# News and Views

## Benefits of PAP Therapy in Patients with Obstructive Sleep Apnea and Nighttime Acid Reflux

Patients with obstructive sleep apnea (OSA) have a higher prevalence of nighttime gastroesophageal reflux (GER) when compared to the general population. They are also more likely to have respiratory symptoms such as wheezing, productive cough. A new single-center study published in *ERJ Open Research* has suggested that consistent use of positive airway pressure (PAP) treatment, which is regarded as the gold standard therapy for these patients, is associated with reduction in nocturnal gastroesophageal reflux (nGER), wheeze and cough.[1]

Researchers from Iceland, Sweden and the United States set out to investigate the effect of PAP treatment on nGER and respiratory symptoms in OSA patients. They enrolled 822 patients, with moderate to severe OSA (apnea-hypopnea index [AHI] ≥15 events/hr), who had been recently diagnosed with OSA and were referred for PAP treatment from September 2005 to December 2009. These patients were a part of the Icelandic Sleep Apnea Cohort (ISAC) study and underwent therapy at the Dept. of Respiratory Medicine and Sleep, Landspitali University Hospital in Iceland.

Out of the 822 participants, follow-up data at 2 years was available for 732, which included 366 full PAP users and 366 partial/non-PAP users. Their mean age was 54 years. Full PAP use was defined as "use of PAP for ≥20 days and ≥4 hours/day on average for the previous 4 weeks based on objective data, or ≥5 nights/week for ≥60% of the night based on questionnaire responses". Those who did not meet these criteria were termed "partial users". Nonusers were those participants who did not use the device after 1 year of starting treatment. Patients who reported having heartburn or belching once a week or more frequently were categorized as "with nGER". Patients who had no such symptoms or used medication for nGER were grouped as "no nGER". The remaining participants were categorized as "possible nGER".

At the start of the study, nearly 12% patients in the full PAP use group had nocturnal acid reflux compared with 16% of those who used the PAP machine only for some time or did not use it at all. At 2-year follow-up, it was found that the risk of experiencing GER diminished among patients who were full PAP users with odds ratio (OR) of 0.58 compared with partial or non-PAP. nGER was present in 14% of full PAP users compared to 36% among the partial or non-PAP users. The presence of wheeze also reduced in this group of patients at the 2-year follow-up (OR 0.56).

Among patients who had had a decrease in nocturnal reflux, the decrease in productive morning cough was more than fourfold with OR 4.70. The risk of chronic bronchitis also reduced nearly 4 times with OR of 3.86. The likelihood of wheezing was also reduced, which was found to be a direct result of PAP therapy and not due to decline in nighttime acid reflux on mediation analysis. However, reduction in productive cough following PAP treatment was found to be mediated through decrease in nGER.

This study shows that OSA patients, who are fully compliant to PAP treatment show an improvement in reflux compared to patients with inadequate adherence to treatment or the untreated patients. Wheezing and productive cough were also found to improve. While nocturnal acid reflux was found to be associated with productive cough, it was not a major cause of wheezing. The treating physicians should be aware of this association and note that in addition to daytime sleepiness and heart disease, OSA may also influence respiratory symptoms. Hence, patients with OSA with significant respiratory and nighttime acid reflux should be offered PAP treatment. It may particularly benefit patients with wheezing or nocturnal acid reflux. "For patients with OSA and productive cough, treatment modalities other than PAP may be needed, especially if nGER is absent", write the authors.

### Reference

1. Emilsson OI, et al. Positive airway pressure treatment affect respiratory symptoms and gastroesophageal reflux. ERJ Open Res. 2023; DOI: 10.1183/23120541.00387-2023.

## Alarming Statistic: 1 in 3 Men Globally Infected with Genital HPV, Lancet Reports

A recent study published in *The Lancet Global Health* revealed that nearly 1 out of every 3 men aged 15 and above carries at least one type of genital human papillomavirus (HPV) infection. This study highlighted the prevalence of genital HPV infections among men.

