DISCUSSION

Obstructive sleep apnoea syndrome is the most common organic disorder of excessive daytime somnolence seen in sleep disorders clinic today. According to different cross sectional studies, the prevalence of obstructive sleep apnoea among adult men is between 1 – 8% (50) (51). In our study where population were surgical patients, prevalence of obstructive sleep apnoea was 5.35%. Male to female ratio in our study was 2:1 comparable with western studies. High prevalence of OSA in males has been attributed to the effects of testosterone on ventilation and chemo sensitivity. The disease is more common in the middle aged individuals as seen in our series (mean age= 50±20)

Various risk factors have been linked with obstructive sleep apnoea. Obesity is an important risk factor for snoring and sleep apnoea. Some data are available that points that apnoea index rises with increase in weight. More than 50 % patients (87 patients) were overweight but not obese (BMI 25-30). Forty seven patients (32.6%) were obese (BMI > 30%) with 6%(9 patients) of patients were morbid obese (BMI>35). Fourteen patients (9.3%) patients were not even overweight. These findings suggest that obesity is not always a contributory factor pointing towards other unknown factors in pathophysiology of OSA. It is now reported that neck size or thick neck is more closely related to severity of obstructive sleep apnoea than the BMI (52). Other risk factors are related to age. In elderly, prevalence is high though it decreases after age of 65 years. One study reported mortality ratio for sleep apnoea in elderly population (mean age at entry: 66 years) was 2.7% (53). Other risk factors associated with obstructive sleep apnoea are cigarette smoking and alcohol (54) (55).

There is definite correlation between snoring, obstructive sleep apnoea and hypertension. A sizeable number of hypertensive cases (30-48%) may have obstructive sleep apnoea and patients with confirmed diagnosis of obstructive sleep apnoea may also have hypertension (55) (56). In our study 28.3% of patients were found to have hypertension. Twelve patients (8%) in our series were found to have ischaemic heart disease whereas in other case centric

studies done in Australia (57) where 101 male patients with myocardial infarction were included. They found that men with apnoea index higher than 5.3 had 23.3 times (95% CI, 3.9 to 139.9) the risk of myocardial infarction than did men with an apnoea index less than 0.4. The mean apnoea index was 6.9 in patients with myocardial infarction versus 1.4 in the control group. After adjusting for other risk factors, authors explain that sleep apnoea acts together with other known risk factors to accelerate atherosclerosis or to precipitate myocardial ischemia in patients with coronary artery disease. The theory that atherosclerosis may be related to hypoxia has received some experimental support (58).

In our series we also found a correlation with upper airway abnormalities and OSA. In 43.3% of patients, mixed syndrome of short neck, large tongue and large uvula was commonest. Beside anatomical abnormality, it is the negative pressure in the pharynx during inspiration which causes collapse and narrowing of lumen along with adherence of uvula and or posterior surface of the tongue resulting into obstruction during sleep (fig-23). A value of morphometric features has been used by many authors for predicting obstructive sleep apnoea syndrome (59).

Obstructive sleep apnoea is of immense importance to anaesthesiologists. There is enough literature now available suggesting that sedatives, tranquillisers and narcotics in particular should be avoided in perioperative period in patients with obstructive sleep apnoea. The recommendations are based on few anecdotal reports in the literature (6) (7) (48) (60) where respiratory obstruction, coma or even death following administration of such drugs has been reported. It is believed that these patients are sensitive to opioids and can cause exaggerated response and adverse effects. These effects could be due to central action or affecting upper airway muscles. There have been no systematic studies of the effect of parenteral narcotics on breathing during sleep or in awake patients with obstructive sleep apnoea.

Parenterally administered narcotics depress hypoxic and hypercapnic ventilatory responses during wakefulness as well as raise base line arterial carbon dioxide tension (61).

