

Imipramine Treatment of Panic Disorder Patients with Frequent Sleep Panic

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SUMMARY

İMİPRAMİN TEDAVİSİNDE PANİK BOZUKLUKLU HASTALARIN TEDAVİSİNDE İMİPRAMİNİN ETKİNLİĞİ

Objective: The aim of this study was to examine the effectiveness of imipramine treatment in the panic disorder patients who had frequent sleep panic attacks as predominant clinical features. **Method:** Thirteen patients whose sleep panic attacks represented their primary complaint at the time of admission were given imipramine for an 8-week trial. **Results:** 150 mg/day imipramine treatment reduced the frequency and the severity of sleep panic attacks in patients. **Conclusions:** These findings suggest that imipramine is useful in the treatment of this subgroup patients of panic disorder.

Key words: sleep panic, panic disorder, imipramine

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ÖZET

İMİPRAMİN TEDAVİSİNDE İMİPRAMİNİN ETKİNLİĞİ

Amacı: Bu çalışmanın amacı önde gelen klinik özellikleri sık gelen uyku panik atakları olan panik bozukluklu hastaların tedavisinde imipraminin etkinliğini araştırmaktır. **Yöntem:** Hastane başvurularında önde gelen yakınmalarını sık gelen panik ataklar olarak tanımlayan 13 hastaya 8 haftalık imipramin (150 mg/gün) verildi. **Bulgular:** Bu tedavi ile panik atakların sıklığı ve şiddeti azaldı. **Tartışma:** Bu bulgular imipraminin panik bozukluğun bir alt tipini oluşturan bu hastalarda yararlı olduğunu göstermektedir.

Anahtar sözcükler: uyku paniği, panik bozukluğu, imipramin

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INTRODUCTION

Recently, there is a considerable progress in understanding the neurobiology of panic disorder. An interesting phenomenon is panic attacks preceded by states of diminished arousal. Mellman and Uhde (1) suggested that there was a relationship between this phenomenon and sleep-related panic. Mellman and Uhde (2) observed that sleep panic attacks typically arose during the transition towards early delta sleep, i. e., during a state of diminishing arousal. One possible explanation for the association of sleep panic with early delta sleep may be related to carbon dioxide sensitivity in panic patients. The possibility of increased sensitivity of central medullary carbon dioxide receptors may be present in some patients with panic disorder (3). Another explanation is that reductions in respiration during deep non-rapid eye movement (non-REM) sleep lead to respiratory acidosis that triggers hyperventilation and subsequent panic (4).

Sleep panic attacks are frequent in patients with panic disorder. There is an association among the severity of illness and sleep panic in panic disorder. In a previous study (5), we found that the patients with recurrent sleep panic had significantly more panic attacks per week than those without sleep panic. In

addition, the patients with recurrent sleep panic had more severe panic symptoms than the others. In a recent study (6), we examined the relationship of sleep panic to major depression in patients with panic disorder and found that the sleep panickers had a higher prevalence of major depression than the other panickers. Moreover, there is an association between recurrent sleep panic attacks and suicidal behavior in patients with panic disorder (7). Thus, it may be suggested that the presence of sleep panic attacks may delineate a subgroup of panic disorder patients.

In the treatment of panic disorder, imipramine is the most widely studied drug and has been effective in multiple double-blind, placebo-controlled studies (8). However, there is no evidence that it is superior (or inferior) to any other tricyclic for panic disorder and there are sometimes individual variations in sensitivity to one or another (9). An interesting topic is that imipramine has specific and significant effects in patients with sleep panic and may be useful for the reduction in the frequency of and the severity sleep panic. The purpose of this report is to demonstrate the response to imipramine treatment in panic disorder patients who reported having the experience of recurrent sleep panic attacks as primary complaint at the time of admission.

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METHODS

The 13 outpatients of this study were outpatients who met the DSM IV diagnostic criteria for panic disorder, whose sleep panic attacks represented their primary complaint at the time of hospital admission. They had at least one sleep panic attacks weekly. They had no a history of psychosis, dementia, bipolar disorder, or melancholia. They were medically healthy and free of psychotropic drugs and alcohol.

The mean age of the subjects was 30.2 (SD=7.5) and the mean age at onset of the illness was 26.9 (SD=7.4). The mean duration of illness was 38.9 months (SD=36.1). Seventy-seven percent (N= 10) of the subjects were women. The 11 subjects (85 %) had also agoraphobia.

Panic attacks were assessed with self-rated questionnaire adapted from the DSM IV criteria for panic disorder. Patients were asked to give "an overall estimate of the severity of your panic attacks during the last 4 weeks" on a scale of 0-8 (0=none, 2=mild, 4=moderate, 6=severe, and 8=very severe). Patients were also asked to give number of their sleep and daytime panic attacks during the last 4 weeks.

All subjects gave informed consent to participate in this study. The initial dose 25 mg/day imipramine for the first 3 days, which was doubled on the fourth day and tripled on the seventh day, with 150 mg/day reached on the tenth day of dosing. At each visit the following second, fourth, and eighth week, the patients were assessed again.

Statistical significance was determined by Wilcoxon Matched-Pairs Signed-Ranks Test. Analyses were performed using the SPSS for Windows v5.01.

RESULTS

The six (46 %) patients had some problematic side effects include sedation, postural hypotension, constipation, dry mouth, and sweating within the

first weeks of treatment. However, all of the subjects completed the 8-week trial period of the study.

Table 1 shows the frequency and the severity of the sleep panic attacks at baseline and after 8 weeks.

As shown Table 1, imipramine treatment reduced both frequency (11±10.5 per month versus 1.2±1.9 month; z= -2.93, p=0.0015) and severity (4.7±0.6 versus 2.8±0.7; z= -3.05, p=0.002) of panic attacks during sleep. When we accept a 50 % reduction in ratings from baseline to signify marked improvement, 11 (85 %) patients had marked improvement.

DISCUSSION

Imipramine has specific and clinically significant effects in the treatment of patients with panic disorder and these effects are dose dependent (10). Patients taking 150-200 mg of imipramine respond better than dose taking either 100 or 50 mg (11). In this study, we presented the significant effects of imipramine in panic disorder patients whose sleep panic attacks represented their primary complaint at the time of admission and their predominant feature is having recurrent sleep panic more than daytime panic. We found that 150 mg of imipramine was effective at the end of 8-week trial. Imipramine treatment was useful for the reduction in the frequency of and the severity sleep panic. In a previous study, Mellman and Uhde (12) presented 12 cases of panic disorder patients whose sleep panic attacks represented their primary complaint and demonstrated marked global clinical improvement and a reduction in the frequency of sleep panic attacks. The present study replicated their study. Although this study was not placebo controlled, it demonstrated that imipramine was effective in sleep panic.

One possible explanation of the effectiveness of imipramine is that sleep panic attacks represent a non-REM event and imipramine may suppress this

Table 1: The frequency and severity of sleep panic attacks in patients at baseline and after treatment Analysis*

	Pretreatment	Posttreatment	z	p
Frequency of sleep panic attacks	11±10.5	1.2±1.9	-2.93	0.0015
Severity of sleep panic attacks	4.7±0.6	2.8±0.7	-3.05	0.002

* Wilcoxon Matched-Pairs Signed-Ranks Test

event. Indeed, Hauri et al. (13) observed that sleep panic attacks occurred in the transition phase between stage 2 and stage 3 sleep. In our opinion, this is very interesting because sleep-related panic attacks appear to clarify the "spontaneous" or physio-

logically based nature some panic episodes and offer novel investigative opportunities for further elucidating pathophysiologic mechanisms.

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