The effect of commonly used antidepressant drug groups on sleep profile with major depression: a case–control study

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Objectives

One of the adjuvant of an ideal antidepressant is its desirable effect on sleep. Nevertheless, head-to-head comparisons between different antidepressants, designed specifically to test their sleep effects in a clinical setting are still scarce. This study aimed at comparing the effect of commonly used antidepressant groups on sleep profile as measured by Polysomnogram of depressed patients in a clinical setting.

Materials and methods

Thirty newly diagnosed nonmedicated depressed patients were recruited from the outpatient and inpatient departments of the Institute of Psychiatry, Ain Shams University Hospitals, in the period May to November 2008. All patients were diagnosed according to International Classification of Diseases-10 research diagnostic criteria of major depression with a score of greater than 14 on the Hamilton Depression Rating Scale, and screened for eligibility in the study using full physical examination, routine laboratory tests, electroencephalogram, and the psychiatric history and mental state examination sheet of the Institute of Psychiatry, Ain Shams University. They were classified according to the prescribed antidepressants according to their treating doctor into tricyclics antidepressants (TCAs) group (15 patients) and selective serotonin reuptake inhibitors (SSRIs) group (15 patients). The control group consisted of 10 healthy individuals matched with patients for age and sex. Recruited depressed patients as well as controls were subjected to (i) structured sheet for sleep disorders, (ii) Hamilton Depression Rating Scale-17 for measuring the efficacy of antidepressants, and (iii) Polysomnographic study. Patients were subjected to these assessments two times, before antidepressant start and 1 month after antidepressant start. Controls were subjected to these assessments once immediately after recruitment.

Results

TCAs improved all sleep parameters, except for sleep stage I and III and slow-wave sleep percentage (SWS %). SSRIs improved all sleep parameters, except for sleep stages I, II, III, and IV and SWS%. TCAs led to a more significant decrease in sleep latency, arousal index, sleep stage I as well as a more significant increase in sleep efficiency, sleep stages III and IV, and SWS% than with SSRIs. SSRIs led to a more significant decrease in rapid eye movement percentage (REM%) and to a more statistically significant increase in sleep stage II than with TCAs. There was no statistically significant difference between the two drug groups regarding their effect on REM density, REM latency, and periodic limb movement index.

Conclusion

Commonly used antidepressants in clinical practice have a positive effect on objective sleep parameters, except for sleep microstructure. TCAs significantly improved objective sleep quality away from its antidepressant therapeutic effect compared with SSRI. Selecting the proper antidepressant for depression with profound sleep problems is an art, which needs future research.

Keywords:
antidepressants, depression, sleep

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Introduction

Sleep disturbance is a prevalent key feature of depression that affects the course of illness, treatment compliance, and treatment response [1]. More than 80% of people with depression experience sleep disturbances, such as early morning waking or frequent awakenings throughout the whole night [2,3]. Even in chronic low-grade depression, which affects roughly 3% of people, insomnia and/or sleepiness may be the most prominent symptom [4].

Disturbed sleep in depression is either objective as shortened rapid eye movement (REM) latency, disruption of sleep continuity, early morning waking, and reduction of slow-wave sleep (SWS) [5] or subjective as total sleep time (TST), difficulty in initiating sleep, and interrupted sleep. This subjective sleep disturbance affects the patient satisfaction by the antidepressant [6,7], that is, does my antidepressant improve my sleep?

One of the adjuvants of an ideal antidepressant is its desirable effect on sleep. Antidepressants that reduce restless sleep and awakening with no REM suppression and that improve alertness are considered ideal [8]. The efficacy of antidepressants generally appears to be equal [9]. However, some compounds claim advantages over others related to specific side effects such as sexual dysfunction and/or sleep disturbance. Nevertheless, head-to-head comparisons between the commonly used antidepressant designed specifically to test these claims in a clinical setting are still scarce [10].

Polysomnogram (PSG) translates subjective sleep complaints to objective findings that help us to quantify the effect of different antidepressants on sleep, which will help in predicting the patient's satisfaction and in enhancing his/her compliance [7,11].

This study aimed at comparing the effect of commonly used antidepressant groups on sleep profile as measured by PSG of depressed patients in a clinical setting.