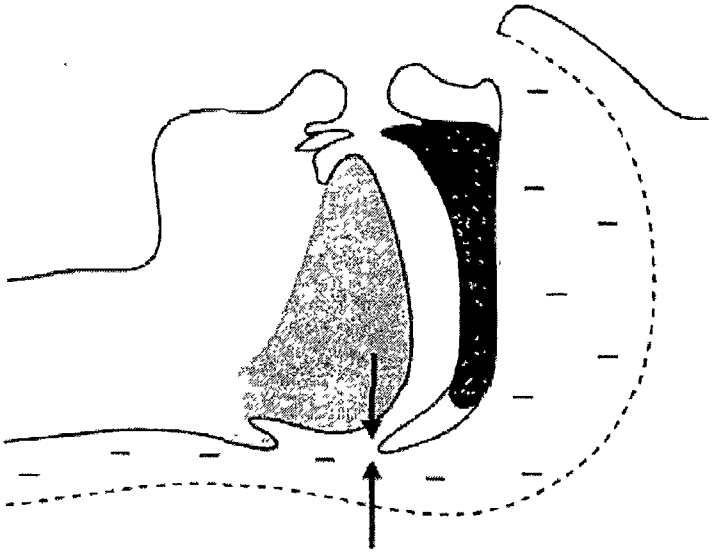

Fig -23: Diagram showing nasopharyngeal cavity and impact of negative pressure on Uvula causing pharyngeal obstruction

In addition, narcotics may impair the compensatory response to increase respiratory resistance. In one study of four subjects, it was found that the combination of morphine and sleep depressed hypercapnic ventilatory response more than either sleep alone or morphine given while awake. Despite these studies, one study of normal adult subjects failed to demonstrate a change in breathing during sleep after administration of oral hydromorphine hydrochloride in 2 and 4 mg doses (8). This occurred despite a depression of awaken minute ventilation and hypoxic response. Author speculated that absence of increased sleep disorder breathing after oral narcotics might be due to a lack of depression of upper airway muscle function by the drug studied. Unlike alcohol no increase in pharyngeal resistance has observed after two oral narcotics doses.

It may not be valid, however, to extrapolate these data to larger doses of narcotics or to their administration of narcotics with pre-existing upper airway dysfunction during sleep. Several case reports have documented the occurrences of severe respiratory depression and upper airway obstruction in patients given narcotics in standard dose perioperatively (60) (62) (63). Data gathered from postoperative respiratory monitoring strongly suggest that narcotics analgesia compared with regional (local anaesthetics) analgesia is associated with considerable more apnoea and greater oxygen de-saturation (6) (64). Ten out of 16 non-obese patients who received morphine infusion mean exceeding dose 18.1 mg and mean infusion rate 0.7 mg/hour after Cholecystectomy or total hip replacement experienced 456 episodes of oxygen de-saturations SaO2 less than 80% during 16 hours of monitoring. These changes occurred only during sleep and were not often associated with obstructive apnoea. A pure narcotic's effects cannot be influenced from study because all patients received general anaesthesia. General anaesthesia decreases neural output to upper airway muscles to a greater extent than they depress phrenic nerve (65).

Use of benzodiazepines, as part of premedication, can cause server upper airway obstruction in patients even when they are awake. Same physiological effects are not seen if morphine is administered in therapeutic

doses. The benzodiazepines have been shown to selectively reduce neural output via hypoglossal nerve and the tone of genioglossus muscle while leaving the output via the phrenic nerve virtually unchallenged (66).

Experience with the perioperative management of sleep apnoea patients is growing and guidelines have been published. They have recommended that preoperative sedation, opioids in particular should never be given in the ward (66) (67). In control group of 50 patients where Inj Ketorolac was used in our series, there was not a single incidence of respiratory depression or obstruction but rise in heart rate and blood pressure was significant (P =0.001). It can be inferred that patients were anxious due to lack of quality premedication.

In study S1 group where 50 patients received Inj morphine 0.10 mg/kg as premedication after shifting the patients in operation theatre had heart rate changes lowest to 60/min and highest 100/min. In terms of number of patients had such changes in S1 group was not statistically significant. It is difficult to explain the incidence of higher heart rate in S1 group of patients. It may be that morphine doses were not adequate to keep them calm. The difference between the two groups as regards to cardiac arrhythmias was not significant.

Higher doses of morphine used in premedication can cause severe respiratory depression or obstruction. In one case report study, where 12 mg morphine with 25 Hydroxyzine was used and patients developed respiratory obstruction after on hour requiring respiratory support (7). In our series in S1 group of patients, incidence of respiratory depression was seen in 6% of patients but requiring no active respiratory support. Narcotics used through epidural route for pain relief postoperatively can also cause respiratory complications (63) Most of the case reports reveal that respiratory complications are much more common if patients received narcotics post operatively and patients are elderly and also suffering from chronic obstructive pulmonary disease (COPD).

