

Drug-Induced Sleep Endoscopy with Target-Controlled Infusion Using Propofol in the Management of Patients with Obstructive Sleep Apnea

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Although it seems to be an exhausted subject at first glance, the therapeutic approach in obstructive sleep apnea syndrome (O.S.A.S.) is still an open subject. The continuous positive airway pressure (C.P.A.P.) represents the gold standard of therapy in O.S.A.S. However, this therapeutic process with C.P.A.P. has a low rate of compliancy, over 50% of patients quit in the first year of use. Implicitly, surgical solutions or mandibular advancement devices remain an alternative for many of these patients. High costs, complexity and risks associated with surgery have led to the identification of more accurate methods for topographic and functional diagnosis in O.S.A.S. Drug-induced sleep endoscopy (D.I.S.E.) with target-controlled infusion (T.C.I.) using propofol in the management of patients with obstructive sleep apnea is a relatively recently introduced method in Romania. The present paper describes our experience with D.I.S.E. for selected patients, who have undergone surgery on the upper airway for O.S.A.S. The D.I.S.E. method has led to the modification of the initial surgical plan in over 60% of patients with multi-level obstruction. Under these conditions, the surgical success rate in patients of the study increased to 80% at 6 months. Considering the specific endowment of each tertiary sleep center, the presence or absence of an operator block and the anesthetist's experience with target-controlled (T.C.I.) infusion using propofol, more extensive and multicenter studies are needed for standardization of D.I.S.E.

Keywords: drug-induced sleep endoscopy, sleep disorders, propofol

The term *apnea* has its origin in Greek, meaning the lack of respiration. An apnea episode is considered to be a lack of air passage through the upper airways (U.A.) for at least 10 seconds. Sleep apnea is characterized by periods of heavy (difficulty) breathing, a progressive snoring (in intensity) followed by silence and then a *deep sigh*.

These breathing pauses have duration between 30-100 seconds, during which time there are compensatory contractions in the thoracic or abdominal muscles. Sleep apnea syndrome is defined as a succession of at least 30 apnea episodes during the usual 7 hours of sleep or more than 5 sleep apnea episodes by hour.

There are two phases of sleep, each one with its own neuro-electrophysiological characteristics. A normal sleep is actually a cyclic progressive passage (90-120 min) from sleep without rapid eye movement (non-REM) to rapid eye movement sleep (REM). Breathing is also different in the waking state compared to sleeping, and the switching to vigilance is by itself a strong respiratory stimulus. In non-REM sleep, the activity of the activation system is extremely strong, asphyxia causes a rapid return to waking state. In contrast, in REM sleep, the activity of the activation system is lower, its mechanisms being largely inhibited; implicitly, a much lower level of peripheral saturation in oxygen is needed to produce a wake-up stimulus. Thus, REM sleep reduces the ability to respond to upper airway obstruction, thus allowing for irregular breathing and sometimes apnea episodes.

Decreasing of the efferent stimuli from the respiratory centers to the upper airway muscles responsible for the open oropharynx / larynx during inspiration, even if it occurs during sleep, is followed by increased resistance at the upper airway level. Relative hypotonia of the soft palate, genioglossus muscle, and posterior pharyngeal muscles can cause passive collapse of the upper airway. Saturation decreases in oxygen and the respiratory center responds by increasing inspiratory effort. When that mechanism is effective, the upper airway is released and the apneic episode ends with a *deep sigh*.

Initially, patients are advised to weaken (if necessary), avoid alcohol and sedatives, and the position of decubitus supine during sleep. The reduced use of coffee and tea (central nervous stimulants) as well as the recommendation that the patient's life partner to go to bed first may be other useful measures.

When it's necessary, the continuous positive airway pressure (C.P.A.P.) is the best way. It is a conservative intervention, used by many specialists. It consists of a mask connected to a pumping system that sends a positive pressure to upper airway (U.A.), practically acting as a pneumatic *prosthesis* that prevents U.A. collapse.

Sometimes it is embarrassing, too expensive or poorly tolerated. Long-term therapeutic compliance is around 58-69%. The theoretical disadvantages of using C.P.A.P. would be the possibility of inducing cardiac or renal decompensation. Other complications, such as pneumothorax, are described.

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Another therapeutic option is to use an oral device. The aim is to move the mandible forward. Made of a plastic, it fastens on teeth similarly to the prostheses used in sports.

In some patients, none of the mentioned therapeutic options is appropriate. For them, surgical option is the best and sometimes the only choice. The patients in question have an obstruction at the U.A. level. By default, surgery will take into account the location of the obstruction, seeking to eliminate it.

