Clinical implications of residual sleep apnoea after chronic CPAP therapy

Several recent studies have documented residual sleep apnoea in continuous positive airway pressure-treated patients, and the term complex sleep apnoea has been used by some to describe this phenomenon. The consequences of residual sleep apnoea are unknown but could be significant, since patients with even mild obstructive sleep apnoea may be at increased risk of cardiovascular complications and motor vehicle crashes. The current study aimed at evaluating the prevalence and clinical implications of residual sleep apnoea.

Materials and methods
Prospective randomised clinical trial in 61 moderate-to-severe obstructive sleep apnoea (OSA) patients who were assigned to standard continuous positive airway pressure (CPAP) titration during polysomnography (PSG) or ambulatory titration using auto-CPAP and home sleep testing at University of British Columbia (Vancouver, Canada). Residual sleep apnoea was defined by an apnoea-hypopnoea index (AHI) of >10 events h⁻¹ on CPAP, after 3 months of CPAP therapy.

Results
30 patients received standard CPAP titration (baseline AHI 37.3 ± 3.6), while 31 underwent ambulatory titration (baseline AHI 43.4 ± 8.1). Residual sleep apnoea was present in seven of 30 PSG patients (23%) and in eight of 31 ambulatory patients (26%), overall in 25% of the study population. Periodic breathing was prevalent among patients with residual sleep apnoea. The most frequently observed residual respiratory events were classified as obstructive hypopnoeas (66% of all events), while central apnoeas accounted for only 10% of events. Age, sex distribution, body mass index, Epworth sleepiness scale (ESS), Sleep Apnea Quality of Life Index (SAQLI) and severity of OSA did not differ at baseline between patients with and without residual sleep apnoea. The combination of an ESS >8 and a machine downloaded AHI >10 had a sensitivity of 45%, a specificity of 97% and a positive-likelihood ratio of 14.5 for the presence of residual sleep apnoea. Outcomes were: ESS (9 ± 6 versus 5 ± 4; p < 0.001), SAQLI (4.6 ± 1.7 versus 5.6 ± 0.8; p < 0.002) and CPAP compliance (4.6 ± 2.2 versus 5.7 ± 1.8; p = 0.04) were worse for patients with residual sleep apnoea compared to those without.

Conclusion
Residual sleep apnoea appears common in patients with moderate-to-severe OSA, despite careful CPAP titration, and is associated with worse outcomes.

Editorial comment
This prospective randomised study in 61 moderate-to-severe OSA patients clearly illustrates the high prevalence of residual sleep apnoea after 3 months of CPAP therapy, independent of pressure or mouth leakage. Equal proportions of residual disease have been reported (17%, predominantly hypopnoeas, AHI >10 [1]; 19%, AHI >15 [2]). A similar phenomenon was described by Gilmartin et al. [3] and termed complex sleep apnoea (CompSAS). Its prevalence reported in some recent papers by different groups was also high (15%, USA [4]; 20%, USA [5]; 13%, Australia [6]). Not all groups have however reported such high prevalence data (6.5%, USA [7]; 5%, Japan [8]; 5.7%, Japan [9]), but can be considered still high when taking into account that the term CompSAS is restricted to persistence or emergence of central apnoeas or hypopnoeas (central apnoea index > 5) on exposure to continuous positive airway pressure in OSA, or at follow up. This also points at a lack of a clear definition to describe persisting events, or may reflect its heterogeneity. There is also some controversy around residual sleep apnoea, especially CompSAS, on whether it actually exists to any great extent and on its clinical relevance [10, 11].

In residual sleep apnoea, Baltzan et al. [1] reported no difference in sleepiness (ESS) between CPAP responders (6.1 ± 3.6) and non responders (7.2 ± 5.4), but more morning headache, nonrestorative sleep, higher CPAP pressures, more mouth leaks and mask leaks and lower compliance) [1]. Surprisingly, residual sleepiness was not associated with an increase in arousals. On the other hand, in the current study more sleepiness (ESS 9 ± 6 versus 5 ± 4), lower compliance and equal pressures were found in residual sleep apnoea. Finally, Pittman et al. [2] found no relationship between sleepiness (ESS 8 [5–12]) and residual AHI. In CompSAS, Pusalavidyasagar et al. [12] found equal therapy compliance and clinical improvement, while Morgenthaler et al. [13] found inferior effects of CPAP in

Message
Residual sleep apnoea presents independent of the chosen CPAP titration procedure, and may have clinical implications. Due to its high prevalence, repeated sleep studies could be recommended.

Competing interests
None declared.

Original article
CompSAS. Kuzniar et al. [14] reported equal compliance after long-term CPAP therapy, but more problems with wearing CPAP, specifically with air hunger, dyspnoea and mask removal, and nearly half maintained a persistently elevated AHI. At the time of the follow-up, there were however no differences in subjective daytime sleepiness as measured by ESS (6 [4-6] versus 6 [5-6.5]; p=0.48). No other studies reported on sleepiness during follow-up. Hence, the question remains open whether it is really a clinical problem, although mean reported ESS values are within the normal range.

Whether residual sleepiness (ESS > 11) is related to residual apnoeas is an open question. Some extrapolations can however be made. Koutsourelakis et al. [15] evaluated adequately treated OSA (baseline ESS > 10, 6 months CPAP compliance >4 h/day) [15]. 55% of their patients showed an abnormal ESS score of >10 (16 ±3) at follow-up, which was related to a history of depression, diabetes, heart disease and a higher ESS score (16 ±3 versus 14 ±3) and lower AHI (44 ±28 versus 59 ±34) on initial assessment. Unfortunately, also patients with mild OSA (AHI >5) were included. Stradling et al. [16] studied 572 patients on CPAP and compared them with a control group of 525 subjects from a community survey. There was no difference in the percentage of patients with an ESS >10 in the CPAP group compared with the controls (16 versus 14%). In the study of Pépin et al. [17] 12% remained sleepy on CPAP, or 6% after exclusion of associated restless-legs syndrome, major depression and narcolepsy. This emphasises that mood disturbance is often involved in residual sleepiness. A link between residual sleepiness and residual apnoeas in selective patients is however not ruled out. Maybe more insight will be obtained when pathophysiology of sleep apnoea identified on CPAP is unravelled.

The contribution of this study is that it did not focus only on central apnoeas, but also took into account other respiratory events as well after chronic CPAP use. This may explain the high prevalence of residual events found in this study, while CompSAS improves over time. The fixed CPAP used in both study groups seems rather high (12 ±2 cmH2O), hence pressure toxicity is not excluded. This idea is supported by the fact that 12 in 15 patients with residual sleep apnoea had periodic breathing on CPAP; three others had predominantly central events, while all four patients with a residual AHI >20 events+h-1 had evidence of periodic breathing on CPAP. However, these pressures were determined according to standard protocols and applied in very obese OSA patients (BMI 37 ±2 kg·m-2), leading to higher pressure needs.

One of the major findings is that despite rigorous CPAP titration and apparent clinical improvement in the group as a whole, residual sleep apnoea on CPAP is common. Moreover, it argues against the hypothesis that residual sleep apnoea is due to inappropriate CPAP titration. For the first time, also the clinical impact has been demonstrated with persistent daytime sleepiness, symptoms of sleep apnoea, and reduced CPAP compliance of nearly 1 h less. The health implications are however unknown, but arguing that residual events should be treated if the patient is not suffering on their account is purely speculative, with no firm evidence to support it. Anyway, prospective trials are warranted, as well as a proactive attitude towards repeated sleep studies.

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References