It emphasized the importance of including them in initiatives aimed at controlling HPV infections and reducing associated diseases in both men and women.

Based on a systematic review and meta-analysis, the study assessed the occurrence of genital HPV infections in the general male population by examining studies published between 1995 and 2022. The findings showed that the worldwide combined prevalence was 31% for any HPV and 21% for high-risk HPV. Among HPV genotypes, HPV-16 was the most common (5%), followed by HPV-6 (4%). HPV prevalence was highest among young adults, peaking between 25 and 29 and then stabilizing or slightly decreasing.

Although most HPV infections in men and women are asymptomatic, they can lead to long-term complications and even mortality. Each year, more than 3,40,000 women lose their lives to cervical cancer. In men, HPV infections often manifest as anogenital warts, causing significant morbidity and increasing the transmission of HPV. HPV infections are also linked to penile, anal and oropharyngeal cancers, with HPV type 16 being a common culprit. In 2018, the International Agency for Research on Cancer estimated that around 69,400 male cancer cases were attributed to HPV. Additionally, the study found that 1 in 5 men is infected with 1 or more high-risk or oncogenic HPV types.

(*Source: https://www.daijiworld.com/news/newsDisplay?newsID=1117159*)

### Lung Conditions and Climate Change: Study Reveals Heightened Risks

An expert analysis recently published in the *European Respiratory Journal* has revealed that individuals with lung disorders like asthma and chronic obstructive pulmonary disease (COPD) face even greater risks due to climate change.

This report titled, "Climate change and respiratory health: a European Respiratory Society position statement" compiled evidence demonstrating how the consequences of climate change, such as heatwaves, wildfires and flooding, will worsen breathing difficulties for millions of people globally, focusing on infants, young children and the elderly. On behalf of the European Respiratory Society, representing over 30,000 lung specialists from 160 countries, the authors urgently call upon the European Parliament and governments worldwide to take immediate action to reduce greenhouse gas emissions and mitigate the effects of climate change.

According to the report, these effects encompass rising temperatures and the subsequent increase in airborne allergens, like pollen. They also included more frequent occurrences of extreme weather events such as heatwaves, drought and wildfires, leading to episodes of severe air pollution and dust storms, as well as heavy rainfall and flooding, resulting in higher humidity levels and mold growth in homes. The report particularly stressed the additional risk babies and children face, whose developing lungs are especially vulnerable to these changes.

(*Source: https://www.hindustantimes.com/lifestyle/health/people-with-lung-conditions-face-extra-risks-from-climate-change-study-101693892221761.html*)

### BMJ Study Shows Startling Rise in Cancers among Under-50 Population

A recent study published in *BMJ Oncology* has revealed a striking 79% increase in new cancer cases among individuals under 50 worldwide over the past three decades. The research highlighted that the most rapid rise was observed in windpipe and prostate cancers, while the highest number of deaths occurred in breast, windpipe, lung, bowel and stomach cancers.

A study conducted by a team of researchers at the University of Edinburgh in Scotland found that in 2019, breast cancer accounted for the highest number of "early onset" cases in people aged 50 and above. Cancers of the windpipe and prostate have experienced the most significant increase in incidence since 1990. The researchers predicted that the global number of new early-onset cancer cases and associated deaths will increase by 31% and 21% by 2030, with individuals in their 40s being the most vulnerable. These findings challenge the conventional understanding of the types of cancers typically affecting individuals under 50. While cancer is generally more common in older individuals, the evidence suggests that cases among those under 50 have increased worldwide since the 1990s.

To arrive at their conclusions, the researchers analyzed data from the Global Burden of Disease 2019 Study, focusing on 29 types of cancer across 204 countries and regions. They examined the incidence, mortality rates, health impacts (measured in disability-adjusted life years or DALYs), and contributing risk factors for individuals aged 14 to 49, estimating the annual percentage change between 1990 and 2019. In 2019, new cancer diagnoses among those under 50 totaled 1.82 million, marking a substantial 79% increase compared to the 1990 figures.