The pharmacological effects of morphine are different when administered in patients with pain and when there is no pain. The clinically significant respiratory depression rarely occurs with standard doses of morphine in the absence of underlying pulmonary dysfunction (69). However, it is combination of other factors like general anaesthetics, tranquillisers, sedatives and hypnotics which present a grater risk of respiratory depression. The maximum respiratory depression occurs 5-10 minutes after intravenous administration of morphine or within 30-90 minutes of intramuscular or subcutaneous administration respectively.

Morphine in humans causes analgesia without loss of consciousness or respiratory depression when administered in therapeutic doses. When morphine in the same doses given in pain free patients as is the case in preoperative period, in awaiting surgical patients, the effect may be different. It may be euphoria, drowsiness and mental clouding. This is explained on the basis of understanding of recently reclassified opioids receptors as OP1 (delta), OP2 (K) and OP3 (M) by an international union of pharmacology. All these receptors have been cloned (70) (71) and have pharmacological characteristics consistent with those of endogenous receptor opioids except a variety of stimulating effects on signal transduction by stimulation of cyclic AMP formation, phospholipid hydrolysis and elevation of intracellular calcium by mobilisation from intracellular stores and by stimulating influx. At cellular level these changes may underline an opioids stimulation of neuronal activity. Studies aimed at unravelling these intricate signalling events may contribute better to our understanding of opioids action (72).

The effects of morphine in snorers and individuals with asymptomatic sleep apnoea syndrome remain unknown. Many authorities in the field have opined that effect of larger doses or parenteral narcotics on breathing during sleep in normal subject has not been well examined.

Obstructive sleep apnoea related heart rate changes are so characteristics that they may suggest the diagnosis of obstructive sleep apnoea syndrome. There are cyclic changes, heart rate decreases during apnoea and

increases abruptly immediately post apnoea. These changes occur during sleep (23). Bradycardia seen in these patients may be due to activation of peripheral chemo receptors or increase in parasympathetic tone due to stimulation of upper airway receptors (74).

Moderate alteration in heart rate in S1 group may be due to mild ranges of respiratory depression associated with fall in oxygen saturation, which occurred in 6% of patients. Significant fall in heart rate has been reported even up to 30/min in 7% of patients seen in series of 400 patients (75).

Many studies have shown that obstructive sleep apnoea affects nocturnal blood pressure (76). Evidence of hypertension in patients with obstructive sleep apnoea can be as high as 45% (77). In our series 21.3% of patients were found hypertensive. The strongest evidence in favour of obstructive sleep apnoea as cause of hypertension can be inferred by significant decrease or even normalisation in blood pressure following nasal continuous positive airway pressure treatment without changes in weight reduction or medication (78).

In our series, 8% of patients were also suffering from ischaemic heart disease. Other workers have also reported marked increase in myocardial ischemia in the nights after oxygen therapy has been stopped. In patients with obstructive sleep apnoea ST wave depression has been demonstrated exclusively if patient also had coronary artery disease, which occurs during long apnoea with profound hypoxia. It is also seen that ischaemic episodes in patients with obstructive sleep apnoea do not respond to nitrates (79)

Premature ventricular contractions in obstructive sleep apnoea have been reported as high as in 40-60% of patients depending upon arterial oxygen saturation, apnoea index and concomitant cardio vascular disease. These changes are more commonly seen if arterial oxygen saturation falls below 60% (79) (80).

Respiratory complications in form of respiratory depression, obstruction are reported to be much common event in patients with obstructive

sleep apnoea than cardiovascular events though latter one may be more dangerous. The lumen of the pharynx is smaller in sleep apnoea patients than in non-apnoeic, non-snoring controls (81). The condition occurs because of increased pharyngeal compliance which is primary pathologic characteristic of sleep apnoea (82). It is caused by relative hypotonia of genioglossus and geniohyoid muscles as suggested by electromyographic findings (82).

