

September 2002

## **Gabapentin and various sexual disorders**

### **Introduction**

Gabapentin (Neurontin<sup>®</sup>) is an amino acid structurally related to the inhibitory neurotransmitter gamma-aminobutyric acid (GABA). Although gabapentin appears to possess GABA-mimetic properties, its precise mechanism of action remains unclear. The drug has no significant effect on GABA transaminase activity, nor does it bind to GABA or benzodiazepine receptors or influence the neural uptake of GABA when given in pharmacologically active doses[1].

It was approved for the Dutch Market in November 1999 *as an add-on anticonvulsant agent in the treatment of patients with refractory partial seizures with or without secondary generalised seizures*[2].

*Adverse events usually are mild and transient. The most frequent adverse events observed during placebo-controlled studies are somnolence, ataxia, dizziness, nystagmus, tremor, dysarthria and fatigue*[2]. Additionally, instances of depression, emotional lability and amnesia have been reported[3].

### **Reports**

Lareb received a report of erectile dysfunction in a 45-year-old man, occurring 3 months after starting treatment for epilepsy with gabapentin 400 mg three times daily. He also suffered from emotional lability, nightmares and dizziness. He used no other medication. After three months gabapentin was replaced by lamotrigine 100 mg daily, after which all symptoms disappeared. Another report was submitted describing a 68 year-old-man who experienced reduced libido and diminished erections after starting gabapentin 1800 mg daily for polyneuropathy. The use of concurrent medication was chronic and included metoprolol, furosemide, quinapril, simvastatin, metformine, glimepiride and phenprocoumon. Gabapentin was discontinued several weeks later, after which he recovered. A diminished libido was also reported in a 58-year-old man immediately after starting gabapentin 1200 mg daily for chronic benign radicular pain. Concomitant medication consisted of betahistine. The decrease in libido was not worsened by dose increase. When the patient was aroused, he did not experience any erection or ejaculation problems.

### **Other sources of information**

#### *Literature*

Erectile dysfunction has been reported in 1.5 % of patients treated with therapeutic doses of gabapentin[3].

Problems in achieving ejaculation and orgasm were described in a 41-year-old man treated with gabapentin 300 mg three times daily for hypomania. After dose increase to 600 mg three times daily the problems worsened. One week after gabapentin discontinuation, he reported normal ejaculation and orgasm[4].

Another report mentioned a case of anorgasmia occurring in a 36-year-old man after titration of gabapentin 400 mg three times a day for hypomania. Within two weeks the patient experienced difficulties in attaining orgasm; his sex drive and erection were not affected. With discontinuation of gabapentin normal orgasmic function returned [5]. Two patients were reported to have experienced improvement of sexual disorder (impotence and anorgasmia) after replacement of gabapentin with lamotrigine[6].

#### *Databases*

The WHO combination database contains 34 reports (12 'sexual function abnormal', 13 on anorgasmia and 9 relating to ejaculation failure) in the organ class reproductive disorders-male, which are disproportionally associated with the use of gabapentin in comparison with all other relevant reports in the database. This also applies to decrease in libido (17 reports) and impotence (32 reports).

### *Mechanism*

Gabapentin is structurally related to GABA. GABA is the major inhibiting neurotransmitter in the central nervous system. In patients taking gabapentin, the *in vivo* occipital lobe concentrations of GABA, measured by magnetic resonance spectroscopy, were higher[7]. It was speculated that gabapentin increases GABA synthesis.

The inhibitory action of GABA (pharmacologically comparable to the effects of benzodiazepines) occurs chiefly in the limbic system, which modulates sexual attention, arousal, cognition and interpersonal reactions. Inhibition and sedation due to benzodiazepines may cause disorientation and disrupt sexual interest and rhythms indirectly. In addition, the dynamic range of sexual responses and reactions may be decreased more directly. It is often difficult to differentiate between deficits in general arousal (sedation) and specific sexual effects[8].

### **Conclusion**

Lareb has received several reports of sexual disorders, including diminished libido, erectile dysfunction and anorgasmia, associated with the use of gabapentin. These associations are supported by publications in the literature and the WHO database. Moreover, there are indications that point to pharmacological plausibility.

### References

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