(*Source: https://www.tribuneindia.com/news/india/cancers-among-under-50s-rose-by-79-per-cent-in-last-30-years-bmj-study-541844*)

### Vaccines not Associated with MS Flare-ups, Study Shows

According to the results of a large national study conducted in France and published in *JAMA Neurology*, getting vaccinated was not associated with increased multiple sclerosis (MS) flare-ups. The study, led by Dr Lamiae Grimaldi, PharmD, PhD, of the Assistance Publique-Hôpitaux de Paris, analyzed data from many MS patients and their vaccination history.

The study relied on the System of National Health Databases registry, covering most French residents, and included data from the national hospital discharge database and death records. It encompassed MS patients diagnosed from January 1, 2007, through December 31, 2017, or those with a history of care during that period if diagnosed earlier.

Over the 11-year study period, the 106,523 MS patients (with a mean age of 43.9 years, 71.8% of whom were female) were followed for an average of 8.8 years. Of these patients, 54.6% received vaccinations at some point, with the most common vaccinations being DTPPHi (diphtheria, tetanus, poliomyelitis, pertussis and *Haemophilus influenzae*), followed by the flu shot and pneumococcus vaccine.

The results revealed that hospitalization for an MS flare showed no indication of a higher likelihood in the 60 days following exposure to any vaccine. This observation held for various common vaccines, including the combination DTPPHi vaccine used in France, the influenza vaccine and the pneumococcal vaccine.

These findings aligned with the American Academy of Neurology guidelines, which recommends routine vaccinations for most MS patients. Exceptions include patients with contraindications, those experiencing an ongoing MS relapse (who are advised to delay vaccination), and individuals receiving immunosuppressive or immunomodulating drugs.

(*Source: https://www.medpagetoday.com/neurology/multiplesclerosis/106190*)

### Topiramate and Pregnancy: PRAC Proposes Stricter Guidelines for Safer Use

The Pharmacovigilance Risk Assessment Committee (PRAC) of the European Medicines Agency (EMA) has issued new recommendations to prevent topiramate use during pregnancy. While it is widely recognized that topiramate can lead to significant congenital deformities and hinder fetal growth during pregnancy, recent data also indicate a potentially heightened risk of neurodevelopmental disorders in children.

The findings of two observational studies have indicated that children born to mothers with epilepsy who were exposed to topiramate during pregnancy may face a two- to threefold increased risk of neurodevelopmental disorders, particularly autism spectrum disorders (ASD), intellectual disability or attention deficit hyperactivity disorder (ADHD), in comparison to children born to mothers with epilepsy who did not use antiepileptic medication.

Based on the findings, the PRAC issued new recommendations advising pregnant women to refrain from its use during pregnancy unless no other suitable treatment options are available. They have also proposed a program to prevent pregnancy while taking topiramate to avoid fetal exposure to the drug.

The EMA noted that these measures will educate women and girls of childbearing age about the risks associated with taking topiramate during pregnancy and the importance of preventing pregnancy while using the medication.

Irrespective of the medical condition for which it is prescribed, the EMA suggested that topiramate should only be used in women of childbearing age when certain requirements of the pregnancy prevention program are met. These conditions include conducting a pregnancy test before commencing treatment, counseling about the risks of topiramate treatment and the necessity for highly effective contraception throughout the treatment, and conducting an annual review of ongoing treatment by completing a risk awareness form.

(*Source: https://www.medscape.com/viewarticle/996113?ecd=a2a*)

### Only 32% of Donated Eyes are Utilized in Eye Transplants Yearly: Department Report

Data from the Department of Health and Family Welfare revealed that only 2,671 of the 8,247 eyes donated in 2022 to 2023 in Karnataka were used for transplantation, or 32% of the total.