One of the best series reported in the literature is of 18 cases of OSA (48). Out of 18 cases, 13 are reported complications, 5 cases did not have complications. None of 5 patients had sedative or opioids in premedication but one case received morphine 4 mg epidurally post operatively (68), one case received Fentanyl intraoperatively (69), one case Fentanyl, Midazolam intraoperatively (49). Other two cases did not receive any opioids intra or postoperatively (7) (83). It is worth noting that out of these 5 patients, 3 cases did receive narcotics intra or post operatively but still did not have respiratory complications. The details of 13 cases that developed respiratory complications are described. One patient received premedication as Temazepam 10 mg(42), 4 patients were given post operative analgesia by epidural infusion of opioids as described (48) and developed respiratory complications 29 – 48 hours after surgery. One case developed respiratory complication following administration of Chloral hydrate 110 mg/kg requiring resuscitation (84). Another case received 3 mg Lorazepam orally and developed respiratory depression postoperatively requiring resuscitation.(63) Other 06 cases received sedation/opioids either intra op or postoperatively . It can be seen from above case report series that sleep apnoea patients are at particularly high risk of post operative respiratory depression from any mode of analgesic therapy. Available literature is basically based on case reports; no formal scientific study has been carried out except in one series of cases (49), where they used freely narcotics in premedication but used nasal continuous positive airway pressure preoperatively as well as soon after surgery. Our results following use of morphine in premedication in mild to moderate doses 0.1 mg and 0.15 mg/kg cannot be compared since such studies are not available in the literature.

Not only opioids, all respiratory depressants such as alcohol, sedative drugs are proscribed for all conditions selected to sleep apnoea (87), (88), (89), (90), (8). It is clear in our study that respiratory complications were evident even when patients were awake while waiting for surgery. The incidence of respiratory complications were not statistically significant in study S1 (6%) but clinically significant incidence of respiratory complications (8%) were seen in S2 group of patients as compared to control group where none of the patient had respiratory complication. However, the difference between the S1 and S2 group as regards to respiratory complications was not statistically significant.

The various modalities of treatment have been suggested to prevent obstruction of airway and apnoea during sleep. Nasal continuous positive airway pressure therapy has been most effective form of non surgical treatment in most of the patients (fig-24).Patients compliance to this mode of therapy has been more than 70-80%(91). Other conservative line of management includes weight reduction, sleeping on the side, sleep sock technique where sock containing tennis ball is pinned to the back of sleep garment A gravity sensitive sleep position monitor alarm has been recommended (92) Alcohol selectively reduces motor activity of upper airway muscle dilators via hypoglossal nerve whereas neural motor output to the diaphragm via phrenic nerve remains unchallenged. This causes increased collapsibility during sleep. It is recommended that alcohol before sleep should be avoided.

Iatrogenic fibrosis of soft palate and uvula with sclerosing agent has been tried recently with some success (Discovery channel 06 July 1998). Pharmacothearpy with progesterone (93), almitrine(94) or other drugs like mazindol ,acetazolamine, nicotine, theophylline, protryptilline, L- tryptophane have been tried but with most disappointing results. Intra oral prosthesis (fig-25) may be tried in some of the patients. Many more dental appliances like adjustable soft palate lifter, mandibular repositioner, snore guard, Tepper oral propioceptive stimulator(TOPS) tongue locking device, tongue positioner and excerciser (TPE) tongue retaining device have been tried with some success. Electrical stimulation of genioglossus muscle has been experimented in limited number of animals (95) There are encouraging results with laser

