenorrhea was struck by lightning as she was standing beside a tree which left her unconscious. She was immediately taken to the emergency department of Maharana Bhupal Govt Hospital (MBGH Hospital), Udaipur, Rajasthan, where she was assessed and admitted in ICU under Department of Medicine.

On examination, her clothes were partially burned. Her vitals on admission were blood pressure 84/56 mmHg, respiratory rate 30 cycles/min, pulse rate 132 beats/min and of low volume. She was put on vasopressor support and was maintaining saturation with 10 L oxygen via face mask. Her Glasgow Coma Scale (GCS) was E2V1M5, pupils were reactive bilaterally and bilateral plantar was extensor, suggestive of brain insult.

Entry wound was from right ear and the exit wound was on abdomen (Fig. 1 a and b). Examination revealed linear first- and superficial second-degree burns. Some blisters were noted on a line traversing from the right ear to abdomen.

The electrocardiogram (ECG) showed deep and symmetrical T-wave inversion in precordial and lateral leads (Fig. 2). There was an associated elevation of troponin T levels (peak: 432 ng/L), suggestive of myocarditis. Laboratory investigations revealed a normal blood count (Hemoglobin – 13 g/dL, white blood cell [WBC] - 13,200, platelet count - 1,80,000), normal renal (Urea - 36, creatinine - 1.24) and liver function tests (SGOT - 38, SGPT - 45, ALP - 54, total protein - 7.4, albumin - 2.8], and no electrolyte abnormalities.

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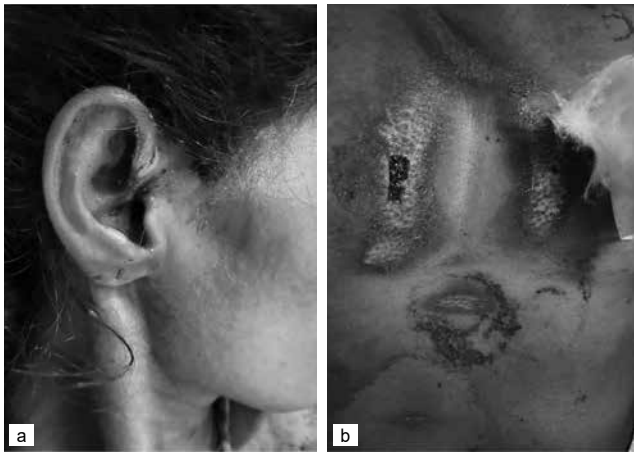

Figure 1 a and b. Entry and exit wounds.

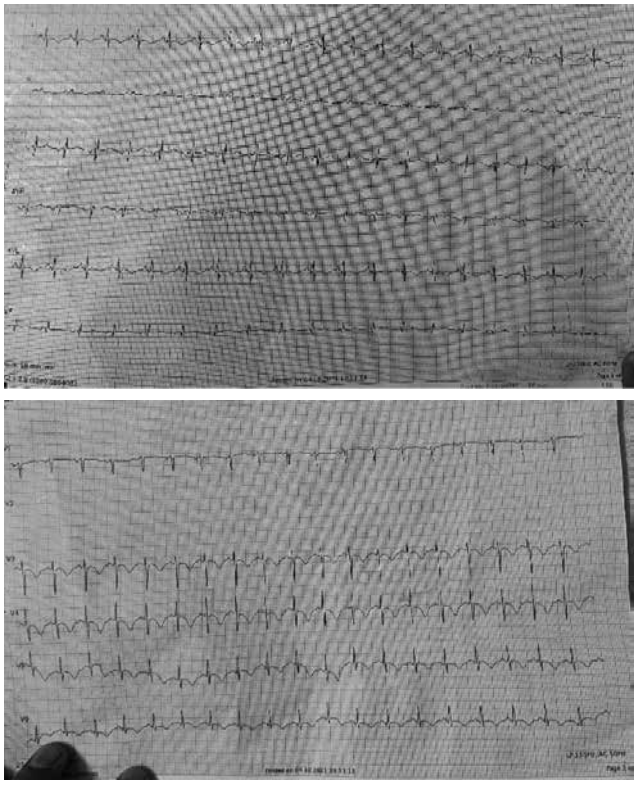

Figure 2. ECG of the patient.

A transthoracic echocardiography revealed reduced ejection fraction of the left ventricle to 25% with global left ventricle hypokinesia, moderate mitral regurgitation and tricuspid regurgitation.

On third day, she started obeying commands and taking food orally, but complained of difficulty in hearing. She was referred to the Department of ENT. On otoscopic examination, she was found to have rupture of tympanic membrane bilaterally. Pure tone audiometry revealed bilateral moderate-to-severe mixed type of hearing loss (Fig. 3) and the patient was advised tympanoplasty.

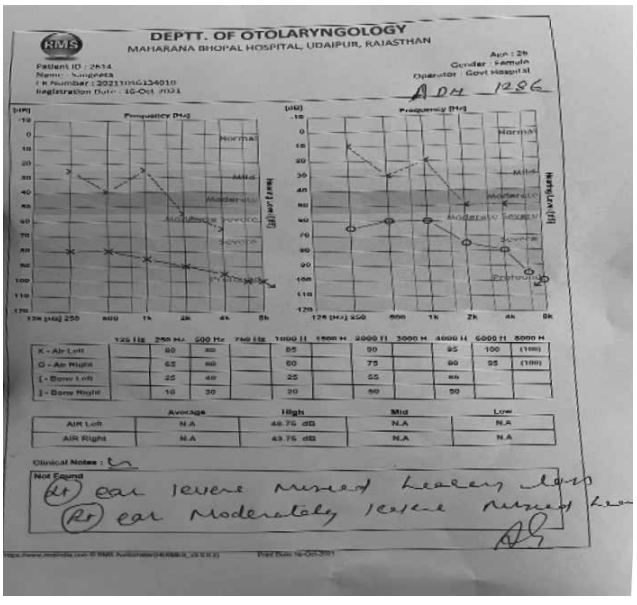

Figure 3. Mixed type hearing loss on audiometry.

On the same day, she complained of bleeding per vagina for which she was referred to Department of OBG. Patient had missed abortion and was terminated medically.

The cardiopulmonary function was monitored at the ICU for 4 days. Hemodynamic parameters became stable and she was weaned off from vasopressor and oxygen support. She was shifted to medicine ward and noncontrast computed tomography (NCCT) head was done, which did not reveal any significant abnormality.

For the burn injuries, the patient underwent conservative management. Dressing was changed daily using a paraffin gauze dressing and topical hyaluronate. She was discharged from the hospital after 7 days and advised to follow-up in medicine OPD.

DISCUSSION

Lightning injuries are categorized primarily into direct strikes, side splash, contact injury and ground current. Ground current accounts for about 50% of cases of lightning injuries and occurs when the lightning strikes near an individual and travels to the person via ground. Side splash accounts for about one-third of cases and occurs when lightning strikes nearby and jumps to a person. Contact injury occurs when an individual is touching an object that has been struck by lightning. Direct strikes account for just 5% of these injuries and occur when lightning directly strikes an individual. The mechanism of lightning injuries may include electrical injury, burns due to heat and mechanical trauma. Lightning injury is diagnosed on the basis of history of

the injury and examination.[3] A direct strike can cause lethal injuries.

Lightning strike patients can present with injuries to several organ systems. Neurological and cardiological complications have often been reported with lightning strike.[4]

The common injuries associated with lightning strike include burns, cardiovascular disorders, neurological disorders, kidney failure and psychological trauma.

Cardiological manifestations of a lightning strike may include myocardial necrosis and rhythm abnormalities. Cardiac arrest and ventricular fibrillation usually have lethal consequences if the patient is not immediately resuscitated. ECG may show mimicking acute coronary syndrome, arrhythmias, myocarditis. Takotsubo cardiomyopathy has been reported following lightning strike.[2]

Neurological manifestations after a lightning strike can range from transient benign symptoms to permanent damage. There may be a temporary loss of consciousness, amnesia, paresis, encephalopathy, etc. Electric current can damage the structural integrity of nerve membranes and muscle tissues.[5]

Burns caused due to a lightning strike are usually superficial second-degree burns and extensive tissue damage or large cutaneous burns are rarely seen. Management of such patients is the same as any other burn victim.

A characteristic skin alteration seen in patients with lightning injuries are Lichtenberg figures, where a transient reddish, fern-like pattern develops on the skin due to lightning strike.[6,7]

Renal failure can be seen in patients with lightning strike on account of myoglobinuria.[8] Renal function of patients struck by lightning should monitored regularly. Our patient had transient episode of oliguria which subsided with fluid therapy.

Psychological impairment is also possible in patients with lightning injury. The neuropsychological and cognitive deficits seen in these patients resemble those observed in traumatic brain injury or post-traumatic stress disorder.[8]

CONCLUSION

This case describes multi-organ injuries in a patient struck by lightning and emphasizes the need for evaluating all possible injuries that can occur due to lightning. Interdisciplinary management of multi-organ injuries due to lightning strike is highly important for early detection and management of the injury.

