



## Gabapentin Efficacy in Reducing Nighttime Awakenings in Premenopausal Women: A Class Effect of GABAergic Medications or Unique Property of Gabapentin Only?

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The recent scientific investigation by Guttuso<sup>1</sup> published in the *Journal of Clinical Sleep Medicine* suggested gabapentin to be effective in reduction of a novel sleep disorder unique to women found to have low serum estradiol and nighttime awakenings. This proposed sleep disorder was coined LUNAs. Gabapentin has been in use for treatment of neurological, psychiatric, chronic pain syndromes, and even menopausal-related hot flashes.<sup>2-4</sup> The mechanism of action of gabapentin in both LUNAs and hot flashes is unclear, however. Gabapentin is a structural analogue of GABA, an inhibitory neurotransmitter. Gabapentin is known to reduce the sleep latency, increase total sleep time, slow wave sleep, and REM sleep. Pharmacologically, it is known to increase GABA in central nervous system.<sup>5</sup>

The theories behind nighttime awakenings and hot flushes in pre menopausal women are hypothesized to be a combination of “narrowing of the thermo neutral zone” (regulated by hypothalamus) along with “increase in sympathetic activity.”<sup>6</sup> Increased firing of GABAergic neurons in the VLPO nucleus of the hypothalamus leads to increase in GABA, resulting in activation of the sleep promoting neurons and suppression of the awake aminergic neurons during NREM sleep. Hypothetically, GABA may also suppress the thermo neutral zone of the hypothalamus during NREM sleep, when night sweats and frequent awakenings are most common. Medications like gabapentin with the potential of increasing GABA in the central nervous system during sleep may help in reducing LUNAs.

Is the action of gabapentin in reducing LUNAs, as reported in this scientific investigation, unique to gabapentin, or do other medications like pregabalin have the potential of increasing GABA in the central nervous system during sleep? Most LUNAs, with or without night sweats, occur in NREM sleep, usually in the first half of the night. Medications such as gamma hydroxybutyrate or pregabalin that consolidate NREM sleep by increasing slow wave sleep may be helpful in reducing these symptoms in this particular group of patients. Additionally, further studies with overnight polysomnogram and qualitative electroencephalograms may help in objective as-

essment of these medications in reducing the night sweats and LUNAs.

Premenopausal women with LUNAs and night sweats have few therapeutic options. It has been reported that the use of medications like selective serotonin receptor agonists such as paroxetine<sup>7</sup> or hormone replacement therapy (HRT) may be helpful in reducing night sweats in premenopausal women. However, many patients are reluctant to use HRT due to concerns of increased risk of breast cancer and cardiovascular events as alluded to in the Women’s Health Initiative report.<sup>8</sup> This scientific report by Dr. Guttuso shows that gabapentin may be an alternative with a more acceptable, mild side effect profile than the present therapeutic options available for this specific group of patients. This may result in improvement in quality of life by reducing LUNAs that may cause fragmentation of sleep and sleep maintenance insomnia.

### CITATION

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