Drug-induced sleep endoscopy (D.I.S.E.) with target-controlled infusion (T.C.I.) using propofol (chemical formula: $C_{12}H_{18}O$, fig. 1) is a method used in the topographic diagnosis of dynamic obstruction of the upper airway, in patients with obstructive sleep apnea syndrome.

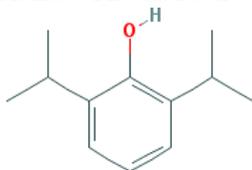


Fig. 1. Propofol
(2,6 Diisopropylphenol) - structural formula

The therapeutic approach for O.S.A.S. is steadily moving from a C.P.A.P. *one-size-fits-all* approach to an individualized treatment of upper airway obstruction during sleep.

In all cases with low C.P.A.P. compliance the sleep surgery or intraoral devices can be the appropriate solution.

In another train of thoughts the existence of different definitions (of successful therapy in sleep surgery) was found in literature. In consequence the comparison of the efficacy in terms of treatment modalities is very confused. Sher's surgical success criteria seem to be the most appropriate in our judgment - a reduction of the apnea hypopnea index (A.H.I.) by 50% and ≤ 20 (in comparison with initial value) in postoperative period.

Experimental part

Besides polysomnography, the complete diagnostic work - up for patients with sleep apnea covered: case history, biometrics, physical examination, lateral telerradiography, Epworth sleepiness scale (ESS), Berlin Questionnaire, STOP BANG Questionnaire, awake and sleep endoscopy.

We used the following inclusion criteria for D.I.S.E.:

- patients with moderate or severe O.S.A.S. without morbid obesity, who cannot tolerate continuous positive airway pressure (C.P.A.P.) as the diagnostic test before appropriate surgical indication or mandibular advancement devices (M.A.D.),

- patients with mild O.S.A.S. or simple snoring with MAD or in which surgical treatment is indicated,

- patients with O.S.A.S. that have not responded to surgical treatment.

We started from the main hypothesis that the D.I.S.E. is a diagnostic tool absolutely necessary for increasing the surgical success rate in patients with O.S.A.S., because it can identify multi-level obstructions and implicitly allows the establishment of an appropriate surgical plan.

The following were used as exclusion criteria for D.I.S.E.:

- the presence of any kind of allergy to the components of propofol (especially soy or eggs),

- the high surgical risk of patient (American Society of Anesthesiologist risk score >3).

Depending on the experience and preferences of the anesthetic-surgical team, D.I.S.E. can be achieved with Midazolam or Propofol (2.5 mg), separately or in combinations.

Our team prefers propofol (target-controlled infusion using propofol and Bispectral index of monitoring sedation depth - BIS) for the following reasons:

- depress reversible and easily controllable the respiratory center,

- pharmacological half-life is from 4 to 6 min,

- plasma clearance is about 55 min,

- suppresses the hypopharyngeal reflexes.

Monitoring the depth of anesthesia was done with the help of bispectral index (BIS) device, which is a system similar to an EEG device. The levels of BIS at which consciousness is lost vary from one individual to another, but from our experience it is located between 50 - 70.



Fig.2. Drug-induced sleep endoscopy (D.I.S.E.) - Somnoscropy



Although it is not necessary to carry out the somnoscropy in the operating theatre, the place chosen has to be equipped with resuscitation devices and with a complete monitoring unit. It should be remembered that these patients, some of them cases of severe O.S.A.S., have a significant potential risk and an airway of difficult intubation. We always choose the operating theatre.

A total of 28 patients were enrolled in the study, in rigorous order of presentation at the somnology department, from June 2013 to June 2015.

The aim of this study was to evaluate the correlation between the location of soft tissue with vibrations (flutter) in the upper airway and the type of obstruction, in patients with sleep apnea syndrome. For each patient the exploration had an average duration of 20 min and was performed prior to planned and consensual surgery.

For most authors, successful treatment of sleep surgery has defined arbitrarily. In the present study, we decided to use the Sher's surgical success criteria.

This protocol was approved by the Ethics Committee at the National Institute of Aeronautical and Spatial Medicine.

Regarding statistical analysis, the majority of data are presented in numeric and percent form. Due to the low number of patients in the study, the statistical tests are meaningless.

Results and discussions

All 28 patients (20 male and 8 women) were initially treated with C.P.A.P. as primary and exclusively treatment by other doctors, in different clinics. All patients met the exclusion / inclusion criteria and agreed to participate at the study.

The mean age was 47.23 years. Must be mentioned the higher incidence in the evaluated group (even without

Group	Vibrations / Flutter %	Obstruction / Collapse %
Uvula / velum or muscular palate	72	16
Pharyngeal lateral walls	32	65
Tongue base	4	60
Epiglottis	3	10

Table 1
THE RESULTS OF D.I.S.E. IN THE STUDY GROUP

statistical significance due to the small number of patients) of clinical cases with indications for D.I.S.E. in men (20 patients).