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■■■■

Too Much Processed Meat Tied to Increased Risk of Death in IBD Patients

Excessive intake of processed meat seems to be tied to a higher risk of death among patients with inflammatory bowel disease (IBD), particularly Crohn's disease patients, suggests new research. Researchers noted that consumption of processed meat for more than 4 times in a week was tied to a higher risk of death among IBD patients (HR 1.53), in comparison with consumption less than once a week. Consumption of only unprocessed red meat, chicken or fish was not associated with any increased risk of death. Consumption of more processed meat was found to be associated with a higher risk of death in patients with Crohn's disease (HR 2.01), but the same wasn't true for those with ulcerative colitis (HR 1.27). The findings were presented during a poster presentation at the virtual Advances in Inflammatory Bowel Disease meeting… (*Source: Medpage Today*)

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- General Weakness
- Chemotherapy-induced anaemia
- Lack of Appetite
- Chronic Kidney Disease

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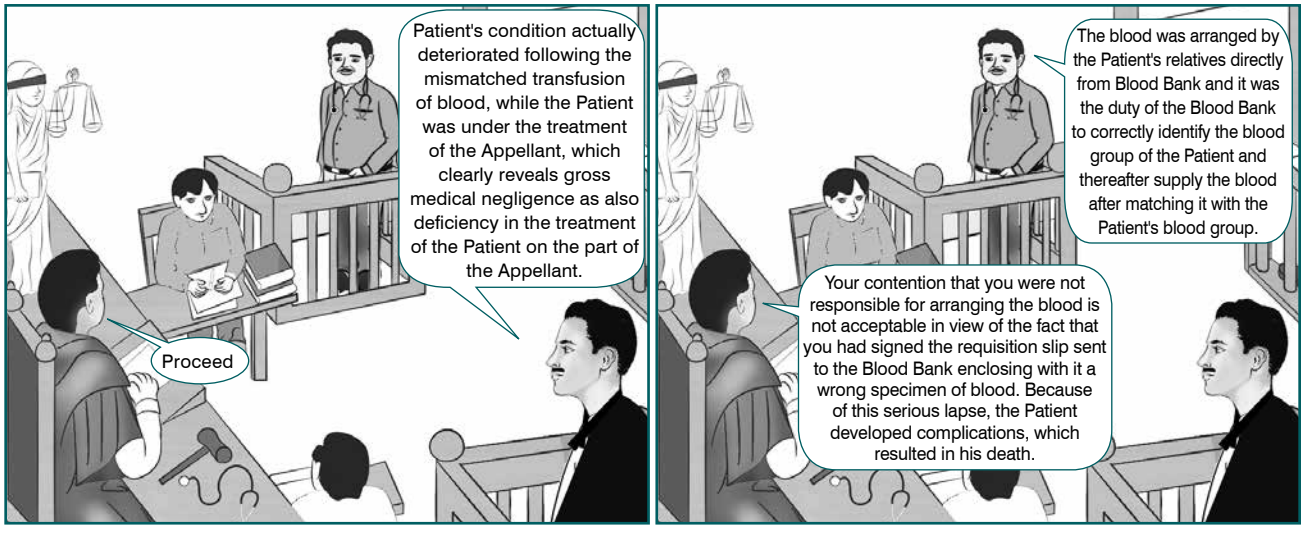
Ipsa Res Loquitur: Wrong Blood Transfusion is a Sure Instance of Medical Negligence



Lesson: Wrong blood transfusion is an error, which no doctor/hospital exercising ordinary skill would have made, and such an error is a sure instance of medical negligence. Counsel for Appellant's contention that Respondent had been unable to produce any medical evidence in support of their case was not tenable because in the instant case, the principle of *ipsa res loquitur* was clearly applicable.

COURSE OF EVENTS

- **14.11.2000:** The Patient, father of Respondent No. 1, fell down from his bicycle and sustained injuries, including a fracture in the neck of the femur. Respondent No. 1 contacted Appellant-Dr A, a Consultant Orthopedic Surgeon attached to Nursing Home A (NH A), on telephone the same night who advised him to bring the Patient for medical examination.
- **15.11.2000:** An X-ray was taken which confirmed fracture neck of the femur and the Patient was admitted in NH A for operation. The Appellant advised before surgery one bottle of blood would be required, which would be provided by NH A. Blood was accordingly supplied.
- **17.11.2000:** Blood transfusion was started and the Patient was operated. The operation was completed by 5.00 p.m.; however, blood transfusion continued even after the surgery. Soon after the blood transfusion, the Patient started frothing from the mouth and complained of difficulty in breathing and shivering.

The next day, he could not urinate and his eyes were deep yellow in color. A Nephrologist examined the Patient and advised that since he might need dialysis and this facility was not available in NH A, the Patient should be shifted to Hospital A, which was done. On request of Hospital A to the Blood Bank attached to it, one bottle of blood of A+ group (blood group of the Patient) was supplied for the Dialysis. The Patient's condition continued to deteriorate and despite being put on a ventilator he passed away on 01.12.2000.

According to the death certificate issued by Hospital A, one of the causes of death was "history of mismatched blood transfusion". It was asserted that while the blood group of the Patient was A+, the blood which was transfused to him at NH A was of B+ group as per the report of the Blood Bank, which supplied the blood on the basis of enclosed blood specimen sent with the requisition slip. It was affirmed that the Patient's condition deteriorated following the transfusion of B+ blood, while the Patient was being treated by the Appellant, which clearly reveals gross medical negligence and deficiency in the treatment of the Patient on the part of the Appellant as also NH A.

Respondent No. 1 filed a complaint before the State Commission on grounds of medical negligence and deficiency in service and requested that the Appellant and NH A be ordered to jointly and severally pay Rs. 6 lakhs as compensation.

Appellant filed a written rejoinder disputing the allegations. He stated that as an Orthopedic Surgeon, he had operated successfully on the Patient and no complaint regarding the surgery was made by Respondent No. 1. As far as the arrangement for transfusion of blood was concerned, it was arranged by the Patient's relatives from Blood Bank and it was the duty of the Blood Bank to identify the blood group of the Patient and supply the blood after matching it with the Patient's blood group. He further stated that it is the duty of doctors and paramedical staff in the operation theater of the Nursing Home to carefully verify the name and blood group of the Patient before transfusion. He stated that the Patient subsequently developed other complications like urination problems, etc., which were not due to any medical negligence or deficiency in service in operating the Patient and, therefore, the allegations of medical negligence and deficiency in service are baseless.

ORDER OF THE STATE COMMISSION

The State Commission after hearing the parties allowed the complaint and held the Appellant guilty of deficiency in service and medical negligence in terms of Section 2(g) of the CP Act, 1986 on the following counts:

"(i) OP No. 2 (Appellant before the National Commission) failed to ascertain the blood Group of the deceased before sending the sample to the Blood Bank despite the fact that there was a reliable document with the complainant's relatives in respect of blood group of the deceased though the Complainant had drawn attention of OP No. 2 to the said document.

(ii) OP No. 2 failed to mention the blood group of the deceased while sending sample to the Blood Bank with a requisition, which is otherwise mandatory.

(iii) OP No. 2 committed gross negligence by accepting and transfusing a blood group other than A+ve, which was the deceased's confirmed blood group.

(iv) OP No. 2 failed to follow instructions contained in the Issue Document of Blood Bank where caution is printed on the Poly Bag containing Blood that in case of any reaction, the Surgeon/Physician must send sample of patient's blood, a small sample of the blood transfused, patient's symptoms evident on transfusion."

The State Commission ordered OP No. 2 to pay a compensation of Rs. 5,28,000/- and Rs. 10,000/- as costs to Respondent No. 1. NH A (OP No. 1 before the State Commission) was also ordered to pay a compensation of Rs. 10,000/- for negligence and deficiency in service for failing to carry the correct blood sample of the Patient to the Blood Bank. OP No. 2 as well as NH A were directed to pay the above amount within 30 days from the date of communication of the order, failing which it was to carry interest at the rate of 12% per annum.

Aggrieved only the Appellant (i.e., OP No. 2 before the State Commission) filed this first appeal.

THE APPELLANT'S ALLEGATIONS

The learned Counsel for the Appellant alleged that the State Commission had given an erroneous finding of medical negligence since his responsibility was that of an Orthopedic Surgeon and the surgery was successfully conducted by him. Provision of blood was the responsibility of the concerned Nursing Home as also the Blood Bank to cross check the blood group with the blood required and mention these requirements in the requisition slip sent to the Blood Bank. In case of any deficiency in doing so, it was the Nursing Home (i.e., OP No. 1 before the State Commission) and the Blood Bank, which were responsible. It was further stated that Hospital A issued a death certificate without carefully considering the facts and, therefore, gave several reasons for the cause of death but it nowhere mentioned that it was because of the faulty surgery. Respondent No. 1 did not produce any expert medical evidence or person to prove his case. The Appellant was a consulting doctor who had been called to NH A to conduct the surgery and was not a regular member of its staff. For any negligence committed by the Nursing Home and its staff in not confirming the blood group before sending it to the Blood Bank, the Appellant could not be held responsible.

REJOINDER OF THE RESPONDENT

Learned Counsel for Respondent No. 1 stated that the Appellant could not take the plea that the blood was arranged for the Patient by his relatives and it was the responsibility of the relatives, the concerned hospital and the Blood Bank to ensure that a correct requisition slip was sent. There was evidence that the requisition slip dated 16.11.2000 to the Blood Bank was signed by the Appellant stating that 1 unit of blood for the Patient was required and a specimen blood sample attached. There was no mention of the Patient's blood group on the requisition slip. The blood sample was

cross-checked in the Blood Bank and found to be of B+ group and blood of B+ group was sent. It was clear that the Appellant had signed the requisition slip without verifying whether the correct blood specimen had been sent and whether any blood group was mentioned. Considering these facts and the death certificate, which confirmed that one of the causes of death was "mismatched blood transfusion", the same was rightly attributed by the State Commission to the Appellant's medical negligence.

OBSERVATIONS OF NCDRC

From the evidence on record, it was clear that a requisition slip was sent to the Blood Bank for blood transfusion required during and after the surgery and specimen attached to it was not of the Patient but of some other Person. Hence, the blood sent by the Blood Bank did not match with the Patient's blood group leading to serious complications contributing to his death. Appellant's contention that he was not responsible for arranging the blood was not acceptable as he had admittedly signed the requisition slip sent to the Blood Bank enclosing with it a wrong specimen of blood. Because of this serious lapse, the Patient developed other complications following the blood transfusion relating to his liver and kidney functions because according to medical literature, there was a relation between transfusion of mismatched blood and renal, urinary and liver problems.