Patients and methods

Consecutive newly diagnosed nonmedicated depressed patients attending both the outpatient and inpatient departments of the Institute of Psychiatry, Ain Shams University Hospitals, in the period May to November 2008 were invited to participate in the study. Depression was diagnosed according to International Classification of Diseases-10 research diagnostic criteria of major depression with a score of greater than 14 on the Hamilton Depression Rating Scale (HAMD).

The depressed patients who agreed to participate in this study were asked for written consent and were screened for eligibility in the study using full physical examination, routine laboratory tests including blood chemistry, thyroid functions, liver functions, urine analysis, electroencephalogram (EEG), and the psychiatric history and mental state examination sheet of the Institute of Psychiatry, Ain Shams University.

Depressed patients were excluded if they were younger than 20 years and older than 40 years, had comorbid psychiatric disorder other than depression (including bipolar depression), were already maintained on antidepressant(s), had a history of use of antidepressants within the last 6 months, had a history of treatment-resistant depression (nonresponsive to a single antidepressant at therapeutic doses for at least 6 weeks), had a past/current history of epilepsy as confirmed by EEG, had a past/current history of head trauma, had comorbid physical condition and/or drugs that could affect the sleep EEG, had a medical contraindication to antidepressant drugs (including pregnancy, lactation, or not using contraception while of childbearing potential in women), had serious suicide risk, were unable to maintain a consistent sleep pattern (such as shift workers), had current sleep/wake disorder, and/or were on psychoactive substances (including benzodiazepines) in the last 6 weeks before the study as a washout period.

Patients were classified according to the prescribed antidepressant according to their treating doctor into two groups: group 1 had been receiving tricyclics antidepressants (TCAs) and group 2 had been receiving selective serotonin reuptake inhibitors (SSRIs). We had 15 patients in each group after dropouts, which were five in each group mainly because of intolerable side effects of drugs and/or severe sleep complaint that needed rapid intervention.

Control group consisted of 10 healthy individuals who were selected from among the hospital employees after being screened for eligibility of the study in the same way similar to patients. They were matched with patients for age and sex.

Recruited depressed patients as well controls were subjected to (i) structured sheet for sleep disorders, derived from the sleep disorder questionnaire of Douglass *et al.* [12] that contained 72 questions regarding past or current history of sleep disturbance, sleep disorder, psychiatric disorder, and drug history; (ii) HAMD-17 for measuring the efficacy of antidepressants; and (iii) PSG study conducted for three successive nights; we considered the values of the last night in order to take the most valid reading after the patient felt comfortable with the study place.

Patients were subjected to these assessments two times: before antidepressant start and 1 month after antidepressant start. Controls were subjected to these assessments once immediately after recruitment.

Tools

HAMD [13] is a valid reliable multidimensional measure covering wide dimensions of depressive symptomatology, including depressed mood, vegetative symptoms, anxiety, agitation, and insight [14] and being sensitive to treatment change [15]. Reduction of 50% of pretreatment depressive symptoms assessment considered response to treatment and score less than or equal to 7 considered clinical remissions [16]. In antidepressant clinical trials, HAMD-17 has been the gold standard instrument for establishing and comparing the efficacy of new treatments [17,18]. Cutoff point and scoring of depression severity as determined by HAMD-17 are as follows: no depression (≤ 7), mild (8–13), moderate (14–18), severe (19–22), and very severe (> 23).

Overnight polygraph sleep recording (PSG) was carried out by a remote cable that used a 16-channel polygraph including EEG, submental chin electromyelogram, and electro-occulogrpahy. Sleep was recorded automatically with visual correction by an experienced sleep scorer according to standard Rechtschaffen and Kales [19]

criteria. Many parameters were derived from the PSG study including sleep staging time, TST, number of awaking, sleep latency, wakefulness after sleep onset, sleep efficiency, REM latency, REM density, periodic limb movement index (PLMI), and arousal index.

Statistical analysis

Data coded and revised were introduced to an EXCEL database to be manipulated and analyzed later using the 16th version of SPSS (SPSS, Inc., Chicago, IL, USA). For the sake of description, categorical data were presented as number and percentage; means, standard deviation, and 95% confidence limit were used to describe continuous variables. One-way analysis of variance was used to test any significant differences between more than two groups. Kruskall–Wallis test was used to analyze differences of continuous variables between more than two groups. The paired *t*-test was used to analyze the difference within individual group before and after treatment of normally distributed variables. Statistically significance level was set at a value of less than or equal to 0.05; highly significant level was at a value less than 0.01; and very highly significant level was at a value less than 0.001.

