

The Swinging Pendulum of Sleep Medicine

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UNDERSTANDING THE FACTORS THAT CAUSE SLEEP APNEA

We know that sleep apnea has to do with the balance of the dilating and constricting muscles in the upper airways. We know that it is a functional problem that is aggravated by some structural issues, but as to what is the precise mechanism that leads to the collapse of the airways? We are still in the dark.

We also know that this is a familial disease, which means that if you have a father with sleep apnea, your own risk of sleep apnea is 10 times higher than if you did not have a father with sleep apnea. But why does the airway collapse when you inhale and start to generate negative pressure in your chest? We still do not know. So this is still a fertile area for research, to try to find out what is the dysfunction of the muscles of the upper airway that cannot sustain the negative pressure.

NON-SLEEP PHYSICIANS AND PATIENTS WITH SLEEP APNEA SYMPTOMS

In Israel, we are seeing a phenomena in which more and more primary care practitioners (PCPs) make a diagnosis of sleep apnea—so we see most of the referrals coming from these family/primary care practitioners. I think that we are part of the process, so we do not see the change clearly. But we are witnessing a change in the field.

I am involved with the Sleep HealthCenters in Boston, of which I was one of the founders in 1997. We now have 16 sleep clinics. We see referrals from family practitioners more and more. So it's not only the ENT that has become sensitive to snoring and sleep apnea—it is the PCP community as well. This will be a slow process, but I think we will start to see a change in the medical field, and the last to come into the game will be the cardiologists. Currently, where I am based in Israel, we are collaborating with the cardiologists and doing sleep studies in the cardiology department. Although it is the beginning of a new process, I believe it will continue.

EDUCATING HEALTHCARE PRACTITIONERS

When I was a dean of medicine at the Technion, Israel Institute of Technology, in Haifa, I changed the curriculum and introduced several courses about sleep medicine. We introduced sleep medicine into what we called the “bridging” course—between the pre-clinical and the clinical years—which every medical student must take. Currently, few medical schools

incorporate sleep medicine into the curriculum; this is something that should be done. When we last polled, it was 10% of medical schools. Even now, it would be no more than 20% of medical schools with any sleep medicine in the curriculum, which leaves 80% doing nothing.

Education is also public awareness, and I think that in the United States the various sleep related organizations are doing an important job. It's getting there, although not at the pace we would like to see. This is a multi-factorial process which should incorporate public appearances, opinion leaders, and scientific meetings to disseminate the knowledge. We are in a much better position now than we were 10 years ago, but we still have a long way to go.

NEW TRENDS DIAGNOSING AND TREATING SLEEP APNEA

The major change in the diagnosis and treatment of sleep apnea is the CMS decision from March 08 regarding positive airway pressure (PAP) devices for obstructive sleep apnea, which is going to open the entire field. Opening the gates of ambulatory monitoring is going to spark change (not right now, but definitely in a few years). Home testing will be more accessible, and I think that the number of people that will join the diagnostic force of sleep apnea is going to be larger, and it will make treatment much easier.

Unfortunately, I do not see any alternative to CPAP, although I am more of a believer in dental devices than I used to be. I saw excellent results when we tested ourselves with dental devices—not only reducing sleep apnea, but also improving cardiovascular function—in a way that we did not anticipate. However, there is no magic pill, at least not in the next 5 to 10 years.

There is no doubt that opening the ambulatory sleep market is going to bring about major change. If you search the literature of the last 5 years, the number of papers on the importance of sleep duration, and how sleep duration interacts with morbidity and mortality, is enormous. There are close to 100 articles linking short sleep and long sleep with a variety of disease conditions and mortality. This is something new, and we still do not understand it. When someone says, “I sleep 9 hours, or I sleep 6 hours,” this is a single question without any objective measurement, but the data is pouring in. So I think the issue of how much you sleep is going to be on the radar screen of clinicians and public health officials over the next 5 years.

THE ISSUE OF COMPLIANCE

More so than a few years ago, the issue of compliance is on the agenda. At the Sleep HealthCenter in Boston, we do treatment and diagnosis under the same roof. We still have laboratories that only perform diagnosis, but many more are moving to the treatment side, which is important. Treatment is being considered more seriously than before, and people are thinking about how to increase and improve compliance—and this was not on the agenda 10 years ago.

