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Obstructive Sleep Apnoea Hypoapnoea Syndrome (OSAHS) and Pulmonary Hypertension (PH): the Link and Possible Management

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ABSTRACT

In past occurrence of pulmonary hypertension (PH) in obstructive sleep apnoea hypoapnea syndrome (OSAHS) had been overemphasized. However sleep apnoea or hypoaponea shall lead to just episodic nocturnal hypoxemia. Whether this alone can lead to permanent i.e day and night PH or other factors are present in OSAHS which lead to permanent PH? This dilemma is actively reviewed in this article and other possible factors contributing to PH are discussed. Finally treatment part emphasizes to search and deal with all these contributing factors along with the conventional treatment of OSAHS.

KEYWORDS : Obstructive Sleep Apnoea, Pulmonary Hypertension, Hypoxemia, Hypercapnia

INTRODUCTION: OSAHS is defined as the presence of five obstructed breathing events in form of apnea i.e more than 10 seconds of no breathing to hypopnea i.e more than 10 seconds of 50% reduction in baseline breathing per hour of sleep. These can lead to pulmonary vasoconstriction, increase in vascular resistance & consequent rise in pulmonary arterial pressure (Ppa) but it should be transient and nocturnal.

How these transient hypoxia causes permanent rise of Ppa causing PH and how other associated factors contribute to PH? What is actual prevalence of PH in different studies? These all have been discussed with review of different researches.

EXACT PREVALENCE OF PULMONARY HT IN OBSTRUCTIVE SLEEP APNEA (OSA): First we will review the study which had reported higher prevalence rate of PH in OSA. Early study by the Stanford group. in 1976, found a high prevalence (near 60%) of awake PH defined as a mean Ppa greater than 20 mmhg in small group (n=22) of patients having OSA, selected from a larger population & probably had observed bias and had not investigated the other confounding factors.Later in the series of Feicher et at which was restricted to 24 patients, exclusively males with an associated respiratory disease , mostly COPD, reported the prevalence of PH to be 73% in patients having OSA. But COPD can lead to persistent hypoxaemia day and night and thus can contribute to persistent PH.

Another study done on the Australian patients (n-100) by Laks and co-workers reported presence of PH in 42% cases of OSA but the mean body mass index was 37 indicating marked obesity & this group also revealed mild hypercapnia (mean SpCO2 was 45 mmHg) suggestive of the presence of alveolar hypoventilation. So the high prevalence was due to obesity related alveolar hypoventilation.

In contrast to this study, the study done by Chaouat done on European patients having OSA (n=220) the prevalence rate of PH was only 17%, the mean BMI was 32 i.e., lesser prevalence of obesity and the mean SpCO2 was 38.6 mmHg (which in the previous obese group having alveolar hypoventilation, it was 45 mmHg).

This in the larger group (n=220) having pure OSA the prevalence of PH was only 17%. This similar figure of prevalence of PH was found in another study ranging from 12 to 20% eg Pudszus (n=65) prevalence 20%,) Weitzenblum (n=46), prevalence 20%), Bradley 10 (n=50, prevalence=12%), Krieger (n=100, prevalence=19%).

The only study which is not consistent with above figure although OSA was not associated with COPD or any cardiovascular disease is the study done by Sajkov et al (n=27, prevalence=45%) but this study was conducted on small group (n=27) and PH was not assessed by catheterisation but by pulsed Doppler measurment .

Patient having PH in pure OSA group is typically considered to be precapillary in type. But there are evidences that PH in OSA can also be caused by and is associated with left sided heart failure and can co-exist with pulmonary venous hypertension. Similar conclusion was observed by Chaouat and co-workers. They had studied the differences in Ppa in patients having OSA and PH (n=37) at rest and during the exercise. It was found that PH worsens during exercise and changes from precapillary type (26 mmHg) at rest to postcapillary type during exercise (46 mmHg) suggestive of the presence of LV dysfunction which manifests during the exercise. Similar conclusion was observed by Tilkian et al and and has been reconfirmed by the recent report by Hawrylkievicz et al.

Co-existing LV dysfunction may be due to associated obesity because majority of OSA patients are relatively obese irrespective of the exact BMI.

Could nocturnal hypoxemia alone can lead to PH?
There is no proof that OSA alone in the absence of day time hypoxaemia is capable of causing stable PH. Most studies have indicated that PH is observed in patients having day time hypoxemia or hypercapnia. Moreover, these studies have failed to find a significant relationship between severity of OSA expressed by apnea index (AI) and the apnoea hypoxemia index (AHI) and presence of PH.

