Imipramine Effects on Sleep in Depressed Adolescents: A Preliminary Report

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Introduction

Antidepressant medications, including tricyclic antidepressants, monoamine oxidase inhibitors, lithium, and fluoxetine, generally have been found to suppress rapid eye movement (REM) sleep (von Bardeleben et al. 1989, reviewed by Saletu 1986), although several unusual antidepressants have been found to increase REM sleep (Wiegand et al. 1986; Di Perri et al. 1987; Soldatos et al. 1988; Monti 1989). Additional evidence that there may be an association between the antidepressant effects of the medications and their REM sleep effects include the following: (1) The extent to which amitriptyline (Kupfer et al. 1976; Gillin et al. 1978; Kupfer et al. 1981) and clomipramine (Höchli et al. 1986) suppress REM sleep was found to predict eventual antidepressant response in depressed adults. Kupfer et al. (1979) extended these findings into depressed children treated with imipramine. (2) Selective REM sleep deprivation improved depressive symptoms (Vogel et al. 1975). Eight of 9 subjects unresponsive to selective REM sleep deprivation were also unresponsive to imipramine.

Characteristic sleep abnormalities found in depressed adults have not been consistently demonstrated in depressed adolescents. In a study consisting largely of outpatients, Goetz et al. (1987) and Appelboom-Fondu et al. (1988) noted only some sleep continuity disturbances and not the other characteristic abnormalities: reduced delta sleep, increased REM density during the early part of the night, and shortened REM latency (Kupfer et al. 1985). Emslie et al. (1987) found all four abnormalities in a sample of inpatients, as did Lahmeyer et al. (1983) in a sample of inpatients and outpatients.

As yet, no studies have found that tricyclic antidepressant therapy is more effective than placebo in the treatment of adolescent depression (Kramer and Feiguine 1981; Ryan et al. 1986). This raises the question of whether or not tricyclic antidepressant medications cause changes in REM sleep parameters in adolescents similar to those caused in adults. REM sleep changes reported in depressed adults on tricyclic antidepressants include increased REM latency and decreased REM time, REM activity, and number of REM periods (Jarrett et al. 1988; Höchli et at. 1986; Kupfer et al. 1981). We are not aware of studies on the effects of these medications on sleep in depressed adolescents. The present study examined the acute effects of imipramine on electroencephalogram (EEG)-monitored sleep in adolescents with major depressive disorder (MDD).

Methods

The subjects were 10 inpatients admitted to the University of Michigan Medical Center Ado-

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lescent Psychiatry Unit, a 14-bed clinical research unit. Informed consent was obtained. The sample included 6 girls and 4 boys, with a mean age of 15.1 years and an age range of 13–17 years. The diagnosis of primary unipolar MDD was made by an attending child psychiatrist according to Research Diagnostic Criteria (Spitzer et al. 1978), using information from a multidisciplinary evaluation and a semistructured interview with the Schedule for Affective Disorders and Schizophrenia (Endicott and Spitzer 1978). Seven of the patients had the endogenous subtype and 4 had distinct comorbid diagnoses, according to DSM-111-R: panic disorder with agoraphobia (3 patients) and a combination of panic disorder with agoraphobia, obsessive compulsive disorder, and conduct disorder (1 patient). All adolescents were depressed throughout an initial 2–6 week medication-free assessment period. On the first week of sleep studies, scores on the 17-item Hamilton Depression Rating Scale (Hamilton 1960) ranged from 11 to 27 with a mean of 19.0.

The adolescents were studied polysomnographically for two pairs of consecutive nights 1 week apart. The studies were performed using an EEG sleep telephone telemetry system (TeleDiagnostic Systems, San Francisco) which enabled data to be telemetered from inpatients in their own beds to the sleep laboratory control room. The studies were otherwise performed and analyzed as described previously (Grunhaus et al. 1988). The patients were psychotropic medication-free on nights 1 and 2. Nights 3 and 4 were the first two nights of treatment with 50 mg of imipramine at 9:00 PM. Nights 1 and 3 were considered adaptation nights. Mean values of selected sleep variables were compared between night 2 (baseline) and night 4 (imipramine) with a two-tailed, paired *t*-test.

Results

Significant REM suppression was found on imipramine compared to baseline (Table 1). We found an increase in REM latency ($p < 0.001$) and decreases in REM time ($p < 0.0001$), REM percent ($p < 0.0001$), REM activity ($p < 0.001$), and number of REM periods ($p < 0.0001$). REM density did not change significantly. Percent of stage 1 sleep increased ($p < 0.05$), with no significant differences in percent of stage 2 or delta sleep. No sleep continuity variables were significantly different, although increased number of arousals showed a trend toward significance.

Discussion

Imipramine markedly suppressed REM sleep in depressed adolescents, and had only minor effects on sleep continuity (a trend toward increased number of arousals) and sleep architecture (increased percent of stage 1 sleep). These findings were similar to those in depressed adults. Jarrett et al. (1988) reported increased REM latency; decreased REM time, REM activity, REM density, and number of REM periods; and no significant sleep continuity changes on the first night of treatment with imipramine. The sleep architecture changes were different in adults: increased percent of stage 2 sleep and no change in percent of stage 1 sleep (Jarrett et al. 1988). Kupfer et al. (1979) found some similarities and differences in REM sleep in depressed children who had been taking imipramine for 3 weeks. Similarities included increased REM latency, and decreased percent of REM and number of REM periods. Differences included not significantly changed REM activity and increased REM density. There were also more imipramine-induced disturbances in sleep continuity and non-REM sleep architecture. The differences with the current findings may have been due to the fact that sleep studies were done after 3 weeks of imipramine, rather than on night 2 of imipramine.

The current findings suggest that effects of imipramine on REM sleep in depressed adolescents are similar to effects on REM sleep in depressed adults. Further work is indicated, including investigations of the association between antidepressant-induced changes in EEG-monitored sleep and clinical response to the medication.

Table 1. Selected Sleep Variables

Sleep variable	Baseline Mean	(SD)	On imipramine Mean	(SD)	t^a	$p<$
Sleep continuity variables						
Total recording period (min)	427.5	(26.7)	439.3	(20.2)	−1.06	NS
Sleep latency (min)	49.9	(30.8)	49.3	(35.2)	0.04	NS
Number of arousals	0.4	(0.7)	2.5	(2.5)	−2.24	0.10
Time spent asleep (min)	372.2	(50.2)	373.5	(40.3)	−0.13	NS
Efficiency (TSA/TRP × 100)	86.9	(8.8)	85.1	(7.9)	0.58	NS
Sleep architecture						
Stage 1%	6.7	(4.2)	14.8	(9.7)	−2.53	0.05
Stage 2%	50.6	(4.7)	54.0	(11.1)	−1.02	NS
Delta %	26.7	(7.2)	27.9	(9.0)	−0.81	NS
REM %	16.1	(3.2)	3.3	(3.5)	9.56	0.0001
REM sleep variables						
REM latency (min)	107.7	(42.9)	312.6	(55.1)	−6.95[b]	0.001
REM time (min)	59.8	(14.2)	12.2	(13.2)	8.90	0.0001
REM activity (U)	61.4	(24.3)	8.7	(11.0)	5.64	0.001
REM density	1.0	(0.4)	0.8	(0.2)	1.42[b]	NS
No. of REM periods	3.5	(0.7)	0.7	(0.5)	9.64	0.0001

[a]Two-tailed, paired *t*-test; df = 9 unless otherwise indicated.
[b]No REM sleep during 3 of the imipramine nights; df = 6.

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