Also, the Counsel for Appellant's contention that Respondent had not produced any medical evidence in support of their case was not tenable because in this case the principle of *ipsa res loquitur* was applicable.

Moreover, the Counsel for Respondent No. 1 had brought to their notice judgments of the National Commission in *Dr. Kam Inder Nath Sharma & Ors. V. Satish Kumar & Ors. [II (2005) CPJ 75 (NC)] and Dr. K. Vidhyullatha v. R. Bhagawathy [I (2006) CPJ 136 (NC)] as also of the Hon'ble Supreme Court in Post Graduate Institute of Medical Education & Research v. Jaspal Singh & Ors. [II (2009) CPJ 92 (SC)]* in support of the contention, which had concluded that wrong blood transfusion is an error, which no doctor/hospital exercising ordinary skill would have made, and such an error is a sure instance of medical negligence.

ORDER OF NCDRC

Considering the facts of this case and respectfully following the judgment of the Hon'ble Supreme Court as also of this Commission, which were relevant in the instant case, NCDRC agreed with the finding of the State Commission that the Appellant was guilty of medical negligence.

This first appeal was found to have no merit and was dismissed and the Appellant was directed to comply with the order passed by the State Commission and pay the amount of Rs. 5,38,000/- (i.e., Rs. 5,28,000/- as compensation and Rs. 10,000/- as cost) to Respondent No. 1.

REFERENCE

1. NCDRC First Appeal No. 175 of 2006; Order dated 29.01.2013.

■■■■

Asymptomatic COVID Infection Rate High

A meta-analysis involving 95 studies with around 30,000,000 individuals has shown that the pooled percentage of asymptomatic COVID-19 infections was 0.25% in the tested population and 40.5% in people with confirmed COVID infection.

The meta-analysis included 29,776,306 tested individuals. Among these, 11,516 had asymptomatic infection. The pooled percentage of asymptomatic infections among the tested subjects was 0.25%. The percentage was found to be higher among nursing home residents or staff, air or cruise ship travelers, and pregnant women, in comparison with the pooled percentage, in an analysis of different study populations. Additionally, the pooled percentage of asymptomatic infections among the confirmed cases was 40.5%. The percentage was again higher among pregnant women, air or cruise ship travelers, and nursing home residents or staff, at 54.11%, 52.91% and 47.53%, respectively. The findings are published in *JAMA Network Open…* (*Source: Medscape*)

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HCFI Dr KK Aggarwal Research Fund Round Table Environment Meet on Challenges in Implementing Climate Action Commitments Made During COP26

28th November, 5th December and 12th December, 2021 (12 noon-1 pm)

- The Conference of the Parties (COP)21 held in Paris in 2015 marked a leap in climate action. It resulted in the most comprehensive international climate agreement. Signatories to the Paris Agreement agreed to limit emissions or global warming to <2°C, ideally 1.5°C. It was also agreed that developed countries would urgently give more resources (financial aid) to climate-vulnerable countries to resolve climate change. Under the Paris agreement, governments devise and present plans for reductions in national emission called the Nationally Determined Contributions (NDC).
- Two-thirds of the global economy is now covered by net-zero targets.
- Progress has been limited and the lack of an effective reporting structure means it is unclear how much money has been contributed so far by high-income countries.
- Developing countries face a lack of funds and the developed countries have not provided aid as they had promised to.
- The Glasgow Climate Pact at COP26 was adopted by almost 200 countries after 2 intense weeks of negotiations. The UN Secretary General said at the conclusion of the conference "It is an important step, but it is not enough."
- The Glasgow Climate Pact recognizes the global climate emergency citing recent findings of Intergovernmental Panel on Climate Change (IPCC). It expressed "alarm and utmost concern that human activities have caused around 1.1°C of global warming to date and that impacts are already being felt in every region". Parties resolved to pursue efforts to keep to 1.5°C. It has urged developed countries to at least double their collective climate finance for adaptation in developing countries from 2019 levels by 2025, to ensure a balance between adaptation and mitigation. It also called on development banks, other financial institutions and private sector to enhance finance mobilization to deliver the scale of resources needed to achieve climate plans.
- COP26 also reached agreement on key provisions of the Paris Agreement Rulebook, which covers issues around market mechanisms and transparency.
- At COP26, it was agreed that the developed countries should deliver more resources to help the climate vulnerable countries.
- Most countries have adopted the target "net zero" carbon emissions by 2050; China has aimed to become carbon neutral by 2060.
- India made 5 commitments towards climate action at COP26.
- India will bring its non-fossil fuel energy capacity to 500 GW by 2030.
- By 2030, India will fulfil 50% of its energy requirement through renewable energy.
- India will cut down its net projected carbon emissions by 1 billion tonnes from now until 2030.
- By 2030, India will bring down carbon intensity of its economy by more than 45%.
- By 2070, India will achieve the target of "net zero" carbon emissions.
- As a party to international conventions, by and large, India has complied with the commitments and obligations despite political diversity.
- India is far ahead of several European countries in terms of compliance to the Minamata convention on mercury. India does not have mercury cell based caustic alkali plants, while Europe still has them despite setting a target of achieving this by 2025. We achieved this target in 2005. Compact fluorescent lamps (CFL) are being used now mainly, which has eliminated another source of mercury.
- India is on track to achieve its NDC under the Paris Agreement, which is to achieve 40% of electric power installed capacity from non-fossil fuel sources by 2030.
- Because of high population density, enough land is not available for alternative power sources such as wind or the sun. To generate 1 KW of solar power, 7-8 sq. m area is required. To generate 1 MW, more than 7000 sq. m of area, so to generate 1 GW of solar

power, lot of land would be required including wasteland and not just rooftop solar panels.

- Land should have multiple uses. Land is also required for forestation, plantation and other development activities. An example is the Canal Solar Power Project in Gujarat, i.e., setting up of solar panels over canals. This not only saved land, but also prevented water evaporation in addition to generating solar power. But this cannot be the only solution.
- Solar energy is useful for individual houses or small communities rather than in a grid, for which nuclear source of energy is suitable. Instead of producing more electricity to charge vehicles, solar panels can be put over parking lots or individual cars. Achieving the solar energy target should be made a mass movement.
- Mapping of energy consumption and requirement of urban, rural and industries will help to find out where and how much of emissions can be reduced.
- Wastage, leakage, pilferage and encroachment, which are known issues, have to be stopped.
- Carbon emission is maximum from biodegradable waste. There are many policies for management of biodegradable waste, but their implementation is poor. Wet waste can be utilized for energy generation. Kitchen waste can be used to produce biogas. If renewable energy is used in solid waste management, lot of issues need to be taken up immediately and standardized.
- Hydrogen technology is an upcoming source of renewable energy, which is still under trial.
- Taking care of soil will not only take care of the air and water pollution problems but also the problem of climate change. In the absence of humus (top soil layer), sunlight is not absorbed and is causing rise in atmospheric temperature. We must also protect the soil while protecting our total environment.
- Preventing soil erosion will also save rivers and in turn lot of biodiversity will be saved.
- There is no shift towards cleaner fuel or renewable energy yet as coal-based plants are still functioning. The dependence on coal is a matter of concern. The changeover has to be done within the next 10 to 15 years otherwise the target of net zero by 2070 might be an unachievable target.
- Forestation has to be a solution. Commercial cropping of wood should be allowed in India. Hard wood is still being imported in the country. This will prevent cutting down of trees (deforestation).
- Planting trees has been proven to reverse the impact of climate change. If we drive average 80 km/day or around 500 km/week, the CO_2 emissions will be 3.17 tonnes/year. If we buy 1 car, on an average, 400 trees need to be planted per person to offset our carbon footprint.
- Industries which use coal and are emitting particulate matter should be asked to plant equal number of trees and maintain them to offset the impact of emissions. This is being done in Delhi, but also needs to be done in other cities.
- Transitioning into electric vehicle needs to be taken up as a serious alternative to diesel or petrol, given their rising costs. There is a lot of hesitancy and apprehensions about adoption of electric vehicles. A charging infrastructure needs to be developed.
- We are dependent on other countries for many resources such as lithium for car batteries used in electric vehicles. For sustainability, dependence on other countries needs to be stopped. But these are not really sustainable solutions as thermal power plants have to work to produce electricity to charge these vehicles. Also, lithium-ion batteries are not recyclable and have limited lifespan. Batteries have to be disposed of in a very scientific manner; end-to-end management has to be worked out.
- Electric vehicles may only be a stopgap measure to what actually needs to be done for a better solution that can last us for decades.
- The recently introduced vehicle scrapping policy has considered the use of different parts of the car. At present, the necessary infrastructure for the new vehicle scrap policy is present in only few states. Hence, its implementation and how its economic value can be improved needs to be worked out. The life of a vehicle now is 10 to 15 years. A balance has to be created between this and carbon emissions.
- Unauthorized sector has to be brought into the mainstream for faster development.
- The Delhi Metro Rail Corporation (DMRC) has 8 climate change projects; 4 under Clean Development Mechanism (CDM) and 4 under Gold Standard. DMRC has till now issued 44 lakh carbon credits. One carbon credit is equal to 1 tonne of carbon dioxide. This means that 44 lakh tonnes carbon emission has been reduced by DMRC. This includes the Regenerative Braking project,

The Modal Shift project and the Energy Efficiency project and Solar Power Plant project. DMRC has to increase the share of renewable energy (solar) by 50 MW up to 2022.

