Abnormal diurnal variation in salt and water excretion in patients with obstructive sleep apnoea

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SUMMARY

1. In healthy individuals, sleep is associated with a fall in urine and sodium output.
2. Seven male patients with obstructive sleep apnoea exhibited a paradoxical rise in both urine and sodium output during the hours of sleep.
3. Continuous positive airway pressure applied via the nose abolished both the apnoea and the nocturnal rise in urine and sodium output, thereby restoring the diurnal pattern towards normal.

Key words: obstructive sleep apnoea, sodium output, urine output.

INTRODUCTION

Urine flow and sodium excretion are subject to a diurnal variation which results in a fall in both during the hours of sleep [1]. This allows uninterrupted sleep, and loss of this diurnal variation, resulting in nocturia, is a feature of cardiac failure and hepatic cirrhosis [2]. In contrast, assumption of the supine posture while awake causes a diuresis and a natriuresis [3, 4]. The mechanisms responsible for the inhibition of sodium and water excretion by sleep have not been fully elucidated.

The syndrome of obstructive sleep apnoea (OSA) is characterized by repetitive upper airway collapse and apnoea throughout the night. Each apnoea leads to arterial hypoxaemia, and arousal is necessary to break the apnoea and enable respiration to restart. Patients are seldom aware that arousals are occurring. Definition of the syndrome is necessarily arbitrary, but it is usually said to be present if the patient has more than five apnoeas per hour of sleep, an apnoea being defined as cessation of airflow for 10 s or more [5]. In its most severe form, when 300 or more apnoeas may occur during the course of a night, the syndrome causes profound sleep disruption, and sufferers usually never achieve stage 3-4 slow wave sleep or consolidated periods of rapid eye movement sleep. The syndrome is thought to have long-term haemodynamic consequences, chief among which is systemic hypertension [5].

We report seven patients with a severe form of the syndrome, but without systemic hypertension. Each exhibited reversal of the normal diurnal variation with an increase in urine and sodium output at night. This was promptly restored by successful abolition of the apnoeas with continuous positive airway pressure (CPAP) via the nose. Although nocturia is not commonly quoted as a symptom of OSA, six patients who had been established on CPAP before the study had all noticed marked reductions in nocturnal urinary production.

PATIENTS AND METHODS

Seven male patients (aged 39-62, mean 54, years) with severe (more than 300 apnoeas per night) OSA documented by full polysomnography were studied over 4 days in hospital. All were overweight (body mass index 26-48, mean 32.3, kg/m²). With the exception of one patient with maturity onset diabetes controlled on glibenclamide, all were otherwise in good health and none had had peripheral oedema at any time. All were normotensive both at the time of the study and before CPAP had been instituted (blood pressure < 150/90 mmHg, mean of at least six readings). Six had been established on nasal CPAP previously. The one remaining was successfully established on treatment in hospital during the course of the study. Each was admitted to hospital in the evening and the bladder emptied before retiring. Thereafter all urine was collected and separated into day and night samples. Thus any urine passed during the night and the first specimen on rising constituted the night samples, and all urine passed during the day, including the last before retiring, the day samples. In order to simulate normal

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circumstances as far as possible, patients were allowed to retire and rise at their own preferred times, samples being timed so that rates of excretion could be calculated. An estimate of normal sodium intake was made for each subject at the beginning of each study and as far as possible this was held constant throughout the 4 days of study by provision of a constant amount of sodium in the diet. Although subjects were allowed a degree of dietary freedom, a dietary assessment was made at the end of each day to estimate sodium and potassium intake and ensure that there had not been any substantial deviation. Each subject recorded his own fluid intake.

During the first 2 nights, patients slept without CPAP, and arterial oxygenation was monitored continuously to confirm obstructive sleep apnoea. For the subsequent 2 nights CPAP was administered, and its efficacy confirmed by oximetry and the patients' own assessment of the quality of sleep. The means of each of the paired values of urine flow and sodium excretion during nights 1 and 2 were compared with the means of the values from days 1 and 2, and nights 3 and 4, using a t-test for paired data.

