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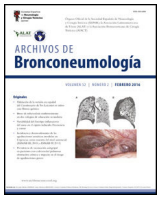

Editorial

What has the ESADA Registry Contributed to the Current OSA Knowledge?

Obstructive sleep apnoea (OSA) affects around 1 billion people worldwide.[1] It is defined by the recurrent collapses in the pharyngeal airways during sleep. Whilst this definition describes the main mechanism, it is important to notice that OSA is a result of complex factors (i.e. environment, gender, obesity, genetic susceptibility, upper airways reactivity to loop gain and arousal) and has heterogeneous consequences (i.e. intermittent hypoxaemia and hypercapnia, daytime sleepiness, comorbidities).

Positive airway pressure (PAP) is the mainstay and the most studied treatment for OSA. Whilst, early observational cohort studies were optimistic that PAP treatment is associated with significant health benefits,[2,3] randomised controlled trials (RCTs), at least in patients with high cardiovascular risk, failed to prove this.[4,5] This is mirrored in the clinical practice, that not all patients experience an improvement in their symptoms and many stop using their devices within a year.[6] The contrasting results between RCTs, observational cohort studies and daily practice highlighted the complexity and heterogeneity of OSA and the unmet need for a personalised treatment approach.

Acknowledging this, the European Sleep Apnoea Database (ESADA), was started as a joint project within the European Union COST action B26 network of nationally appointed sleep apnea experts in 2007. Up to February 2024, there are 41 contributing and 29 actively recruiting centres across Europe and data from in excess of 41,000 patients with over 70,000 visits have been entered so far. Since 2016, the ESADA has been supported from the European Respiratory Society (ERS) through Clinical Research Collaboration (CRC) grants.

The study is unique compared to the Wisconsin Sleep Study and the Sleep Heart Health Study, as it represents a population which attends a sleep laboratory and it also allows analysing the effect of a broad range of socioeconomic, cultural and healthcare-based factors.[7] The ESADA has wide inclusion (all patients referred with symptoms suggestive for OSA, they need to speak, read, and understand the local language and possess the ability to respond to questions and follow instructions) and very narrow exclusion (limited life expectancy due to illness unrelated to sleep apnoea, documented history of alcohol or drug abuse up to 1 year) criteria and uses powerful bioinformatics to overcome limitations due to its study design compared to RCTs.[7]

As of February 2020, 40 original research papers were published as part of the ESADA study. One of the main outcomes is the comprehensive description of the link between OSA and its cardiometabolic and pulmonary comorbidities. A recent review paper summarised these studies[8] and concluded that this association is primarily driven by the chronic intermittent hypoxaemia rather than the number of obstructive events measured by the apnoea hypopnoea index (AHI). This concept is in line with the results in other databases[9] and may form a principle for future study designs (i.e. using overnight hypoxaemia as an inclusion criterion rather than AHI).

In addition, ESADA has helped us to understand which patients would most likely benefit from PAP therapy. Using cluster analysis, Bailly has demonstrated that patients with OSA can be classified to different clinical phenotypes depending on their age, gender, body mass index, Epworth Sleepiness Scale (ESS), AHI and comorbidities. Importantly, this analysis has shown that in most patients, symptoms, disease severity measured by AHI and comorbidities do not strongly correlate.[10] A follow up study by Yassen et al. has concluded that the physiological and symptomatic changes following PAP treatment depend on the clinical phenotype and can be predicted before initiation of PAP.[11] Both studies challenged the concept of treating OSA based on the number of obstructive respiratory events (i.e. AHI). This was supported by the validation study of the Baveno classification (Fig. 1) which uses AHI only as a prerequisite for OSA diagnosis, but treatment recommendation is based on the burden of symptoms and comorbidities.[12] The study showed that whilst AHI is only minimally different, and the adherence to PAP is similar among the four Baveno groups, patients in groups B and D had higher symptomatic benefits, and blood pressure improved only in groups C and D.[12]

Acknowledging the fact that some patients will more likely benefit from PAP than others, clinicians may focus on providing extra support for these individuals. However, the long-term adherence to PAP is suboptimal[4–6] and poorly predictable at baseline as it does not correlate with clinical phenotypes determined either by powerful bioinformatics[11] or consensus.[12] This highlights, that we need different tools to predict which patient will benefit and which patient will use PAP treatment. A potential guide could be the Clinical Global Impression Scale (CGI-S) which reflects on the clinician's assessment of the disease impact on patient's functioning. Assessing 1455 patients, the CGI-S has outperformed AHI or ESS when predicting adherence to CPAP.[13] A frequent reason for stopping PAP early is if a patient does not perceive significant improvement in their sleepiness. Analysing 4853 subjects treated with PAP, Bonsignore et al. concluded that a significant proportion of patients (28%) report of excessive daytime sleepiness despite treatment.

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Reassuringly, with prolonged treatment duration, the prevalence of residual sleepiness has improved.[14] Due to the inverse relationship between duration of the treatment and percentage of patients complaining about existing symptoms, it was suggested to reevaluate alternative reasons for sleepiness after 3 months of treatment. Acknowledging that some patients may experience only minimal benefit from pursuing treatment,[11,12] a clinician may device to either allocate extra resources in treating these individuals, or to consider discharging them. Another potential barrier for suboptimal adherence could be the coexisting presence of insomnia which affected around 50% of patients in ESADA.[15] Indeed, compared to patients complaining about excessive daytime sleepiness, patients with insomnia were less likely using their PAP device.[15] This is concerning, as these individuals more likely suffer from psychiatric and cardiovascular comorbidities,[15] therefore a personalised approach using cognitive behaviour therapy for insomnia may be needed to help overcome difficulties.

In summary, apart from helping us understanding the link between OSA and its comorbidities on a population level, the ESADA has demonstrated that not all patients would equally benefit from PAP treatment, highlighted that some patients may require increased support to achieve clinical outcomes, and introduced a simple way to predict adherence to PAP. More importantly, although further validation is needed, the based on the results of ESADA we could also identify those patients would not require PAP treatment for their OSA. The ESADA is an ongoing collaboration that has served platform for dynamic interactions, facilitated collaborations between sites, contributes to guidelines and continuously provides data for further funding applications for clinical trials. Further results originating from this cohort could help us choosing the optimal PAP modality and non-PAP therapy allowing personalised treatment for patients with OSA.

Conflict of Interests

The authors state that they have no conflict of interests.

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