- If the environmental problems are not handled today, the health problems will not be overcome.
- We must find which policies can be adopted in a traditional way. Until we work at the local level, we will not be able to resolve the global issues.
- Scientists must think about how the gap between the commitment and availability in Indian conditions can be minimized.
- Acceptability and implementation are the blocks and the challenge lies in how this gap can be reduced.
- All commitments made by developed countries should be fulfilled and they have to set an example for the developing world. Developed nations must present actions taken by them, which can be followed by the developing countries.
- The world has to realize that progress will be made by taking care of the environment and not against the environment.
- A distinction has to be made between human need and human greed.
- Focus has to be on restoration of ecology, control of emissions, use of renewable energy and sustainable economy, alternative power sources, etc.
- The commitment made at COP26 by India is tough to achieve. But the targets have to be accepted and the responsibility to achieve them is to be shared by all citizens. Any change that has to come should come from within us and we should start from our homes.
- Each and every citizen of the country has a responsibility to prevent climate change and start work from the local level for the restoration of ecology, reduction of emissions, use of natural energy for development.
- The targets set out by India in COP26 are achievable provided there is a will to do so. We have to move forward as a nation.
- Associated economic benefit, ease of doing business and betterment of public life may help achieve the target even earlier than 2070.

Participants: Dr Anil Kumar, Mr Vivek Kumar, Mr Paritosh Tyagi, Mr Ashish Gulati, Dr Dipankar Saha, Mr Ankit Sethi, Mr Neeraj Tyagi, Mr Varun Singh, Mr Vikas Singhal, Dr Ravindra Kumar, Dr Saroj Kumar, Mr VK Tyagi, Mr Pradeep Khandelwal, Dr SK Gupta, Mr Raghav Khemka, Mr Rajesh Arora, Ms Ira Gupta, Dr S Sharma

Minutes of an International Weekly Meeting on COVID-19 Held by the HCFI Dr KK Aggarwal Research Fund

Topic: Post-COVID Sequelae – Hearing Loss, Tinnitus and Vertigo

Speaker: Prof Dr JM Hans, *Padma Shri Awardee, Director Dr Hans Centre for ENT, Hearing Care & Vertigo, New Delhi*

18th December, 2021 (Saturday, 9.30 am-1 am)

- There has been a 10-15% increase in patients suffering post-COVID sequelae of hearing loss, tinnitus, vertigo. The age variants are disturbing; now these problems are seen in persons as young as 18 to 20 years.
- Viruses such as rubella, rubeola (measles), mumps, varicella zoster virus (VZV), cytomegalovirus (CMV) have a predilection for the inner ear. They directly affect any part of the inner ear like the stria vascularis, organ of Corti or nerves and indirectly they decrease immunity in the host. COVID virus behaved similarly to other respiratory viruses causing cochlear symptoms or vestibular symptoms or both. The most important part of the inner ear is the endolymph, which is formed inside the cochlea by the stria vascularis and is also absorbed by the stria vascularis. We do not know where the coronavirus is acting, but based on what we know about the earlier respiratory viruses, we know that they act at the stria vascularis and endolymphatic duct.
- The most common ear conditions seen are endolymphatic hydrops/Meniere's disease, labyrinthitis, vestibular migraine and benign paroxysmal positional vertigo (BPPV).
- The first symptoms are fullness, pain, deep seated vague burning sensation. The disease has to be picked up at this initial stage. Once the disease is established, i.e., when the endolymphatic duct is totally occluded, the condition becomes irreversible.
- Vestibular migraine can be in the vestibular nuclei. The precipitating factor is either endolymphatic (hence called the Migraine Meniere's syndrome) or working for long hours on the computer or using the mobile phone.

- BPPV is now known to be in any canal, multiple canals; it could be bilateral. Hence, the maneuvering exercises also vary. There are 15 types of BPPV and there are about 15 types of maneuvering exercises. So, it is very important to pinpoint where exactly the BPPV is.
- The virus directly damages the intracochlear structure and induces inflammatory response leading to formation of debris inside the inner ear, which block the drainage of endolymphatic system causing hydrops. It also causes immunosuppression leading to increased susceptibility to bacterial infections.
- In post-COVID stress, the plasma levels of stress-related hormones such as antidiuretic and catecholamine are raised. They alter the inner ear fluid dynamics and may cause endolymphatic hydrops. Disease may worsen the emotional state, which in turn may worsen the symptom perception.
- Predisposing factors are genetic, autoimmune state, ototoxic drugs and hormonal imbalance.
- Many people had underlying allergies, which made them vulnerable after exposure to the COVID virus. People on aspirin were more predisposed to develop endolymphatic hydrops.
- High estrogen levels cause sluggishness of blood flow in stria vascularis, which changes the fluid balance of the inner ear leading to endolymphatic hydrops. Low estrogen may weaken the otoconia and produce symptoms such as BPPV.
- The three major symptoms of Meniere's disease are episodic vertigo, fluctuating hearing loss, roaring tinnitus. But the blocked ear, which is the initial symptom, is the most important. Most blocked ears are treated as eustachian catarrh. If tympanic membrane and impedance are normal, this should raise suspicion of endolymphatic hydrops.
- Causes are genetic, vascular (stress-induced vasoconstriction), viral infection, allergic/auto-immune, environmental (increased salt and water intake). Secondary endolymphatic hydrops may occur following trauma, otitis media, otosclerosis, internal auditory canal (IAC) lesions or mass. Asians are more prone to this disease than their western counterparts.
- Etiopathogenesis is the formation or excretion of the endolymph; Radial flow where the endolymph is formed and absorbed in the stria vascularis and longitudinal flow where the endolymph is formed in the stria vascularis and absorbed in the endolymphatic duct. Debris are entangled in the endolymphatic duct, which is narrowed by mastoid hypocellularity. Other factors are hypodeveloped Trautman's triangle and anterior displacement of lateral sinus.
- Meniere's disease has to be diagnosed at the prodromic stage, where the patients come with vague symptoms like fullness in the head, etc. In stage 1a (fluctuating stage), there is fluctuating hearing loss and roaring tinnitus. This is followed by the disabling stage (stage 1b), where destruction is evident. The hearing loss further deteriorates each time there is an attack. In stage 2, the disease is stable, there is no vertigo but the disease might recur after few years. This latent period keeps on decreasing. The third stage is the contralateral ear stage.
- The disease is most damaging in the first year. Symptoms are blocked ear/deep seated ear pain/burning sensation, Tullio phenomenon (dizziness when there is loud sound), hyperacusis (irritation to the sound - one of the cardinal symptoms of endolymphatic hydrops). Once tinnitus, vertigo and hearing loss occur, this means that the destruction has already started and the disease is becoming less reversible.
- Diagnosis is based mostly on history. Audiometry shows flat curve in 60%, rising curve in 17% (low frequency hearing loss) and falling curve in 12% (high frequency hearing loss). Electrophysiological tests include Short Increment Sensitivity Index (SISI), Electrocochleography (EcocG), Vestibular Evoked Myogenic Potential (VEMP). If EcocG/VEMP is positive, it is a sure case of endolymphatic hydrops. However, a complete vestibular assessment is essential to rule out associated conditions such as BPPV, vestibular migraine.
- In BPPV, the otoliths could be in the canal called canalithiasis or in the cupula called cupulolithiasis. They are most commonly in the posterior canal but lateral or anterior canals may also be involved. There are about 15 types of BPPV, including multicanal BPPV. And there are different repositioning exercises. The Dix-Hallpike Test is to be done to pinpoint the otoliths and by which exercise they can be repositioned into the utricle so that they become ineffective. Other tests include thyroid function tests, vitamin B12 and D3, pANCA/cANCA, skin prick allergy tests, hormonal assay, HRCT (temporal bone) and MRI (IAC).

- Earlier surgical treatment was stressed upon, but this is not the case now. Management involves Meniett's device, psychotherapy and drugs including intratympanic instillation.
- The drugs include betahistine, piracetam, diuretics (acetazolamide) and steroids. Give all four together to treat endolymphatic hydrops, then the results are very good. Betahistine increases cochlear/vestibular and cerebral blood flow; diuretics reduce formation of endolymph; piracetam reduces erythrocytes adhesion, hinders vasospasm and improves microcirculation.
- Intratympanic steroid increases vascularity, reduces inflammation in the labyrinth, restores normal functioning of stria, regulates inner ear *de novo* protein synthesis and improves excretion via longitudinal flow.
- If post-COVID acute tinnitus is not treated properly, it becomes chronic, which cannot be treated by intratympanic steroids. The phantom noise has to be treated by tinnitus matching and masking.
- Tinnitus can be matched from 50 Hz to 13,500 Hz with One Hz steps. Advanced audiometers can match till 16-18,000 but with only 500 Hz. Tinnitus masking app can be downloaded on mobile, which has 250 environmental and 250 filtered musical masking tracks.
- Acute tinnitus, which is due to the distension of the endolymphatic system and stretching of the neural element inside, can be very well treated by diuretics and intratympanic steroid.
- Medications have to be stopped as early as possible after tapering the dose and start vestibular rehabilitation.
- Cervical spondylosis is no more a cause of vestibular vertigo. It causes vertebrobasilar insufficiency and pain. The vertebrobasilar insufficiency may cause vertigo, which has a very characteristic feature that there is blurring of vision for few seconds and then it becomes alright. In vestibular vertigo, there is no blurring of vision or sinking sensation. Cervical spasm is secondary to the vertigo. The straightening of the cervical spine is due to the spasm of the muscles.