BBMP districts alone witnessed the collection of 5,127 eyes, despite the fact that there are 49 eye banks in Karnataka that are registered under the Human Organ Transplantation Act, including nine state-run ones. The utilization percentage of corneas at Narayana Nethralaya, which collects around 2,500 to 2,800 eyeballs annually for transplantation, ranges from 25% to 40%. Doctors claim that occasionally, donated eyeballs are wasted

because the corneal tissues produced via the donation procedure do not always match the requirements for transplantation. Sometimes, the condition of the cornea or the kind of corneal structure renders the eyes unsuitable for transplantation. According to stakeholders, a delay in transporting the cornea to the eye bank might also result in rejection.

Dr Pallavi Joshi, consultant in cornea, ocular surface and refractive surgery at Sankara Eye Hospital, responded that it is their duty as ophthalmologists to carefully examine the tissues obtained from donated eyes to determine whether they meet the quality criteria. Following the requirements guarantees that only the best tissues are chosen for transplantation.

The head of Narayana Nethralaya, Dr Rohit Shetty, stated that the eyeballs not utilized for transplantation are used for research. They frequently serve as a training ground for the upcoming cornea surgeons. The ability to do any study is attainable with these tissues. They make sure the given eyeballs are used effectively. Hundred percent of cornea is used for academic, training or research purposes.

(*Source: https://timesofindia.indiatimes.com/city/bengaluru/only-32-of-eyes-donated-in-1-year-used-for-transplantation-dept-data/articleshow/103448838.cms*)

### Blood Clot Risk Spikes with Painkiller and Contraceptive Pairing

According to a Danish research that was just published in *The BMJ*, women who use hormonal contraception and nonsteroidal anti-inflammatory drugs (NSAIDs) have a slightly increased chance of getting venous thromboembolism (VTE) or blood clots.

The risk is more pronounced in women who use third- or fourth-generation progestins in combination with oral contraceptives, but it is relatively lower in women who use progestin-only tablets, implants or coils in combination with NSAIDs like ibuprofen, diclofenac and naproxen. It's crucial to remember that, even for women on high-risk hormonal contraception, the chance of developing a serious blood clot is still quite low.

Using national medical information, the study tracked the first-time diagnoses of venous thromboembolism among 2 million Danish women between the ages of 15 and 49 between 1996 and 2017. Based on earlier research, the risk levels of hormonal contraception were classified as high, medium and low based on their connection with VTE.

The study found that 5,29,704 women who used hormonal contraception also took NSAIDs during the research. Ibuprofen (60%) was the most popular NSAID among them, followed by diclofenac (20%) and naproxen (6%); 8,710 venous thromboembolic episodes were reported during a 10-year period, and 228 (2.6%) of the diagnosed women died within 30 days.

NSAID usage in women with hormonal contraception is linked to increased VTE events per week, with 11 extra events in medium-risk women and 23 extra events in high-risk women.

Experts recommend investigating alternatives for analgesia and integrating these findings into safety assessments of over-the-counter diclofenac.

(*Source: https://medicalxpress.com/news/2023-09-common-painkillers-hormonal-contraception-linked.html*)

### Study Finds Regular Exercise Reduces Stress in Children

A study published in the *Journal of Science and Medicine* in Sport found that daily exercise boosts resilience and reduces stress in school children.

The study revealed that participants who engaged in over an hour of daily exercise, in line with World Health Organization (WHO) guidelines, exhibited lower cortisol levels during stress-inducing tasks than their less active peers.

Experts stated that regularly active kids appear to have less physiological stress reactivity. Children who routinely exercise, swim, climb, etc., teach their brains to link an increase in cortisol to good things. The body's response is always cognitive, and this positive relationship lessens the likelihood that cortisol levels may spike during test scenarios.

The study included 110 kids between 10 and 13 years who wore sensors to measure their everyday movements for a week. The participants were then brought into the lab on 2 consecutive occasions to perform a challenging challenge and a less challenging control task.

The amount of the stress hormone cortisol in the kids' saliva was used to gauge how physically the kids would react to stress.