In Israel, after a patient gets a sleep recording, if there is a diagnosis of sleep apnea, we then open the laboratory to all companies with CPAP products. We let the patient see each one of them, and the patient picks what suits him. The lab does the titration, and we then accompany the patient for 1 year to assist him with his therapy and attend to his needs. A similar procedure is followed at the Sleep HealthCenters in Boston. The titration is done in the sleep health center, we provide the patient with CPAP, and we accompany the patient with any problems that he may have. This is not a DME company, that has nothing to do with sleep, and only provides a kind of technical service. At Sleep HealthCenters, we provide medical and technical consultation under the same roof. This is much better than separating the two components of diagnosis and therapy, which leads to situations where the person making the diagnosis does not know who is making the treatment and how it will be provided.

NEW SLEEP FRONTIERS CAN BE FOUND AT OUR FINGERTIPS

Itamar brings a new medical signal to the sleep medicine field. We can extract from the tip of the finger, not only arousals and apneas, but REM sleep and light sleep and deep sleep. Using the same technology, we can understand the function of the vasculature and endothelial function, and maybe even get information about blood pressure.

My vision is that in the next 5 to 10 years, patients will go to sleep with the PAT probe, and in the morning we will have information not only about their sleep, but also about a person's risk of developing hypertension or other cardiovascular diseases based on a dynamic test done while he is asleep. I believe this is achievable within 5 years or so.

In a recently published paper in *Sleep Medicine*, Jan Hedner of Gothenburg Sweden analyzed the WatchPAT signal during sleep in a unique way that provided a prediction of hypertension. Thus, he could predict from the apneas related vascular constrictions during sleep, measured by the PAT probe on the finger, which patients will develop hypertension. This is exciting. (Nocturnal pulse wave attenuation is associated with office blood pressure in a population-based cohort).

ITAMAR INTRODUCES A NEW MEDICAL SIGNAL

Whenever you come up with a new medical signal, you must educate the field. Most people do not understand the basic physiological principle behind the WatchPAT, so it's important to talk about the physiology and how we use the physiology to get the clinical information from the finger. You cannot do this without education, and this is a major investment for Itamar.

The WatchPAT is not a "black box." It is a "clever box," because it relies on basic physiological principles. When you use a new medical signal, it does not come out of nowhere. The finger is a unique site that is almost "tailor-made" to measure autonomic nervous system activity. Sticking a needle in the autonomic nervous system is painful, so why not use the finger? This is what the WatchPAT does, and this is why we need

more education. More research is also important because we still do not maximize the potential of this signal. I believe that in 5 years, one will wake up from sleep with a signature not only of sleep apnea or insomnia, but also of how bad the vasculature is responding to stress. This is going to be important with respect to the prevention of cardiovascular diseases.

One common thread to many conditions is oxidative stress—the production of free radicals. Sleep apnea is an oxidative stress disease, which means that every night there are free radicals produced in the blood stream. The same principle applies to diabetes, hypertension, Parkinson's, and metabolic syndromes. Some of these conditions have a link with sleep apnea in a sequential way, because we believe that glucose intolerance and insulin sensitivity is linked with sleep apnea. All these diseases share a common thread and act in a synergistic way. This is why we believe that sleep apnea is a bad comorbidity to any of these diseases, because they act in a synergistic way.

SLEEP DISORDERS AND CARDIOVASCULAR DAMAGE

The risk is a major one, because every night for many years there is a bombardment of free radicals on the inner surface of the vasculature that is lined with endothelial cells. The cells die, vessels lose their flexibility, plaque is formed, and atherosclerosis progresses leading to stroke and myocardial infarction (MI). I should add that at the same time, there may be a parallel process of adaptation. Thus, sleep apnea may progress in different pathways, one is the damaging arm with triggered by the production of free radicals, and the other arm is the adaptive/protective arm—and the balance between the two will determine if you will have cardiovascular consequences or not.

Surprisingly, results from our laboratory show that patients that survive the age of 50 and 60 and reach elderly age with sleep apnea, do not have excess mortality risk in comparison with patients without sleep apnea. Moreover, our results also showed that in fact they are in a much better shape than their counterparts in the general population. We believe that this old age protection is explained by a process called ischemic preconditioning, that may play a major role in sleep apnea. Therefore, young patients have the highest risk of dying because of sleep apnea, up to the age of 50. Once you pass the age of 50, it is most likely that your adaptive/protective arm is functioning, and ischemic preconditioning is working. Similar results were reported in the Sleep Heart Health Study. Their mortality data presented in the last APSS meetings showed that there is no relationship between sleep apnea and mortality in patients 70 year old or older.