First of all, it is worth noting the high incidence of soft tissue with vibration / flutter at the level of uvula / velum or muscular palate (72% of patients). The total obstruction at this level is much smaller (16% of patients).

D.I.S.E. has been able to identify areas of collapse in the pharyngeal lateral walls (65% of patients) and at the level of the tongue base (60% of patients).

As an immediate consequence for all patients which were planned to be operated of uvulopalatopharyngoplasty (U.P.P.P) as first line of surgical therapy for O.S.A.S. it was decided to awaken the patient and to re-prioritize the operator plan. It became obvious that without an adequate assessment of obstruction site(s) and regardless of predictive factors such as obesity the surgical result for isolated U.P.P.P is often unsuccessful in treating O.S.A.S.. By reformulating the operative plan, the surgical success rate in the patients included in the present study increased to 80% (22 patients) at 6 months, according to Sher's surgical success criteria.

Although the type of obstruction is not always identical, the information obtained by endoscopy with the patient in the waking state is similar to D.I.S.E. only at the oropharynx level.

Somnoscopia appears to be necessary to identify the dynamic obstacles located at the level of the tongue base and the hypopharynx.

There are also a number of criticisms about it D.I.S.E. First of all, there were doubts about the equivalence between natural sleep and drug induced sleep. Rabelo concluded that there are no significant differences between natural sleep and drug induced sleep, in terms of the respiration parameters and upper airway obstruction areas. The patient under D.I.S.E is in most of the time in sleep phase N2 [1].

Kellner appreciated that D.I.S.E is a test with good reliability (because there is a good intra and inter-observer concordance) and that the tongue base is the most difficult to evaluate. The reliability of the sample is also supported by the monitoring of the anesthetic depth, the collapse of the upper airway being directly proportional to the depth of anesthesia [2].

Steinhart has demonstrated that a multi-level collapse identified by D.I.S.E is directly proportional to the severity of the O.S.A.S. The best indicator of O.S.A.S. severity was the transverse or circular collapse of the pharynx walls [3].

Gillespie compared the indication of surgical treatment after endoscopy in the awake state with that obtained in D.I.S.E. in 38 patients with sleep disorders. The author has shown that the D.I.S.E. changes the surgical plan in 62% of patients, both to increase and decrease the treatment at the tongue base and soft palate. The epiglottis is the most responsible for the surgical change, being responsible for 61% of the changes [4].

Golbin et al. also shows some interesting results on this topic. They compared the surgical results between a first group of 40 patients who had been diagnosed by normal endoscopy and a second group of 64 patients who were diagnosed by D.I.S.E. The author concluded that D.I.S.E. does not improve the surgical success rate of surgery, but when more surgery is indicated, the rate of complications also increase [5].

Vanderveken et al, have evaluated the D.I.S.E. findings in 21 patients undergoing to hypoglossal stimulation and find that patients with complete circular collapse of the palate are failures in 100% of cases. Therefore, D.I.S.E. was considered as a selection criterion for this surgery [6].

Zhang et al, assess the successes and failures in case of 43 patients who undergo oropharyngeal surgery according to the length and height of the collapse of the soft palate seen in the D.I.S.E.. The presence of a longer collapse with a higher start have been identified as factors of failure in oropharyngeal surgery [7].

On the other hand, Soares et al, found that the patients with complete hypopharyngeal collapse due to pharyngeal lateral walls and patients with complete supraglottic collapse do not respond well to multilevel surgery [8].

Koutsourelakis et al found greater surgical failure in patients with complete circular collapse of the soft palate and those who had a complete antero-posterior collapse on the basis of tongue [9].

Conclusions

In our study the D.I.S.E. has changed the surgical indication in over 60% of patients. This modification was based mainly on the findings regarding the tongue base and epiglottis. In the case of a unique obstacle at the level of the tongue base the U.P.P.P results were very poor. Patients with significant collapse due to pharyngeal side walls also have had poorer surgical results. Probably the most important finding has been the fact that the patients with complete circular collapse in the area of the tongue base do not respond well to multilevel surgery of the upper airway and therefore should be candidates for another alternative treatment. Under the mentioned conditions, the surgical success rate in the patients included in the present study increased to 80% at 6 months. Considering the specific endowment of each tertiary sleep center, the presence or absence of an operator block and the anesthetist's experience with target-controlled infusion (T.C.I) using propofol, more extensive and multicenter studies are needed for standardization of D.I.S.E.

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