Possible causes of day time hypoxemia/ hypercapnia :--
Following factors may play role in day time hypoxemia:-
Diminished sensitivity to hypoxemia and hypercapnia:- Gary et al has shown a decrease of ventilator response to hypoxia and hypercapnia (n=13) but in this study number of participants were small (n=13) and all were obese. And obesity may behave as a confounding factor causing alveolar hypoventilation. But this hypothesis is confirmed by other study also, e.g.- by Berthan Jones where diminished ventilatory response to CO2 was found in OSA with PH and it rapidly improved in patients kept on CPAP ventilation. In other study patients of OSA tracheostomy, this improvement took a longer time to occur.

Role of obesity:- historically, the obesity-hypoventilation syndrome has been described as the Pickwikian syndrome. Obesity is the classical cause of hypoventilation. However, the data of different study is conflicting and all the studies have not confirmed this association.

Role of COPD:- the co-existence of COPD and OSA which has been called "overlap syndrome" by Flenley is likely to cause day time and night time hypoxemia along with the OSA causing episodic nocturnal hypoxemia and hypercapnia.

Interplay of hypoxemia & pulmonary vascular responsiveness:
Alveolar hypoxemia can lead to PH both by pulmonary vasoconstric-

tion and "remodelling" of pulmonary vasculature and there could be marked differences in individual responsiveness to alveolar hypoxia both in normal individual and in COPD patients. This could be a reason to explain why only 12 to 20% persons with pure OSA develop PH. Saikov et al speculated that in "responder" OSA, the repeated nocturnal rise in Ppa during sleep may lead to pulmonary vascular remodelling with time leading to fixed PH and Laks and co-workers observed that some OSA patients have an exaggerated pulmonary vascular responsiveness to hypoxia and hypercapnia which may return to normal with long term treatment with nocturnal CPAP ventilation.

Investigations:- Besides polysomnography to detect OSA, arterial blood gas analysis, pulmonary function test, BMI estimation, echocardiography for LV dysfunction and non-invasive measurement of Pap, in selected cases of catheterisation may be required to differentiate between precapillary and post capillary PH.

Therapeutic implication:- Even in patients having OSA without PH the treatment with nCPAP should get started which is the first line treatment of OSA and it will help the patient in many ways e.g. it will increase day time alertness, will treat associated hypertension and will decrease the risk of stroke (40% risk) and acute coronary syndrome (20% risk) associated with OSA. Those who can not afford or tolerate nCPAP treatment, can use Mandibular Responding splint (MRS) or mouth device which is the evidence based second line treatment of OSA.

Regarding correction of PH associated with OSA, there are very few data in the literature making possible to answer this question. Seorza et al investigated 54 patients treated with nCPAP for atleast one year. For the group as a whole Ppa was unchanged after a mean follow up period of 554+/-28 days. This result has been confirmed by a further study by the same group in which long term (5 years) effect of CPAP were investigated in 48 OSA patients. The number of PH patients at the onset (n=4) was too limited to allow estimation of the evolution of Ppa. Both studies have indicated that PaO2 increases significantly in those patients exhibiting significant hypoxaemia at the onset. If PaO2 improves significantly with long term CPAP treatment, one could expect an improvement or at least stabilisation of PH similar to that observed in COPD patients under long term O2 therapy.

Finally, there could be a sub group of OSA patients having associated COPD and /or obesity-hypoventilation syndrome who inspite of nCPAP therapy at night, may reveal hypoxaemia particularly during REM sleep and then it will be necessary to give supplementary oxygen therapy (1.5 to 3 L/min) during sleep or shift the patient to bilevel positive airway pressure ventilation. If yet such patient reveal day time hypoxaemia then conventional >18 hr/day oxygen therapy will be required in addition to nCPAP or bilevel positive airway pressure ventilation. These patients are most likely to develop PH and long term oxygen therapy may help or at least stabilise pumonaryl arterial pressure.

SUMMARY—While dealing with a case of OSA, all the other factors like COPD, obesity, LV dysfunction etc. should be thoroughly searched and treated and treatment should start with nCPAP. If hypoxaemia persist then supplemental oxygen therapy should be added to treatment so that pulmonary hypertension can be treated or at least stabilised.

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