Participants – Member National Medical Associations: Dr Yeh Woei Chong, Singapore, Chair-CMAAO; Dr Alvin Yee-Shing Chan, Hong Kong, Treasurer-CMAAO; Dr Marthanda Pillai, India Member-World Medical Council, Advisor-CMAAO; Dr Wasiq Qazi, Pakistan, President-elect-CMAAO; Dr Angelique Coetzee, South Africa; Dr Akhtar Hussain, South Africa; Dr Salma Kundi, Pakistan; Dr Ashraf Nizami, Pakistan; Dr Qaiser Sajjad, Pakistan; Dr Md Jamaluddin Chowdhury, Bangladesh; Dr Debora Cavalcanti, Brazil

Invitees: Prof Dr JM Hans, New Delhi; Dr Monica Vasudev, USA; Dr Eng Chang Ng; Dr Ng Hwee Hin; Dr Nisha Jacob; Dr Yeo Khoonhui; Dr Patricia La'Brooyi; Dr Gaurav Chaturvedy; Dr Xinhuo Peter Liao; Dr LC Lim; Dr Ashok Gupta, India; Dr Hwee Yee Lai; Dr S Sharma, Editor-IJCP Group

Moderator: Mr Saurabh Aggarwal

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Delayed Umbilical Cord Clamping Tied to Improved Outcomes in Very Preterm Infants

Delayed umbilical cord clamping for at least 60 seconds following birth could lead to a significant reduction in death or disability in very preterm infants, suggests a new study.

Investigators randomized 767 very preterm infants to delayed cord clamping at least 60 seconds after birth, while 764 were randomized to immediate cord clamping. Death or disability at 2 years of age was the study's primary outcome.

Death or major disability was noted in 29% of infants who were randomized to delayed clamping compared to 34% of the infants subjected to immediate clamping (relative risk 0.83, p = 0.010). By 2 years of age, 8% of infants who were assigned to delayed clamping and 11% of the infants who underwent immediate clamping had died, while 23% and 26%, respectively, had major disability. The impact of clamping the cord at least 60 seconds after birth reflected a 30% reduction in relative risk of death at 2 years of age. The study is published in *The Lancet Child & Adolescent Health*… (*Source: Medscape*)

79th AIOC 2021: All India Ophthalmological Society

MANAGEMENT OF CORNEAL THINNING AND PERFORATIONS IN SEVERE ACUTE CHEMICAL INJURIES

Dr Tuhin Chowdhury, Kolkata

In his talk, Dr Tuhin Chowdhury said that proper management in the acute state is most important and determines the long-term outcome. Corneal thinning or perforation, when associated with large areas of sclera ischemia, if left untreated, can lead to various complications such as total melt with extrusion of intraocular contents, anterior staphyloma, secondary glaucoma.

The primary goal of surgery in severe ocular burn cases is globe preservation and ocular surface maintenance. When the globe integrity is saved and the ocular surface is stable, further surgeries can be planned for better visual rehabilitation. The most common comorbidity is glaucoma and needs to be managed aggressively. He emphasized the need for a close follow-up after the initial injury for management of possible sequelae – corneal ulceration or perforation, corneal scarring with limbal stem cell deficiency (LSCD), secondary open-angle glaucoma, conjunctival scarring, dry eye, etc. Oral mucous membrane grafting is combined with tenonplasty for repair of sclerocorneal melt caused by chemical burns. Tenonplasty improves local environment and microcirculation, while oral mucous membrane grafting provides many cells for repair and re-epithelialization.

CAN STEREOACUITY REPLACE VISUAL ACUITY IN AMBLYOPIA RISK FACTOR SCREENING AMONG PRESCHOOLERS?

Sanitha Sathyan, Mathew Kurian, Rosemary C Antony, Angel Edward; Kochi

A combination of visual acuity and stereoacuity test is better, according to a presentation, which addressed the question of whether stereoacuity could replace visual acuity in amblyopia risk factor screening among preschoolers. Combined screening reduces false positives and increases true negatives. If the combination is not possible, then in 3 and 4 year-olds, TNO is better and in 5 and 6 year-olds, TNO or visual acuity charts may be used. 'Pass' in the distance visual acuity screening test or TNO stereo test individually, does not eliminate the need for further evaluation.

CLINICAL, PATHOLOGIC FEATURES AND MANAGEMENT OF ADVANCED EYE AND ORBITAL PLASMACYTOMA

Dr Ankita Aishwarya, Dr Harika Regani, Dr Santosh G Honavar; Hyderabad

Dr Harika Regani presented the findings of a retrospective observational and interventional case series comprising 6 patients, which evaluated the clinical, pathologic features and management of advanced eye and orbital plasmacytoma. She said that although plasmacytoma of the orbit is rare, ophthalmologists should be aware of it. It should be one of our differentials in a case of bony triradiate lesion irrespective of age group.

Dr Regani emphasized the need for a systemic workup for multiple myeloma not only as a treatment guide but also to prognosticate the disease. A detailed histopathological evaluation with immunohistochemistry is important. She further said imaging should focus on the early detection of additional or recurrent lesions, which influence clinical management. Aggressive and early initiation of multimodal treatment is warranted.

PHACO IN HARD CATARACT

Dr Mahipal S Sachdev, New Delhi

Dr Mahipal S Sachdev gave a presentation on phaco in hard cataract. He said the hard cataract is a challenge. The white and brunescent/hard cataracts are associated with increased risk of capsule complications. He also discussed the problems encountered intraoperatively such as incomplete separation of nuclear fragments following chopping, absence of an epinuclear cushion for protection of posterior capsule, posterior capsular tear. Early detection of the posterior capsular tear leads to optimal management, which depends on the stage of surgical procedure at which the tear is detected. He said the use of dispersive ophthalmic viscosurgical device (OVD) tamponades a posterior capsular tear, enabling completion of phacoemulsification and preventing vitreous prolapse. If vitreous prolapse occurs, anterior vitrectomy is done.

SURGICAL MANAGEMENT TIPS – PUK

Dr Ishantha Jayasekara, Sri Lanka

Peripheral ulcerative keratitis (PUK) is a destructive inflammatory disease of the juxtalimbal corneal stroma

that is associated with epithelial defect, presence of inflammatory cells in the stroma and progressive stromal melting. Delivering his presentation, Dr Ishantha Jayasekara further said that PUK is a potentially blinding disease, sometimes proving to be recalcitrant to all modes of therapy. The imbalance between collagenase (MMP-1) and its tissue inhibitor (TIMP-1) has been proposed as the reason for rapid keratolysis, which is a hallmark of the condition, he added. Timely diagnosis, detection of underlying systemic inflammatory disease and proper treatment can prevent complications. Dr Jayasekara also said that it is often associated with potentially life-threatening systemic vasculitic autoimmune diseases and needs to be treated with a systematic approach. Hence, a thorough systemic history is very important. He suggested that surgical management, even though technically challenging, can give a better prognosis in all stages of disease.

PEDIATRIC HSV

Dr Kathryn Colby, USA

Dr Kathryn Colby said during her presentation that herpes simplex virus (HSV) is an important disease in children, adding that a high percentage have stromal disease. She emphasized that there is a high risk of recurrence, with significant risk for corneal scarring, induced astigmatism and reduced vision. Dr Kathryn said that we must always consider HSV whenever there is unilateral, recurrent disease in the anterior segment, no matter what the manifestation. She added that a trial of acyclovir (ACV) can be very helpful in challenging pediatric cases.

She said that oral ACV can be used and the dosage must be adjusted as the child grows. She advised to consider long-term ACV prophylaxis if there is stromal disease. She also advised to be careful while using topical steroids and said that amblyopia management is key.

APPLICATION AND RELIABILITY OF CORVIS ST IN CLINICAL SCENARIOS

Dr Namrata Sharma, New Delhi

The CORVIS ST allows dynamic and noninvasive imaging of deformation of cornea in response to a puff of air, said Dr Namrata Sharma in her presentation on the application and reality of CORVIS ST in various clinical scenarios. Further describing its features, she said that the high-speed Scheimpflug camera records deformation at 4,330 frames/sec over a horizontal range of 8.5 mm. Recording measurement time is 30 ms with acquisition of 140 digital frames. It is used in the evaluation of biomechanical response, tonometry and pachymetry.

An important clinical use of biomechanics is to overcome well-known errors in the measurement of intraocular pressure (IOP) with the common applanation tonometer. Additionally, it can be used to screen for diseases such as keratoconus and glaucoma, predict response to corneal procedures such as laser vision correction and corneal collagen cross-linking. Biomechanics should be more inclusive to include cases of other disease pathology, corneal transplants including donor corneas, she added. Although we are still in a stage of infancy, there is a potential to change the whole new world of biomechanics.

ABUSIVE HEAD TRAUMA: WHERE DOES TRUTH LIE?

Dr Donny W Suh, USA

During a presentation, Dr Donny discussed about abusive head trauma (AHT). He said that it has different names – Battered infant, Battered child syndrome, Whiplash shaking infant, Shaken baby syndrome (SBS), Nonaccidental trauma and AHT. He said that AHT is the most common cause of traumatic death in children below 12 months of age.

He discussed the pathophysiology of brain injury – 2 types of injury by acceleration and deceleration. He mentioned that vessel bifurcations experience greater stress. In peripheral retina, there are greater number of bifurcating vessels. This may explain the diffuse nature of retinal hemorrhages in SBS. He added that all pre-, intra-, subretinal layers experience similar stress. He said that computer and animal models support the hypothesis that shaking an eye at a frequency as low as 2.2 cycles/sec can produce stress levels that exceed the minimum threshold for producing VR separation in young sheep and monkey eyes due to mechanical failure. Similar mechanical failure may occur in human eyes if stress levels exceed vitreoretinal adhesion.

Dr Donny said that their finite element can be used to recreate the trauma based on history provided and calculate the force/pressure applied to the retinal structures. This information can be useful for deciding whether to further pursue the extensive and careful medical and social history investigation of circumstances surrounding a trauma event.

