

LETTERS TO THE EDITOR

The relationship between insomnia and endometriosis

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Endometriosis, a progressive disease with features of chronic inflammation, is characterized by the presence of functional endometrial glands and stroma outside the uterine cavity.¹ It affects 10% of women at reproductive age, being one of the most common benign gynecological conditions.² Many studies have been performed to understand the etiology of the disease but the results have been contradictory. The oldest and most widely accepted hypothesis for the pathogenesis of the condition is the retrograde menstruation concept.² Because the signs and symptoms of endometriosis may vary widely from one woman to another, the diagnosis is often delayed, with women experiencing debilitating pain and infertility for years without treatment.² Most of the symptoms, including dysmenorrhea, chronic pelvic pain, infertility, and dyspareunia are well recognized symptoms of endometriosis; however, little attention has been given to insomnia symptoms.³

The high prevalence of insomnia in women is often attributed to hormonal fluctuations, mood disorders, or gynecological dysfunctions, such as premenstrual syndrome and dysmenorrhea.^{4,5} Although there is a lack of studies in the literature addressing the possible association between endometriosis-related symptoms and insomnia, there are two relevant studies that used questionnaires to examine insomnia in endometriosis patients. The first study, from Maggiore's group (2017), found higher Insomnia Severity Index and Epworth Sleepiness Scale scores in an endometriosis group than in a control group.⁶ Additionally, patients with endometriosis experienced subthreshold insomnia and moderate clinical insomnia significantly more frequently than those in the control group. In agreement with these findings, Ramin-Wright (2018) also observed a negative relationship between endometriosis and insomnia.⁷ Although her group applied a distinct questionnaire developed by the universities in Zurich, they also pointed equivalent results from those observed by Maggiore's group. The data showed that insomnia and fatigue were twice as frequent in patients with endometriosis than in a control group.⁷ Both sleepiness and fatigue can be signals of insomnia and lead to impairment in daytime function.⁶

The insomnia symptoms observed in these studies might have been triggered by endometriosis-related pain. It is well known that any pain condition can affect sleep, leading to sleep disturbances and impairment in sleep quality.⁸ In turn, sleep disruption can activate inflammatory mechanisms by triggering changes in the effector systems that regulate the immune system,

resulting in abnormal increases in inflammatory responses⁸ that can stimulate or increase pain. This can result in the creation of a vicious cycle, with pain causing sleep disturbance that increases inflammation, leading to increased pain. Moreover, experimental studies have shown that the association of sleep loss and inflammatory markers are stronger in females than males,^{9,10} suggesting that women with both insomnia and endometriosis complaints are more susceptible to symptoms of pain.

Endometriosis induces several debilitating symptoms that affect women's lives, including insomnia; however, there have been very few studies of this association. The insomnia associated with the condition can result in disease progression and increased pain. Sleep-related symptoms are often not considered in regular gynecological consultations, especially with patients of reproductive age. Nevertheless, given the growing body of evidence concerning sleep and endometriosis, there should be more awareness of this relationship among clinicians and we suggest that they should:

- Suspect endometriosis whenever they face women of reproductive age with sleep- or insomnia-related symptoms. Despite not being pathognomonic, these sleep complaints, especially when associated with other symptoms such as dysmenorrhea, might reinforce the diagnosis of endometriosis.
- Look out for sleep-related symptoms when diagnosing and treating endometriosis patients. These symptoms may be alleviated by referring these patients to a specialized sleep professional for effective insomnia treatment. Sleep-related symptoms and complaints are important and debilitating in women with endometriosis, and require proper appraisal and treatment for a complete medical approach.

Treating insomnia would reduce the negative outcomes related to the inflammatory- and pain-related aspects of endometriosis and would contribute to an improvement in mental health and daytime function. We hope that this letter helps to increase awareness about the importance of sleep assessment in the clinical evaluation of patients with endometriosis, thereby facilitating treatment to reduce pain symptoms and disease progression, and improve daytime function and overall quality of life in this group of women.

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REFERENCES

- Méar L, Herr M, Fauconnier A, Pineau C, Vialar F. Polymorphisms and endometriosis: a systematic review and meta-analyses. *Hum Reprod Update*. 2020;26(1):73–103.
- Falcone T, Flyckt R. Clinical management of endometriosis. *Obstet Gynecol*. 2018;131(3):557–571.
- Bellelis P, Dias JA Jr, Podgaec S, Gonzales M, Baracat EC, Abrão MS. Aspectos epidemiológicos e clínicos da endometriose pélvica: uma série de casos. *Rev Assoc Med Bras*. 2010;56(4):467–471.
- Mauri M, Reid RL, Mac Lean AW. Sleep in the premenstrual phase: a self-report study of PMS patients and normal controls. *Acta Psychiatr Scand*. 1988;78(1):82–86.
- Baker FC, Driver HS, Rogers GG, Paiker J, Mitchell D. High nocturnal body temperatures and disturbed sleep in women with primary dysmenorrhea. *Am J Physiol*. 1999;277:E1013–E1021.
- Maggiore ULR, Bizzarri N, Scala C, Tafi E, Siesto G, Alssandri F, Ferrero S. Symptomatic endometriosis of the posterior cul-de-sac is associated with impaired sleep quality, excessive daytime sleepiness and insomnia: a case-control study. *Eur J Obstet Gynecol Reprod Biol*. 2017;209:39–43.

- Ramin-Wright A, Schwartz ASK, Geraedts K, et al. Fatigue – a symptom in endometriosis. *Hum Reprod*. 2018;33(8):1459–1465.
- Irwin MR. Sleep and inflammation: partners in sickness and in health. *Nat Rev Immunol*. 2019;19(11):702–715.
- Miller MA, Kandala NB, Kivimaki M, et al. Gender differences in the cross-sectional relationships between sleep duration and markers of inflammation: Whitehall II study. *Sleep*. 2009;32(7):857–864.
- Irwin MR, Carrillo C, Olmstead R. Sleep loss activates cellular markers of inflammation: sex differences. *Brain Behav Immun*. 2010;24(1):54–57.

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