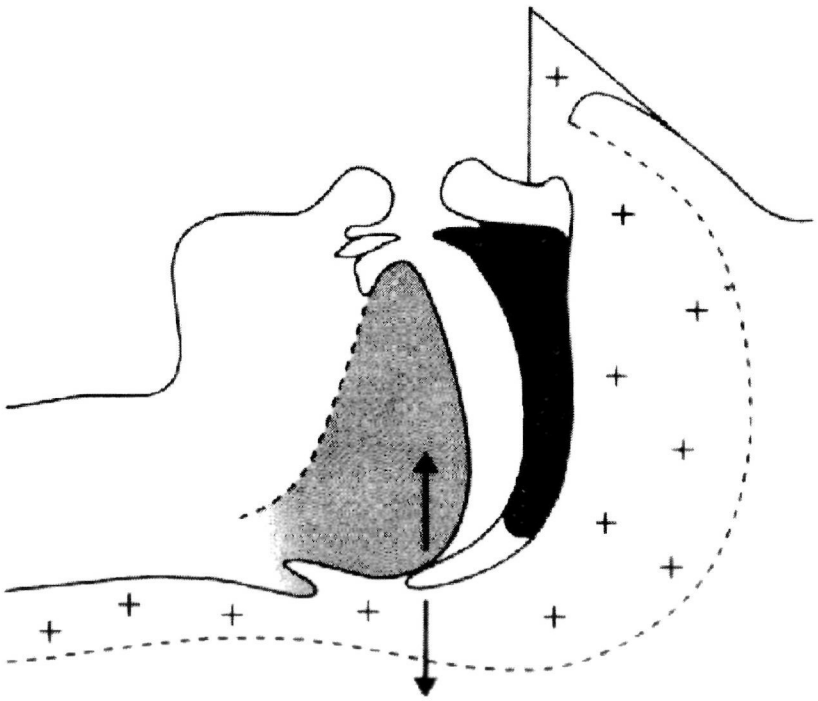

Fig 24: Diagram showing effects of nasal positive airway pressure (CPAP) on the patency of upper airway

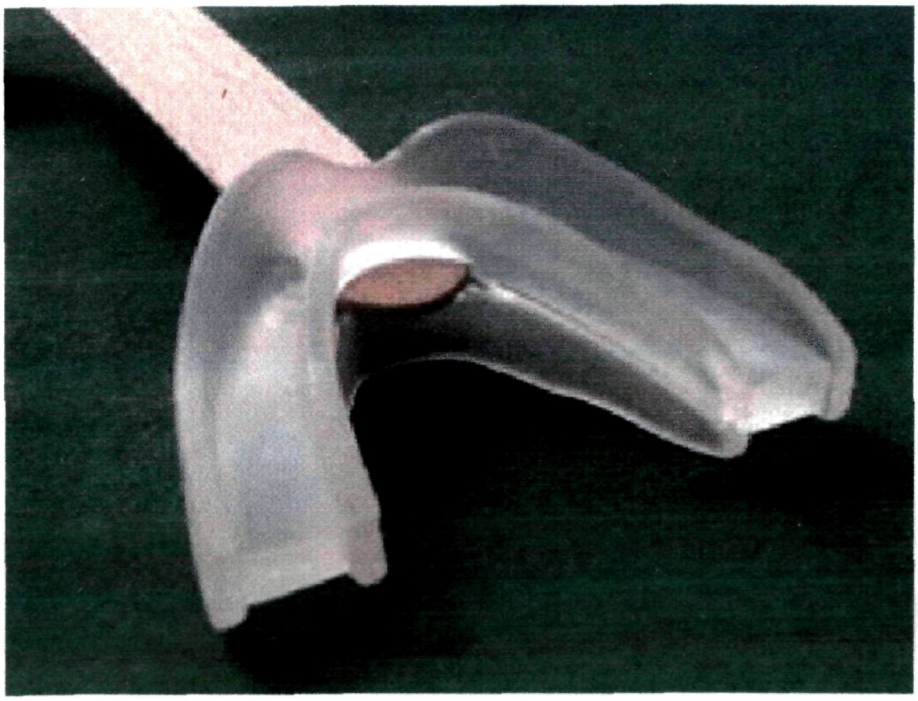

Fig 25: Intra oral device(Dental appliance)

uvulopalatoplasty(96,97) Surgical intervention like uvulo-palato-pharyngo - plasty(UPPP) is reserved only in very severe form of OSA(98) The selection of patients is very important as failure of UPPP to relive the symptoms would also make nasal CPAP ineffective following this kind of major surgery.

We applied nasal CPAP therapy in one of our patient who developed respiratory obstruction. Symptoms were relieved and patient could be taken for surgery. In addition to CPAP therapy, other conservative form of therapy should be considered in patients for elective surgery depending upon the severity of disease. Patients with known or suspected OSA for emergency surgery should not be administered opioids unless absolutely necessary and to be put on prophylactic CPAP pre and postoperatively irrespective of they received opioids or not in premedication.