Drug-induced sleep endoscopy (DISE) as a guide towards upper airway behavior and treatment outcome : the quest for a vigorous standardization of DISE

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Editorial OV SLBR

DISE phenotyping as a guide towards upper airway behavior and treatment outcome in patients with SDB: The quest for a vigorous standardization of the implementation of DISE

Since its first description in 1991 (1), drug-induced sleep endoscopy or DISE has been progressively advocated as a useful pre-assessment before choosing the most suitable treatment option for the individual patients with sleep-disordered breathing seeking a non-positive airway pressure (PAP) therapy (2). With the increased use of DISE in both clinical practice and research projects, the need for standardization of the technique in terms of technical equipment and staffing, patient positioning and diagnostic maneuvers during DISE, drugs usage, observation window, target events, scoring and classification systems for DISE got collectively recognized (3). These considerations resulted in publication of the 'European position paper on DISE' in 2014 (4), with an update that was recently published (5).

This issue of the journal *'Sleep and Breathing'* contains up to seven manuscripts that all address different issues regarding DISE and its standardization in one of these perspectives.

Vonk *et al.* provide an assessment of DISE as selection tool for oral appliance therapy (OAT) and positional therapy in obstructive sleep apnea (OSA) by evaluating the effect of different passive maneuvers such as manually performed jaw thrust and lateral head rotation on upper airway (UA) patency during DISE in two-hundred OSA patients (6). The analysis of the results revealed that overall the effect of jaw thrust on UA patency during DISE was more pronounced and that the effect size of the lateral head rotation maneuver alone was smaller. In another paper of the same group, Beelen et al. (7) were able to further evaluate the influence of these two maneuvers during DISE. In this same cohort it was shown that the combination of both maneuvers resulted in the most pronounced increase in UA re-opening at all collapsible levels within the UA. On the other hand, the authors noted that jaw trust led to a significant decrease in collapsibility at all collapsible levels whereas with lateral head rotation only an increase in obstruction was observed at the oropharyngeal level while the other levels of UA collapse showed significant improvement in terms of UA opening with lateral head rotation (7).

Nowadays, midazolam and propofol are the most widely used for DISE, either to be used as a single agent or in combination (4). Alternatively, a combination of these medicines with other drugs such as remifentanil or ketamine has been described (5). In this issue of the journal, Kim et al. report on a placebo-controlled comparison of the effect of remifentanil on propofol concentrations during DISE (8). Interestingly, the results of this study suggest that the additional use of remifentanil, a short-acting synthetic opioid analgesic drug, together with propofol significantly reduces the target concentration of propofol with about 0.5 µg/ml

on average without respiratory depression. Moreover, the authors state that the time needed for sufficient sedation to be reached was significantly shorter, a mean difference of about three minutes, in the remifentanil-propofol group as compared to patients receiving propofol alone (8). The findings of this trial are relevant and the future research agenda should include further comparison of this regime with other combinations of drugs for DISE with a simultaneous attempt for further standardization of the drug regimen to be used (5).

The main indication to schedule a patient for DISE in clinical routine practice is when a decision needs to be made towards PAP alternatives, such as upper airway surgery, including palatal surgery, tongue base surgery and hypoglossal nerve stimulation, oral appliance therapy (OAT) or positional therapy (PT) or a combined approach including different treatment modalities (2, 4, 5, 9-11). Evidence in literature indeed suggests that the pre-operative findings during DISE relate to the final surgical outcome and that awake assessment of the upper airway does not accurately correlate with the exploration of the UA in SDB patients during DISE (12-14). In this issue of *'Sleep and Breathing'*, additional evidence on the added value of DISE towards UA surgery for adult OSA patients is provided in the paper by Wang *et al.* (15). In their retrospective study including eight-five patients with moderate to severe OSA that underwent tonsillectomy and/or uvulopalatopharyngoplasty (UPPP) the non-responders were more likely to be diagnosed with a complete circular collapse at the level of the palate (CCCp) and/or a complete tongue base collapse during DISE. The responders, on the other hand, were more likely to have a partially anteroposterior palatal collapse as documented during their pre-operative DISE. These results, again, provide evidence that DISE has the clear potential to guide surgical treatment decision making in SDB patients (15).

The specific DISE-phenotype of the occurrence of complete concentric or circular collapse at the velopharynx or palate, referred to as CCCp, has been defined as an exclusion criterium for upper airway stimulation (UAS) therapy, using electrical neurostimulation of the hypoglossal nerve synchronized with ventilation (11, 16, 17). In their paper, Hasselbacher *et al.* (18) were able to explore whether UPPP with tonsillectomy (UPPP-TE) would be able to remove the CCCp DISE-phenotype in fifteen OSA patients with CPAP intolerance in order for these patients to fulfill the inclusion criteria for UAS after UPPP-TE. Before the treatment with UPPP-TE all patients presented with the CCCp phenotype during pre-operative DISE, while after UPPP-TE only one patient still exhibited CCCp during DISE. As a result, a large majority of

these CPAP intolerant OSA patients would fulfill the criteria to be included in the UAS clinical program after UPPP-TE (18).

Kastoer *et al.* report on a comparison of patients' characteristics in terms of UA collapse patterns in a large series of patients with and without OSA undergoing DISE with a special focus on positional OSA or POSA (19). The presence of collapse at the level of the palate and/or the level of the oropharynx was found to increase the likelihood of OSA, while CCCp was found significantly more in non-POSA patients. In addition, while no differences were described in terms of OAT outcome using mandibular advancement device (MAD) treatment, a lower efficacy of UA surgery was observed in POSA patients as compared to non-POSA. The latter finding again confirms the potential of residual POSA after UA surgery and the conceivable benefit of positional therapy in these patients afterwards (20).

Finally, an interesting paper by Lan *et al.* reports on the evaluation of DISE for the prediction of CPAP titration in OSA patients (21). Interestingly, patients with CCCp or a lateral oropharyngeal collapse during DISE were subject to significant higher CPAP pressure after CPAP titration during polysomnography. The authors state that DISE findings could provide better understanding of the need of higher CPAP pressure setting in subgroups of OSA patients. At the same time, DISE can be a tool to identify the indications for OAT or surgery in order to lower CPAP titration levels and, thereby, improve adherence and compliance with CPAP (21). Again, these findings illustrate the need for a prospective upfront decision making in the individual patient without excluding potential combination therapies for SDB in order to improve the true clinical effectiveness of the treatment (22).

More importantly, treatment for OSA may become more effective, being tailored to each patient's need.

All together the collection of papers on DISE in this issue of the journal illustrate the actual interest in the further standardization and exploration of this evolving technique in terms of predicting non-PAP treatment outcome in patients with SDB. The results are highly promising towards a more personalized approach being aware of the fact that the personalized medicine approach is highly relevant for this patient group, given the complex pathophysiology, the variable clinical presentation, the relevant comorbidity, and the potential contribution of undiagnosed or untreated SDB to poor outcomes (23). In the future era of theragnostics DISE will potentially play a key role in the clinical evaluation of patients

with snoring and OSA. From the editorial board of *'Sleep and Breathing'* we do hope that the readership of the journal enjoys reading this collection of recent papers on DISE.

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