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News and Views

Insomnia in Healthcare Workers Deteriorated During Pandemic

A study looking into the association of quality of sleep with psychological distress among healthcare workers in New York City during the coronavirus disease 2019 (COVID-19) pandemic noted that those who don't sleep well have double the odds of reporting symptoms of depression compared to their colleagues who sleep better.

The study, published in the *Journal of Affective Disorders*, noted that the healthcare workers with sleep disturbances have a 50% higher likelihood of reporting psychological distress and are 70% more likely to experience anxiety. Investigators carried out a series of surveys to evaluate the sleep habits and psychological symptoms experienced by healthcare workers during the first peak of the pandemic in New York City.

More than 70% of healthcare workers were found to have at least moderate insomnia. The number came down as COVID-19 cases declined; however, about 4 in 10 still had insomnia 10 weeks after the first survey, when the first wave was over and work schedules were back to normal… (*Source: Medscape*)

New Zealand Plans to Ban Cigarettes for Coming Generations

New Zealand plans to ban the sale of tobacco to its future generation, in order to eventually eliminate smoking. Anyone born after 2008 will not be able to buy cigarettes or tobacco products during their lifetime, under a law which is expected to come into effect this year. The country's Minister of Health, Dr Ayesha Verall, said that they want to ensure that young people never start smoking. The country's health ministry announced a sweeping crackdown on smoking recently. The government also introduced certain tobacco controls, as a part of which, it has significantly restricted the places where cigarettes can be sold, to remove them from supermarkets and corner stores. The number of shops authorized to sell cigarettes will be brought down to less than 500 from about 8,000 at present… (*Source: BBC*)

Children with Type 2 Diabetes should be Frequently Screened for Diabetic Retinopathy

A retrospective review published in *JAMA Ophthalmology* reveals that eye complications occurred more often and earlier with type 2 diabetes (T2D) compared to type 1 diabetes (T1D) in the young.

Medical records of persons from Olmsted County, Minnesota spanning five decades (from January 1970 to December 2019) were reviewed to examine the risk of developing diabetes-associated ocular complications; 606 patients diagnosed with T1D or T2D before 22 years of age were finally included in the analysis. The average age at the time of being diagnosed with diabetes was 12 years. The incidence of T1D was determined to be 26 per 1,00,000 children annually; for T2D, the incidence was 5 per 1,00,000 children per year. The prevalence of T2D was higher in girls versus T1D.

Diabetes-related eye complications occurred more commonly in T2D patients (26.6%) compared to T1D patients (31.2%). More than half of those (52.7%) with T2D developed retinopathy after 15 years of diagnosis versus 30.6% of those with T1D; the hazard ratio (HR) for any diabetic retinopathy (nonproliferative or greater) was 1.88 and 2.33 for proliferative diabetic retinopathy (PDR). They were also at a greater risk of developing other eye complications such as visually significant cataract (HR 2.43), diabetic macular edema (HR 1.49), or needing pars plana vitrectomy within 15 years of diagnosis (HR 4.06).

This study has shown that among the young persons diagnosed with diabetes, the risk for diabetic retinopathy within the first 15 years of disease was 88% higher in those with T2D compared to those with T1D. Hence, children with T2D need to undergo more frequent ophthalmoscopic examinations for timely detection of retinopathy and treatment to prevent or delay the risk of loss of vision.

Reference

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Persistent Dyspnea in Long COVID Patients may Indicate Subclinical Cardiac Dysfunction

Patients who continue to experience breathlessness on physical activity even after 1 year of recovering from COVID-19 may have sustained some residual heart damage, suggests a new study from Belgium, presented at EuroEcho 2021, the annual echocardiography conference of the European Society of Cardiology (ESC).[1,2]

Sixty-six patients, with no past history of any cardiopulmonary disease, were selected for the study to detect any subclinical heart dysfunction in those complaining of dyspnea. Around 67% of participants were men; 23 patients (35%) had dyspnea as part of long COVID. Their average age was 50 years. These patients had been hospitalized with COVID-19 between March and April 2020 at University Hospital, Brussels. Spirometry and chest CT scan were done at 1-year post-discharge to evaluate pulmonary functions and detect any residual lung damage. Assessment of cardiac function was done by ultrasound and myocardial work, a new echocardiography-based measure of cardiac function. Global work index (GWI) and global constructive work (GCW) were used to evaluate myocardial work performance.

Results showed that compared to patients with no dyspnea, those who had persistent dyspnea at 1 year after recovery displayed diminished heart function on cardiac imaging as measured by GWI and GCW (odds ratio [OR] 0.998) after adjusting for age and gender. At 9 months, the probability of having a normal respiratory pattern also showed a reduction (OR 0.195). Almost half of the patients showed myocarditis and ischemic injury at 1 and 2 months after hospital discharge. Although more than a quarter of the participants had residual ground glass opacities at 6 months and 10% had pulmonary fibrosis at 1 year, no association was observed with dyspnea.

The findings of this study show a significant association of subclinical cardiac dysfunction incurred due to COVID-19 and persistent breathlessness during physical activity at 1 year. Such patients require long-term regular monitoring. It proposes a likely explanation of why some long COVID patients continue to experience shortness of breath even after recovering from the infection. All patients should undergo cardiac evaluation using myocardial work as a new diagnostic aid for early identification of abnormalities in heart function. Such patients require long-term regular monitoring.

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2. https://www.ajmc.com/view/investigators-ask-if-covid-19-infection-is-to-blame-for-cardiac-dysfunction.

Give Two Doses of Same COVID-19 Vaccine Rather Than Mix-and-Match Approach, Says WHO Panel

An expert panel of the World Health Organization (WHO) has said that it is best to administer two doses of the same COVID-19 vaccine; however, mixing and matching seems good for countries which face supply issues.

Alejandro Cravioto, the panel's chairman, said that the best approach seems to be using the same vaccine for the two doses in the primary series. Using vaccine combinations, by mixing and matching, could be beneficial for low- and middle-income countries which are dealing with vaccine shortages amid the spread of the Omicron variant.

Cravioto stated that if countries consider a mix of vaccines, it is best to administer a second dose of a messenger RNA or vector-based vaccine if the first jab was that of an inactivated vaccine. Messenger RNA vaccines can be followed by vector-based shots... (*Source: NDTV – Bloomberg*)

Bariatric Surgery Tied to Increased Epilepsy Risk

A new research presented at the American Epilepsy Society (AES) 2021 Annual Meeting suggests that bariatric surgery is tied to a significantly increased risk for epilepsy.

In order to assess the link, investigators identified 16,958 adult patients from linked databases at the Institute for Clinical Evaluative Sciences (ICES) who underwent bariatric surgery from July 2010 to December 2016. Data were also analyzed for 6,22,514 obese patients who had not undergone the surgery. The study participants were followed till December 31, 2019 for new-onset epilepsy. A total of 73 (0.4%) participants who underwent bariatric surgery developed epilepsy (50.1 per 1,00,000 person-years). The risk for epilepsy was significantly raised among subjects who underwent bariatric surgery compared to those who didn't (HR 1.45)... (*Source: Medscape*)

Boosters Provide 70-75% Protection Against Mild Disease from Omicron: UK Health Agency

Citing preliminary results from a real-world study, the UK Health Security Agency said that booster COVID-19 vaccine doses provide around 70% to 75% protection against mild disease caused by the new Omicron variant.

The early data from real-world evidence indicate that although Omicron variant of the coronavirus could decrease the protection against mild disease offered

by an initial two-dose vaccination series considerably, booster doses could restore the protection to a certain extent.

In an evaluation of 581 individuals with confirmed Omicron infection, two doses of AstraZeneca and Pfizer-BioNTech COVID vaccines provided much lower levels of protection against symptomatic infection in comparison with that provided against Delta. When boosted with a dose of Pfizer vaccine, about 70% protection was noted against symptomatic infection for those who were initially administered AstraZeneca vaccine, while there was nearly 75% protection for individuals who had received the Pfizer vaccine initially… (*Source: ET Healthworld – Reuters*)

Two Common Drugs Appear Effective Against COVID in Preliminary Testing

In early tests, two over-the-counter drugs appear to inhibit the replication of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), reports a study.

Investigators at the University of Florida found that the combination includes diphenhydramine, an antihistamine agent. When combined with lactoferrin, the compounds inhibited the virus during tests in monkey cells as well as human lung cells.

Individually, the two compounds were found to each inhibit SARS-CoV-2 virus replication by around 30%; however, on adding them together, the virus replication was diminished by 99%. The findings are published in the journal *Pathogens*. The investigators stated that further research into the effectiveness of the compounds to prevent COVID-19 infection is being done in mouse models… (*Source: The Hindu – PTI*)

Longer Interval Between COVID-19 mRNA Vaccine Doses may Reduce Myocarditis Risk

According to a preprint research study, rates of myocarditis or pericarditis across all ages and sexes combined were found to be lower for those who had a longer interval between the two doses of an mRNA vaccine.

This was a population-based study of people in Ontario, Canada, who were administered at least one dose of a COVID-19 mRNA vaccine from December 14, 2020 through September 4, 2021. A total of 19.7 million doses of Moderna or Pfizer/BioNTech mRNA vaccines were identified to have been administered during the study period in the Ontario Ministry of Health's COVaxON database. Overall, 417 cases of myocarditis or pericarditis were reported. Of these, 297 reports met the inclusion criteria. Among all ages and sexes combined, myocarditis or pericarditis rates appeared to be higher among people who had a shorter interval between the two doses (≤30 days vs. ≥56 days). Moreover, the rates were similar for the Moderna (rate ratio [RR] 5.2) and Pfizer (RR 5.5) vaccines… (*Source: Medscape*)

Duration of Bisphosphonate Therapy to Prevent Osteoporotic Fractures in Postmenopausal Women

The benefits of bisphosphonates in postmenopausal women with osteoporosis may become evident only after 1 year, according to a recent meta-analysis reported in *JAMA Internal Medicin*e.

