

## Sodium Oxybate and Sleep Apnea

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The gamma-hydroxybutyric acid (GHB) is a short chain fatty acid, an endogenous metabolite of gamma-aminobutyric acid. Sodium Oxybate (SO) is the sodium salt of the GHB, approved by the FDA (Food and Drug Administration) for the treatment of narcolepsy with cataplexy in patients over 16 years of age [1].

Its prescription in narcoleptic patients with breathing disorders is controversial.

GHB was used in the 70s and 80s as a general anesthetic, either in the induction or in the anesthesia maintenance, being the anesthetic of choice in the event of respiratory insufficiency [2,3].

Also it was used in ICUs for years, to provide suitable sedation in those patients under controlled ventilation or fighting against the respirator, who were to be converted to spontaneous breathing [4].

The action of SO at CNS level in sedation or sleep is depending of pharmacokinetics: the SO has a short half-life (30-60 min) and is metabolized in the tricarboxylic acid cycle (Kreb's cycle) to H<sub>2</sub>O and CO<sub>2</sub>. During sedation and NREM sleep, breathing is regulated almost exclusively by the metabolic control system. CO<sub>2</sub> plays a prominent role in this metabolic control and in the maintenance of breathing rhythm during sleep [5].

In central sleep apnea syndrome, the metabolization of SO and its subsequent production of CO<sub>2</sub> stimulates breathing and increases the "central apnea threshold" i.e. the CO<sub>2</sub> level below which the apnea occurs. There are published report of cases in which central sleep apnea has been treated with SO [6]; however, there have been isolated cases that central apneas were triggered by lower doses of SO [7]. It seem reasonable that the increase in CO<sub>2</sub> production due to metabolization of the high doses of SO triggers an increase in breathing during sleep, with a decrease in CO<sub>2</sub> levels, an inhibition of respiratory effort and the onset of central apnea.

In dual diagnosis of obstructive sleep apnea and narcolepsy data are scarce and/or contradictory, and SO should be used with caution as the literature contains conflicting results [8].

The matter is complicated as we know that the apnea-hypopnea index (AHI) during sleep is elevated in many patients who suffer from narcolepsy. Some 31% of patients show as AHI >5 [9] and some 24.8% show an AHI >10 [10]. It's possible that exists a dysfunction in brain areas where respiratory and sleep-waking systems are interrelated (nucleus tractus solitaries and ponto-medullary reticular formation [11].

On the other hand, there is a high prevalence of obesity (25%) and

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overweight (29.2) in patients with type 1 narcolepsy in childhood and adolescence, which favors the development of SAHS, and the SO treatment be associated with a significant BMI reduction [12].

There are a number of recommendations that should be observed in cases of overlap between SAHS and narcolepsy, to assess how and when to start treatment with OS.

As a general rule: OS doses, administration time and possible adverse effects should be monitored at baseline and avoid concomitant intake of alcohol and sedatives, particularly benzodiazepines.

If the SAHS is moderate or severe, it is a priority to ensure compliance with CPAP, avoiding OS treatment if the device is not used. We also recommend PSG study with CPAP, titration of pressure, and observe the presence of central apneas and/or arterial oxygen desaturations. The next day develop MSLT (multiple sleep latency tests).

After starting treatment with OS, monitor the presence of oxygen desaturations by home nocturnal pulse oximetry, cardio-respiratory polygraphy or, preferably, PSG.

Special attention should be paid to the follow-up of obese patients with neuromuscular disorders or secondary narcolepsy.

If SAHS is mild, clinical follow-up after initiation of treatment.

## References

- 1 Thorpy M (2007) Therapeutic advances in narcolepsy. *Sleep Med* 8: 427-440.
- 2 Zverev VV (1985) Clinico-physiological substantiation of using various methods of anesthesia in operations on the lungs in patients with chronic respiratory insufficiency. *Vestn Khir Im Grek* 134: 118-121.
- 3 Hasenbos MA, Gielen MJ (1985) Anaesthesia for bullectomy: A technique with spontaneous ventilation and extradural blockade. *Anaesthesia* 40: 977-980.
- 4 Entholzner E, Mlieke L, Pichlmeier R, Weber F, Schneck H (1995) EEG changes during sedation with gamma-hydroxybutyric acid. *Anaesthesist* 44: 345-350.
- 5 White DP (2005) Pathogenesis of obstructive and central sleep apnea. *Respir Crit Care Med* 172: 1363-1370.
- 6 Kovacevic-Ristanovic R (2010) Use of sodium oxybate (Xyrem®) in patients with dual diagnosis of narcolepsy and sleep apnea. *Sleep Med* 5: 6.
- 7 Frase L, Schupp J, Sorichter S, Randelschofer W, Riemann D, et al. (2013) Sodium oxybate-induced central sleep apneas. *Sleep Med* 14: 922-924.
- 8 Jullian-Desayes I, Revol B, Chareyre E, Camus P, Villier C, et al. (2017) Impact of concomitant medications on obstructive sleep apnoea. *Br J Clin Pharmacol* 83: 688-708.
- 9 Pizza F, Tartarotti S, Poryazova R, Baumann CR, Basetti CL (2013) Sleep-disordered breathing and periodic limb movements in narcolepsy with cataplexy: A systematic analysis of 35 consecutive patients. *Eur Neurol* 70: 22-26.
- 10 Sansa G, Iranzo A, Santamaría J (2010) Obstructive sleep apnea in narcolepsy. *Sleep Med* 11: 93-95.
- 11 Chokroverty S (1986) Sleep apnea in narcolepsy. *Sleep* 9: 250-253.
- 12 Ponziani V, Gennari M, Pizza F, Balsamo A, Bernardi F, et al. (2016) Growing Up with Type 1 Narcolepsy: Its Anthropometric and Endocrine Features. *J Clin Sleep Med* 12: 1649-1657.