



## Letter to the Editor

## Oral L-carnitine as treatment for narcolepsy without cataplexy during pregnancy: A case report



### 1. Introduction

Narcoleptic symptoms persist during pregnancy; however, the mutual influences between pregnancy and narcolepsy are poorly evaluated. Several drugs for narcolepsy are designated Class C in pregnancy, and there are few data regarding their effects on the developing fetus or neonates [1]. Prematurity, low birth weight and withdrawal symptoms have been reported in infants born to women taking amphetamines for recreational purposes or addiction disorder, but lacking data in narcolepsy. Recently a retrospective study of narcoleptic pregnancies reported only few cases of narcolepsy with cataplexy (NC) or without cataplexy (NwC) under stable treatment for the entire duration of pregnancies [2].

Recently, low serum acylcarnitine levels were associated with narcolepsy, demonstrating a dysfunctional fatty acid beta-oxidation pathway present in the disease [3]. Therefore, a randomized placebo-controlled trial in narcolepsy patients showed the efficacy of oral L-carnitine in reducing somnolence in narcolepsy patients [4]. **In addition gestation is a physiological state that leads to lower plasma carnitine concentrations and its supplementation is safe during pregnancy [5].**

**We present a single case of a narcoleptic pregnant patient successfully treated with oral L-carnitine throughout the entire pregnancy.**

### 2. Report of case

We report the case of a 32-year old woman affected by NwC (HLA DQB1\*0602 negative). She was diagnosed at age 25 years, according to the ICSD-2 (mean sleep latency 3.2 min; Sleep Onset REM Periods, SOREMPs 3). She presented at the time of diagnosis severe daytime somnolence, episodes of sleep paralysis and hypnagogic hallucinations. She was successfully treated with modafinil titrated up to 400 mg/daily showing a mild residual daytime somnolence (Epworth Sleepiness Scale, ESS score 11). The patient manifested the need to be pregnant for the first time thus modafinil was slowly withdrawn. After conception we performed a multiple sleep latency test (MSLT) (11-week pregnancy) because the patient complained of a severe daytime sleepiness combined with an increase night-time sleep. Nocturnal cardiorespiratory monitoring excluded the presence of sleep apnea and/or snoring, although periodic limb movements were not evaluated by means of polysomnography. MSLT showed a mean sleep latency of 4.2 min and three SOREMPs, while ESS was 19. Therefore after a clear explanation regarding the unknown teratogenic risk by anti-narcoleptic drugs, she refused drug treatment. Notwithstanding we proposed oral L-carnitine as a safe compound in pregnancy, probably effective for narcolepsy. An informed consent was obtained. Oral L-carnitine therapy was titrated up to 500 mg b.i.d. Patient well tolerated the therapy and referred a progressive improvement of daytime somnolence and showed a regular night-time sleep schedule. The patient referred a subjective reduction

of diurnal time for dozing off and of the number of diurnal naps. At the end of the second trimester (24-week pregnancy) MSLT showed a normal mean sleep latency (16 min.) lacking SOREMPs, and ESS was 14. Fetal echographies, echocardiography and cardiocotography were unremarkable until delivery. At 32-week pregnancy ESS score was 11. The patient did not report restless legs symptoms during the entire gestation. At 39-week pregnancy the patient delivered without childbirth complications. The treatment was still effective at a 6-month follow-up (ESS 12) without clinical impairment of sleepiness.

### 3. Discussion

Sleep quality in healthy women may be impaired during both the first and the second trimester due to high levels of progesterone in women. During the third trimester, sleep disturbance and sleepiness usually increase due to sleep disorders (i.e. restless legs, sleep-related breathing disorders) and/or leg cramps and fetal activity [6]. The nocturnal sleep and daytime sleepiness symptoms in narcolepsy women have not been characterized during pregnancy but they appear to follow the pattern seen in healthy women with higher variability [1]. The management of narcolepsy during pregnancy is still debated [1,2]. We described a significant improvement of sleepiness in our pregnant narcoleptic patient after the L-carnitine intake. Our report suggests considering oral L-carnitine to treat daytime sleepiness in narcoleptic pregnant patients. It is difficult for a clinician to make an appropriate assessment of the benefit–risk ratio of narcolepsy medications during pregnancy [1,2]. It is ideally recommended that the narcolepsy treatment should be discontinued during the time of conception, pregnancy and lactation [2]. However, the decision to use or not to use medications should be made on an individual basis. There are scarce data about the use of medication during pregnancy from the European Narcolepsy Network [2]. This study recorded only few cases of treated patients during the entire pregnancy (5 NC and 2 NwC) lacking significant differences in complication rates with the more represented untreated group [1].

It was demonstrated that serum acylcarnitine levels are reduced in narcolepsy related to total carnitine insufficiency, reduced both carnitine palmitoyltransferase 1B and choline kinase beta activity, and decreased availability of the substrate (acyl-CoA) [3]. Moreover, very recently we found lowered CSF beta-amyloid levels in narcolepsy that may be probably linked to the impairment of the alpha-secretase activity due to low acylcarnitine levels [7]. Hence dietary or supplemental L-carnitine intake could be useful to normalize the acylcarnitine levels, probably reducing narcoleptic symptoms. A randomized placebo-controlled trial suggests that oral L-carnitine can be effective and well-tolerated in reducing sleepiness in narcoleptic patients [4].

It is well known that women are getting more sleepy and tired when pregnant [8], but some studies showed a possible relationship between sleep apnea and/or snoring and sleepiness during pregnancy [9]. Acylcarnitine serum levels were reduced during pregnancy and L-carnitine integration in pregnant women may be safe and advantageous

[5]. In addition, low L-carnitine levels were recently associated with obesity at term pregnancy, representing a significant risk factor for sleep apnea and sleepiness [10]. Perhaps, an inadequate iron status may impair carnitine synthesis, which in turn provides an explanation for the low plasma carnitine concentrations observed in pregnant women [5]. Although narcolepsy is a rather rare disorder, daytime sleepiness is not. It is possible that low levels of carnitine could be a cause of fatigue and daytime sleepiness. For example, low serum carnitine levels have been observed in patients with chronic fatigue syndrome — a clinically defined condition characterized by severe disabling fatigue and a combination of symptoms, such as musculoskeletal pain, difficulty in concentration and sleep disturbances [11].

In conclusion, we are aware that a single case does not allow generalization, however narcolepsy treatment during pregnancy is still puzzling. Our case suggests that L-carnitine may improve excessive daytime sleepiness in pregnancy, although the mechanisms underlying its benefit should be clarified.

Further randomized controlled studies with large sample of narcoleptic pregnant patients could demonstrate efficacy, tolerability and safety of L-carnitine also related to acyl-carnitine serum levels and confirm that pregnancy should not be discouraged in narcoleptics.

### Conflict of interest

No conflicts of interest declared.

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