**RESULTS**

Fluid and sodium intake remained constant throughout the 4 days of study (Table 1). In all cases oximetry confirmed severe OSA during nights 1 and 2. In six cases CPAP was successful on night 3 and in one patient a leak prevented the total abolition of apnoea. In all cases apnoea was completely abolished on night 4, as evidenced by a normal oximetry trace and self-reported excellent sleep quality. Urine production and sodium excretion rates are shown in Fig. 1. Sodium excretion is only available for five subjects. Although there was considerable variation, all subjects exhibited the same pattern. Compared with nights 1 and 2, both sodium and urine output were significantly lower on days 1 and 2 (P<0.05), and nights 3 and 4 (P<0.02). Although both urine and sodium output were less on nights 3 and 4 than on days 3 and 4, the difference did not reach statistical significance.

**DISCUSSION**

Stanbury & Thomson [1] observed as much as a fourfold fall in both urine production and electrolyte excretion during the hours of sleep in normal subjects. In contrast, the patients in this study exhibited a significant rise in nocturnal urine and sodium output when experiencing obstructive sleep apnoea. Although we did not observe such profound falls in relation to daytime levels during the nights on treatment, every patient conformed to the same pattern in that a highly abnormal situation, in which urine production and sodium excretion was high at night, tended to reverse toward normal on the treatment nights. It would be necessary to repeat the study with more rigidly controlled sodium and fluid intake to quantify the changes more accurately.

**Table 1. Fluid and sodium intakes over the 4 days of study**

<table>
<thead>
<tr>
<th></th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluid intake (ml)</td>
<td>1100±21</td>
<td>1293±18</td>
<td>1476±27</td>
<td>1280±38</td>
</tr>
<tr>
<td>Sodium intake (mmol)</td>
<td>117±30</td>
<td>113±31</td>
<td>116±31</td>
<td>102±33</td>
</tr>
</tbody>
</table>

Fig. 1. Urine production (n=7) and sodium excretion (n=5) rates for all patients over 4 continuous days and nights of study. Shaded columns represent nights. Values are means and SEM. CPAP was administered on nights 3 and 4 (N3 and N4, arrowed). Compared with nights 1 and 2 (N1 and N2), values of both urine flow and sodium excretion are significantly lower on day 1 and day 2 (D1 and D2) (P<0.05), and on N3 and N4 (P<0.02). The daytime rates are not significantly different from each other. Values for N3 and N4 are less than those on day 3 and day 4 (D3 and D4), but the difference is not significant.

As well as profound sleep disruption, OSA has two other major pathophysiological characteristics: recurrent (and often severe) arterial hypoxaemia, and the repetitive generation of abnormally large negative intrathoracic pressure during attempted inspiration through an obstructed pharynx [6]. Hypoxaemia is a potent stimulus to chemoreceptor discharge and has been shown to promote sodium and water excretion in the cat [7]. This was
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seen in both intact and denervated kidneys, and appeared not to be mediated through suppression of aldosterone secretion alone [8]. Conversely, stimulation of renal sympathetic nerves causes renin release and inhibits sodium and water excretion [9]. A recent publication [10] has demonstrated high urinary levels of noradrenaline in OSA which returned towards normal after tracheostomy.

The persistent and repetitive generation of large negative intrathoracic pressures during OSA may cause sufficient cardiac distension to stimulate the release of atrial natriuretic peptide. A preliminary experiment in our laboratory suggests that breathing through an inspiratory resistance, generating pleural pressures of up to −40 cmH₂O (similar to values seen in severe obstructive apnoea [6]) causes a small rise in distending pressure across the wall of the superior vena cava and therefore presumably the right atrium.

Further studies are necessary to elucidate the mechanisms responsible for these results. It is of some interest that none of the patients studied had significant arterial hypertension. We do not know what long-term implications OSA and its treatment may have for sodium and water balance, and it remains to be determined whether our patients differ in some way from those in whom hypertension and obstructive sleep apnoea coexist.

REFERENCES