The researchers used electroencephalography (EEG) to monitor participant brainwaves while doing the stress task to investigate participants' cognitive responses. To conclude, the experts suggested that stress might affect one's thinking ability. The research team is now trying to determine if these cognitive impacts of stress are also influenced by physical exercise.

(*Source: https://www.daijiworld.com/news/newsDisplay?newsID=1117704*)

### Children with Moderate Croup may Benefit from Exposure to Outside Cold Air

Exposing children to the cool night air is an old wives' tale. Perhaps giving credence to this, a recent study reported in the journal *Pediatrics* found that almost half of the children exposed to outdoor cold air showed improvement in their symptoms compared to children who were exposed to indoor ambient air.[1,2] This effect was more pronounced among children with croup of moderate severity.

A total of 118 children with croup attending a pediatric emergency department in a tertiary hospital were selected for this single-center, randomized controlled trial. Their ages ranged from 3 months to 10 years and all had a Westley Croup Score (WCS) ≥2. In the emergency department, after administration of a single-dose of oral dexamethasone, the participants were immediately randomized 1:1 to exposure to outdoor cold (<10°C) air or to indoor ambient room air for 30 minutes.

After 30 minutes, a decrease in the WCS ≥2 points from baseline was noted in 49.2% of the children exposed to outdoor cold air compared to 23.7% children in the indoor air at 30 minutes after triage with a risk difference of 25.4% after they had been administered a single dose of oral dexamethasone. The beneficial effect of cold air was most evident in patients with moderate croup, with WCS 3 to 5, with risk difference of 46.1%. In this group, 63.3% in the outdoor group showed a reduction in WCS ≥2 from baseline versus 17.2% in the indoor group. After 1 hour, the effect of outdoor cold air was mitigated with no difference noted between the two groups. No adverse events occurred. When these children were examined after a week, 44% in the cold air group showed no residual symptoms compared to 32.1% in the indoor air group. But the total scores were comparable between the two groups.

This study demonstrates that exposure to outside cold air may reduce the severity of symptoms in children with moderate croup. Hence, this may also be a strategy to manage cases of moderate croup as an adjunct to oral dexamethasone.

### References

1. Siebert JN, et al. Outdoor cold air versus room temperature exposure for croup symptoms: a randomized controlled trial. Pediatrics. 2023;152(3):e2023061365.
2. Henderson J. Medpage Today. August 1, 2023. Available at: https://www.medpagetoday.com/pediatrics/generalpediatrics/105714. Accessed September 7, 2023.

### Memory-appetite Connection Unveiled: Insights into Obesity

New research from the Perelman School of Medicine at the University of Pennsylvania and published in *Nature* reveals a direct correlation between disrupted connections within the brain circuits responsible for memory and appetite regulation and body mass index (BMI). This correlation is particularly prominent in individuals grappling with disorders related to overeating, such as binge eating disorder (BED), which can lead to obesity.

The research highlights the impaired connectivity between the dorsolateral hippocampus (dlHPC) and the lateral hypothalamus (LH) in obese individuals. These disruptions may influence their capacity to manage and control emotional reactions when anticipating pleasurable meals or snacks.

Researchers at the Epilepsy Monitoring Unit found that the hypothalamus-hippocampus circuit, which regulates feeding behavior, activates simultaneously when patients anticipate receiving a sweet treat. The dlHPC and LH regions exhibited robust connectivity, and the impairment of this circuit was directly proportional to BMI in individuals with high BMI.

Scientists employed a "brain clearing" technique to examine brain tissue, verifying the association between the dlHPC and melanin-concentrating hormone (MCH). This approach confirmed the presence of MCH in the dlHPC, affirming a connection between these regions. Remarkably, the method revealed MCH originating exclusively from the LH, a known regulator of eating behavior, and its presence in the dlHPC underscored the pivotal link between these two brain areas.

The research further aims to identify individuals at risk for obesity and develop novel therapies to improve the function of the hippocampus, a critical circuit often faulty in obese patients, by identifying potential targets for future treatment.

(*Source:https://www.sciencedaily.com/releases/2023/08/230830131943.htm*)

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