The gamma-hydroxybutyric acid (GHB) is a short chain fatty acid, an endogenous metabolite of gamma-aminobutric 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 H2O and CO2. During sedation and NREM sleep, breathing is regulated almost exclusively by the metabolic control system. CO2 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 CO2 stimulates breathing and increases the “central apnea threshold” i.e. the CO2 level below which the apnea occurs. There are published reports 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 CO2 production due to metabolization of the high doses of SO triggers an increase in breathing during sleep, with a decrease in CO2 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 pontomedullary reticular formation [11].

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