The meta-analysis of 10 randomized clinical trials involved postmenopausal women with T scores ≤–2.5 or a vertebral fracture to determine the time to benefit of bisphosphonate use – alendronate, risedronate and zoledronic acid – to prevent fractures. Overall, 23,384 women, age ranging between 63 and 74 years, were included in the meta-analysis. The follow-up duration was 12 to 48 months. Pooled analysis of data revealed that taking bisphosphonate for 12.4 months would reduce the risk of 1 nonvertebral fracture per 100 postmenopausal women at an absolute risk reduction of 0.010. By 18 months, 1.5 fractures per 100 osteoporotic postmenopausal women taking bisphosphonates were prevented. Researchers also looked at specific fractures. To prevent one hip fracture in 200 postmenopausal women with osteoporosis, it would take 20.3 months of treatment with bisphosphonates at an absolute risk reduction of 0.005. On a similar note, 12.1 months of bisphosphonate therapy would be required to prevent one clinical vertebral fracture in 200 postmenopausal women with osteoporosis at an absolute risk reduction of 0.005.

Bisphosphonates are considered the first-line drugs for the treatment of osteoporosis in postmenopausal women. In this study, bisphosphonates were beneficial when used for a longer period of time. However, potential adverse effects may occur even with short-term use such as upper gastrointestinal irritation and musculoskeletal pain (which may be severe enough to necessitate discontinuation of the drug). These have to be weighed in with the benefits of long-term use. Treatment, therefore, must be individualized and based on the patient's preference.

Reference

1. Deardorff WJ, et al. Time to benefit of bisphosphonate therapy for the prevention of fractures among postmenopausal women with osteoporosis: a meta-analysis of randomized clinical trials. JAMA Intern Med. 2021 Nov 22;e216745.

Yoga as Adjunct Therapy in Recurrent Vasovagal Syncope

A small, open-label trial, conducted in India, suggests that addition of yoga to conventional therapy for vasovagal syncope (VVS) can decrease the symptoms and improve the patients' quality of life.

The study participants who practiced yoga had an improvement in VVS symptoms after just 6 weeks, with a reduction of 1.82 events at 1 year. Participants who practiced yoga also had significantly improved quality of life (QoL) scores by the end of the study.

Fifty-five patients were randomized to receive either a specialized yoga training program besides guideline-based therapy, or guideline-based therapy alone. At 12 months, the mean number of syncopal or presyncopal events was 0.7 ± 0.7 in the yoga group, compared with 2.52 ± 1.93 in the control group ($p < 0.05$). The reduction in events started by 6 weeks. About 43.3% patients in the intervention group and 16% patients in the control arm remained event-free at 12 months ($p = 0.02$). The findings were published online in *JACC: Clinical Electrophysiology…* (*Source: Medscape*)

Sun Exposure Tied to Reduced Risk of Pediatric-onset MS

In a recent case-control study, sun exposure was found to be associated with a lower risk of pediatric-onset multiple sclerosis (MS).

Researchers noted that spending 30 minutes to 1-hour outdoors every day during the most recent summer was linked to a 52% lower likelihood of developing pediatric MS, when compared with spending lesser than 30 minutes outside daily (adjusted OR [aOR] 0.48). Spending time outdoors for 1 to 2 hours per day reduced the odds by 81% (aOR 0.19), reported researchers. Additionally, summer ambient ultraviolet ray dose was also found to protect against MS (aOR 0.76/kJ/m^2).

Investigators assessed 332 patients aged between 3 and 22 years who had MS for a median of 7.3 months. They were compared with 534 age- and sex-matched controls without MS. Questionnaires were filled by the study participants or their parents. The responses showed that 18.7% of young MS patients spent less than 30 minutes outdoors every day during the previous summer, compared with 6.2% of controls. The findings are published in the journal *Neurology…* (*Source: Medpage Today*)

Sleep Disturbances More Intense in Older Adults with Atopic Dermatitis

According to the results of a cross-sectional study presented at the Revolutionizing Atopic Dermatitis virtual symposium, patients with atopic dermatitis (AD), aged 65 years and above, have similar disease severity as that in younger adult patients; however, the sleep disturbances in older patients are more profound, particularly difficulty staying asleep.

Researchers enrolled AD patients, 18 years of age and above, who were assessed at an academic medical center from 2014 through 2019. They noted that being 65 years of age or older was not tied to AD severity on the Eczema Area and Severity Index (EASI) (aOR, 1.47); total Scoring Atopic Dermatitis (aOR, 1.10), and itch subscore (aOR, 1.00); Investigator's Global Assessment (IGA) (aOR, 1.87); patient-reported Global Assessment of AD severity (aOR 0.80), or the patient-oriented eczema measure (aOR, 0.55). The associations were not statistically significant.

Older adult age; however, was linked to an increased number of nights with sleep disturbance from AD in the past week (aOR, 2.14; $p = 0.0142$), increased fatigue in the last 7 days (aOR, 1.81; $p = 0.0313$), difficulty sleeping in the last 7 days (aOR, 1.98; $p = 0.0118$), and trouble staying asleep in the last 7 days (aOR, 2.26; $p = 0.0030$). It was not associated with difficulty falling asleep in the last 7 days (aOR, 1.16; $p = .5996$)... (*Source: Medscape*)

HIV Testing Declined During Pandemic, Raises Transmission Concerns

In new research presented at the United States Conference on HIV/AIDS (USCHA) 2021 Annual Meeting, investigators reported that HIV testing centers across the country witnessed a decline in testing of around 50% during the peak of the COVID-19 pandemic in 2020. This has raised concerns about a surge in transmission by people who are not aware of their HIV-positive status.

According to data from the National HIV Prevention Program Monitoring and Evaluation (NHM&E) system, the number of CDC-funded HIV tests was reported to drop by over 1 million in 2020 when COVID restrictions were in place. A total of 1,228,142 tests were conducted that year compared to 2,301,669 tests in 2019, with a decline of 46.6%. The number of people newly diagnosed with HIV, based on the tests, dropped by 29.7%, from 7,692 in 2019 to 5,409 in 2020, reported the investigators... (*Source: Medscape*)

The Spiritual Prescription "I am Sorry"

Two hardest words for a doctor to say: "I'm sorry". Most defense lawyers counsel doctors to not apologize to patients. Their view is that if you say you're sorry for something, you are implicitly taking some degree of responsibility for whatever has happened. In other words, you are pleading guilty. The complainant's lawyers may use a doctor's apology to the maximum extent possible to show the doctor knew what they did was wrong. The usual approach is to deny and defend. But,

- Apologizing after a medical error is the humane thing to do.
- Patients often sue simply because it's the only way to find out what went wrong.
- Erecting a wall of silence is enough to make someone very angry. And it's awfully easy for an angry person to find a lawyer who will listen to them. At that point, it's too late to say sorry.
- Over 35 states in the USA have passed laws prohibiting doctors' apologies from being used against them in court. (Apology laws)
- By promptly disclosing medical errors and offering earnest apologies and fair compensation, one can hope to restore integrity to dealings with patients, make it easier to learn from mistakes and dilute anger that often fuels lawsuits.

Apology, the spiritual answer

- The word 'sorry' is synonymous with apology.
- To err is human, and to admit one's mistake is superhuman.
- Sorry should be heart-felt and not ego-felt. You should not only say sorry but also appear as being genuinely sorry.
- A huge amount of courage is required to face the victim of our wrong doing and apologize.
- Those who are in harmony with their life, and consequently with themselves, find it easier to say sorry. They are the positive, conscientious people who are at peace only after making amends for their wrong doing.
- The word 'sorry' in itself is instilled with tremendous potential and power. Within a fraction of a second, grave mistakes are diluted, estranged relations are brought alive, animosity and the bitterness are dissolved, misunderstandings are resolved and tense situations ease out, giving way to harmony and rapprochement.
- To forgive and forget is a common spiritual saying.
- Remember, we all make mistakes and seek forgiveness from GOD every day.

■■■■

Molnupiravir Tied to Modest Benefit in High-risk Outpatients

An interim analysis of the phase II/III MOVe-OUT trial of molnupiravir revealed considerable benefit with a 5-day course of drug, initiated within 5 days of onset of symptoms in ambulatory, high-risk, unvaccinated adults, reported researchers in the *New England Journal of Medicine.*

Hospitalization for any cause and death through day 29 were reduced to around half in comparison with placebo (7.3% vs. 14.1%, p = 0.001) in the first half of patients randomized, with a 6.8% point advantage. However, this declined to 3.0% points (6.8% molnupiravir vs. 9.7% placebo, p = 0.001) in the analysis of all the 1,433 participants randomized before the trial was terminated early for efficacy.

A subgroup analysis of the trial did not favor the drug for patients with prior SARS-CoV-2 infection, those who had low baseline viral load, and people with diabetes… (*Source: Medpage Today*)

INSPIRATIONAL STORY

Laughter is the Best Medicine

Several years ago, Norman Cousins was diagnosed as being terminally ill and was given 6 months to live. He was told that his chance for recovery was 1 in 500. He came to realize that worry, depression and anger in his life had contributed to his disease. He started wondering that if illness could be caused by negativity, could wellness be created by positivity. He thought of making an experiment of himself. Laughter was among the most positive activities he could think of. He rented several funny movies including those of Keaton, Chaplin, Fields and the Marx Brothers. He read funny stories, asked his friends to call him whenever they said, heard or did something funny. He could not sleep many a times due to his pain, but he noted that laughing for 10 minutes relieved his pain for several hours, and he could sleep. Eventually, he completely recovered from his illness and lived another 20 happy and healthy years. He talked about his journey in his book "Anatomy of an Illness". He credits his recovery to visualization, the love of his family and friends, and laughter.