SNORING AND SLEEP APNEA

Not every snorer has sleep apnea, but almost every person with sleep apnea is a snorer. When snoring is ongoing, monotonous, and without interruptions, this is a benign snoring because of the vibrations of the soft tissue in the upper airways—it does not necessarily mean they have sleep apnea.

POLYSOMNOGRAPHY IN MODERN SLEEP MEDICINE

Polysomnography should be reserved for complicated or uncertain cases. In many cases, we are over diagnosing sleep apnea. In some individuals, insomnia resulting in an instability of the sleep process is responsible for apneic events they may amount to at least 5 per hour. This is not sleep apnea. This is respiratory instability because of sleep fragmentation. However, to prove it you must use polysomnography.

Thus, in an obese patient who may fall asleep anytime or anyplace, and snores like a tractor; there is no need for polysomnography. In such patients with high likelihood of disease, ambulatory monitoring can be used with high reliability and accuracy. But in patients where there is a discrepancy between the complaints and objective findings, and in patients that have instability of the sleep process—these are the patients that need polysomnography—in addition to patients who may have narcolepsy or epilepsy in sleep, or any other sleep related diseases.

As I mentioned before, in recent years, the old question of sleep quality—how many hours of sleep we get—is surfacing again. In our recent paper (to be published in *Journal of Sleep Research*) on mortality in the elderly with sleep apnea we found that sleep apnea played no role in mortality. In addition to co-morbidities, the most important predictors of mortality were sleep quality as indexed by sleep efficiency and sleep latency. If you have a sleep latency of more than 2 hours, your risk of dying within 5 years is threefold higher than someone with less than 30-minute sleep latency. So we need to measure sleep to calculate the risk. This is why I think polysomnography is important, because it can provide us with an objective presentation on sleep quality.

THE FUTURE OF AMBULATORY MONITORING

Ambulatory monitoring is here to stay. The future will depend on the reliability of the system and the amount of information it provides. First, we don't want to use a system where you have to repeat every third or fourth study, because this would make it cumbersome and expensive. Second, I would like to use a system that provides me with information about patient's sleep, particularly in view of the fact that sleep quality has shown important prognostic value. Finally, if my system can provide me in addition to apneas and sleep quality also with information about the cardiovascular system, this would probably be the holy grail of ambulatory monitoring. We are not there yet.

I am fond of the WatchPAT not only because the technology was developed in my laboratory in Israel, but because the WatchPAT gives me REM sleep, light sleep, and deep sleep, something that no other ambulatory device can provide unless it uses electroencepholgraphy. Using the WatchPAT I can look at the sleep structure and say if this patient has a normal pattern, or this patient is an insomniac, and maybe his sleep apnea has nothing to do with sleep apnea—but instead is due to the instability of his sleep structure. Ambulatory systems will thrive based on what type of information they provide and the reliability of the system.

GENETIC LINK TO SLEEP DISORDERS

Sleep apnea is a familial disease. This has been shown in more than one study. We are still in the dark with regards to narcolepsy and whether it is familial. Although there is still much debate, I am convinced that some insomnia has also a familial origin. The more we will apply modern genetic techniques to large patient populations, the more we will learn about the genetic link to sleep disorders. I believe this information should be put to clinical use by health care professionals today.

If you are a sleep specialist treating a 60-year-old patient with severe sleep apnea, and ask him how many children he has. If he responds that he has two sons aged 27 and 24, insist that they be studied also because severe sleep apnea is a familial disease.

My laboratory is conducting an ongoing study in Israel on behalf of the department of transportation. Whenever you apply for a professional driving license, ambulance, bus, taxi, or trucking, you must pass a medical exam. We know what the scaling questionnaire is for adults in their 50s with sleep apnea, but we do not know what type of questionnaire to use for someone in their 20's or 30s. We are running a study in which we sample candidates for professional driving licenses aged 20–30 and correlate their subjective responses to questionnaires in the sleep study.

We begin with questionnaires, and then we study them with the WatchPAT. So far, out of the first group of 158 candidates, we identified 13% with sleep apnea. At this young age, apneas were not related to BMI or excessive sleepiness, it was the existence of a father who was a heavy snorer and occasionally fell asleep in passive situations that predicted the results of the sleep study. This was the only distinguishing question: "familial history." As such, we believe this should be put to clinical use in a proactive way.