People sometimes think that laughter is a waste of time. It is a luxury. But that's not the truth. Laughter is essential for our equilibrium and our wellbeing. Laughter helps us get well and stay that way. Since Cousins' work, scientific studies revealed that laughter has a curative effect on the body, the mind and the emotions. Indulge in laughter as often as you can.

Use whatever makes you laugh – movies, sitcoms, books, cartoons, jokes and friends. Laugh long and loud. People may think you're strange, but sooner or later they'll join in even if they don't know what you're laughing about.

Some diseases may be contagious, but none of them is as contagious as the cure… laughter.

(***Source:*** *Peter McWilliams. Chicken Soup for the Cancer Survivor's Soul: Healing Stories of Courage and Inspiration By Jack Canfield, Mark Victor Hansen, Patty Aubrey, Nancy Mitchell, Beverly Kirkhart*)

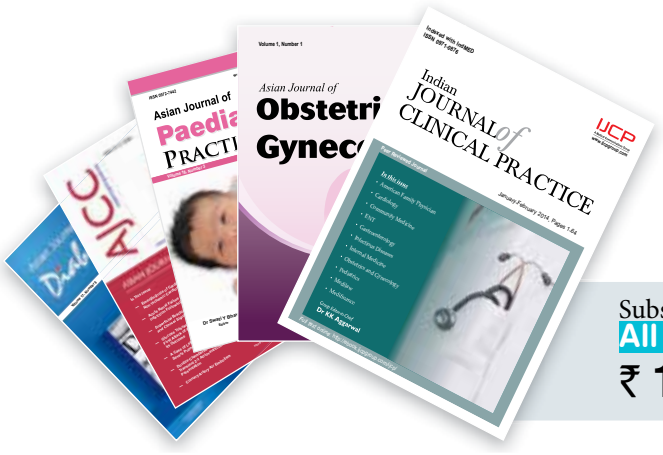
■■■■

Lifestyle Choices may Offset Genetic Risks for Cancer

According to a new study, healthy lifestyle choices, including physical activity and a diet rich in whole grains, fruits and vegetables, may be able to counteract the genetic risks for five cancers.

A survey was conducted with around 2,00,000 individuals in the UK Biobank about their lifestyle habits from 2006 to 2010. The baseline genetic risks for various cancers were evaluated for the participants and they were assessed for new-onset cancer through 2019. It was noted that unhealthy habits heightened the overall risk of cancer by 32%. Unhealthy habits were associated with a heightened risk of eight types of cancer, including lung cancer, with a HR of 3.5, bladder cancer (HR 2.03), pancreatic cancer (HR 1.98), kidney cancer (HR 1.91), pharyngeal cancer (HR 1.69), uterine cancer (HR 1.63), colorectal cancer (HR 1.42) and breast cancer (HR 1.42). Of note, healthy lifestyles did not appear to diminish the risk of melanoma, non-Hodgkin lymphoma, ovarian cancer or lymphocytic leukemia.

Healthy lifestyle choices appeared to be of greater benefit among people who have a high genetic susceptibility to colorectal, breast and pancreatic cancers, and may completely negate the genetic risk for lung and bladder cancers, stated authors… (*Source: Medscape*)



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Lighter Side of Medicine

HUMOR

BAD EATING HABITS

Complaining to her consultant about her daughter's strange eating habits, a woman said that the daughter lies in bed all day and eats yeast and car wax. What will happen to her?

The consultant said, "She will rise and shine."

COSMETIC SURGERY

A sign on a cosmetic surgery clinics says:

"If life gives you lemons, a simple operation can give you melons."

HEALTHY LIVING TIPS

Does an apple a day keep the doctor away?

Only if you aim it well enough.

WHAT'S THE BEST TYPE OF DOCTOR?

"The best doctor in the world is the veterinarian. He can't ask his patients what is the matter – he's got to just know."

— *Will Rogers*

WHAT A SPECTACLE

Q: Did you hear about the optometrist that fell into his lens grinding machine?

A: He made a spectacle of himself.

FUNNY ONE LINERS

Artery: The study of fine paintings

Bacteria: Back door to cafeteria

Barium: What doctors do when patients die

Cat scan: Searching for kitty

Cauterize: Made eye contact with her

Coma: A punctuation mark

D&C: Where Washington is

Enema: Not a friend

ER: The things on your head that you hear with

Fester: Quicker than someone else

Genes: Blue denim slacks

GI Series: World Series of military baseball

Hemorrhoid: A male from outer space

Impotent: Distinguished, well-known

Medical Staff: A doctor's cane

Morbid: A higher offer than I bid

Nitrates: Cheaper than day rates

BUT WHERE WERE YOU YESTERDAY?

John would always get up late in the morning and was always late for work. His boss was annoyed and threatened to fire him if he didn't do something about it. John went to his doctor who gave him a pill and told him to take it before he went to bed. John slept well and beat the alarm in the morning. He had breakfast and drove to work. He went to his boss' cabin and told him that the pill actually worked. The boss said, "That's fine, but where were you yesterday?"

Dr. Good and Dr. Bad

SITUATION: A 52-year-old, type 2 diabetic male was suggested to eat a starch-restricted, fiber-rich functional bread, with an increased β-glucan/starch ratio.

LESSON: It has been reported that a starch-restricted, fiber-rich functional bread, with an increased β-glucan/starch ratio helps in ameliorating long-term metabolic control. Thus, it could be regarded as a beneficial dietary treatment for T2DM.

Nutrients. 2017;9(3):297.

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- The introduction should state why the study was carried out and what were its specific aims/objectives.

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- These should be described in sufficient detail to permit evaluation and duplication of the work by others.
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Results

- These should be concise and include only the tables and figures necessary to enhance the understanding of the text.

Discussion

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References

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Paintal AS. Impulses in vagal afferent fibres from specific pulmonary deflation receptors. The response of those receptors to phenylguanide, potato S-hydroxytryptamine and their role in respiratory and cardiovascular reflexes. Q. J. Expt. Physiol. 1955;40:89-111.

Books

Stansfield AG. Lymph Node Biopsy Interpretation Churchill Livingstone, New York 1985.

Articles in Books

Strong MS. Recurrent respiratory papillomatosis. In: Scott Brown's Otolaryngology. Paediatric Otolaryngology Evans JNG (Ed.), Butterworths, London 1987;6:466-470.

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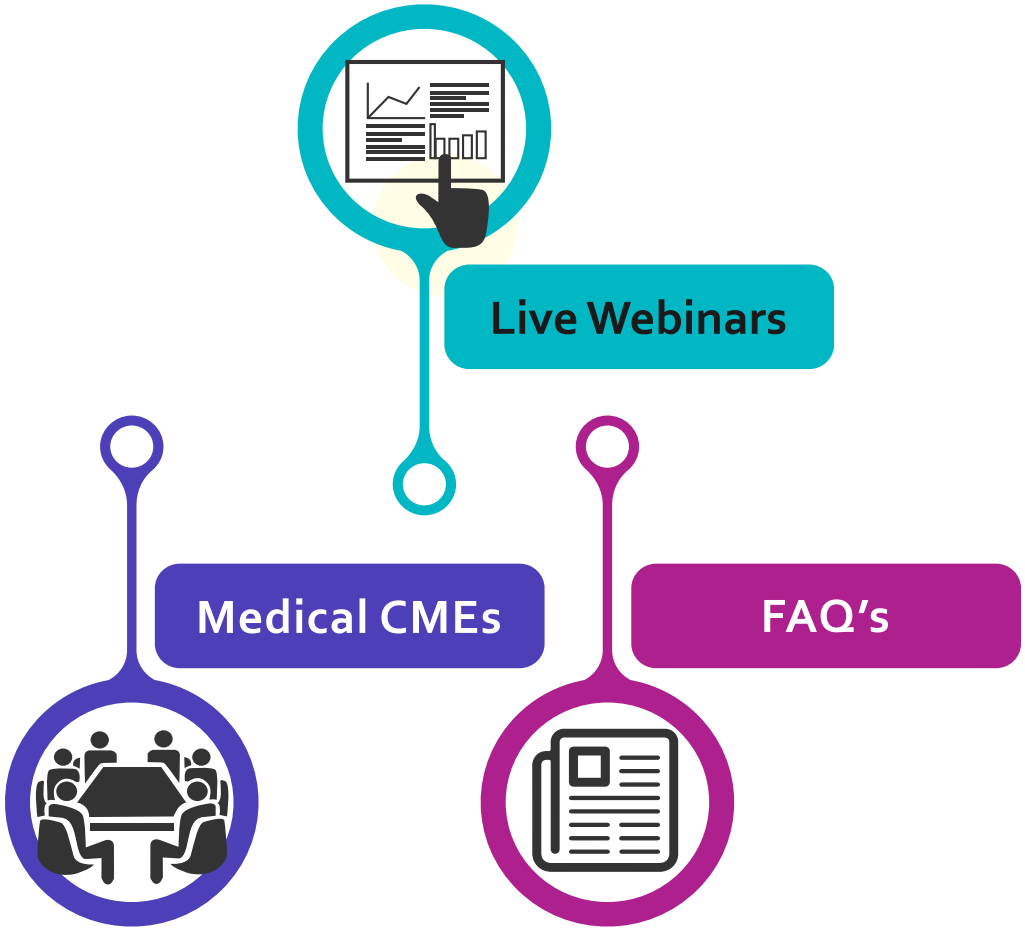

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