Results

Two groups of depressed patients were identified in our study. Each group included 15 patients. The first group (1) received TCAs (11 received amitriptyline and four received imipramine) within the therapeutic dose (75–100 mg/day); their mean age was 34.73 ± 4.89 years with eight of them being women (53.3%) and seven of them being men (46.6%). The second group (2) received SSRIs (12 received paroxetine and three received citalopram) within the therapeutic dose (20 mg/day); their mean age was 34.60 ± 5.36 years with nine of them being women (60%) and six of them being men (40%).

The third group in our study was of healthy controls (3) matched with patients for sex and age. Their mean age was 33 ± 4.42 years with five of them being women (50%) and five of them being men (50%). There was no statistically significant difference between patients and controls regarding age and sex ($P > 0.05$).

In comparing sleep parameters of both TCAs group (1) and SSRIs group (2) versus controls (3) at the baseline (pretreatment), there was statistically significant longer sleep latency, poorer sleep efficiency, higher arousal index, longer stage one, shorter stage three and four and SWS, higher REM percentage and density, and shorter REM latency in patients than in controls. With regard to PLMI, it was higher only in group 1 than in controls with no statistically significant difference ($P = 0.357$) found between group 2 and controls (Table 1).

In comparing sleep parameters of TCAs group 1 versus SSRIs group 2 at the baseline (pretreatment), there was no statistically significant difference in all parameters between the two groups, except for significantly longer stage four and higher SWS percentage (SWS%) and PLMI in group 1 than in group 2 (Table 2).

In assessing the response to treatment in the two groups by comparing the scores on HAMD before and after treatment, there was statistically significant lowering of the HAMD score in both groups; however, it reached the response level (lower than 50% from the initial score) only in group 1. There was no statistically significant difference between the two groups after treatment as regards the HAMD score (Table 3).

With regard to the effect of TCAs on sleep parameters, all parameters were improved after receiving TCAs, except for sleep microstructure where stage one showed no statistically significant shortening after treatment and stage 3 and SWS% showed significant prolongation but still below the normal values (Table 4).

With regard to the effect of SSRIs on sleep parameters, all parameters were improved after receiving SSRIs, except for sleep microstructure, where stage one showed no statistically significant shortening after treatment, stages 2, 3, and 4 showed significant prolongation, and SWS% showed a significant increase, but all were still below the normal values (Table 5).

Table 1 Comparing sleep parameters of depressed patients maintained on TCAs (group 1) versus controls and depressed patients maintained on SSRIs (group 2) versus controls at the baseline pretreatment level

Sleep parameter	TCAs group (mean ± SD)	SSRIs group (mean ± SD)	Controls (mean ± SD)	*P* value
Sleep latency	42.53 ± 7.74	41.6 ± 10.7	19 ± 2.4	0.000
Sleep efficiency	37.35 ± 5.08	40.58 ± 7.3	91.18 ± 2.47	0.000
Arousal index	17.93 ± 1.31	17.4 ± 1.79	5.78 ± 1.83	0.000
Sleep stage 1	8.19 ± 1.2	10.18 ± 3.49	7.78 ± 12.04	0.00
Sleep stage 2	51.41 ± 0.92	52.55 ± 3.17	19.43 ± 2.6	0.00
Sleep stage 3	6.67 ± 10.07	3.87 ± 0.96	9.99 ± 0.71	0.00
Sleep stage 4	3.77 ± 0.71	2.76 ± 1.03	10.12 ± 0.52	0.000
SWS%	7.87 ± 0.87	6.63 ± 1.41	20.17 ± 0.61	0.000
PLMI	2.73 ± 0.65	2.29 ± 0.47	2.08 ± 0.46	0.006 0.357
REM%	31.87 ± 3.25	30.65 ± 5.25	25.21 ± 1.20	0.001
REM density	26.75 ± 0.74	26.03 ± 1.63	20.74 ± 0.83	0.000
REM latency	44.40 ± 12.40	46.24 ± 13.03	68.4 ± 5.93	0.00

Statistical significance level was set at a value ≤ 0.05, highly significant level at a value < 0.01, and very highly significant level at a value < 0.001. PLMI, periodic limb movement index; REM, rapid eye movement; SSRIs, selective serotonin reuptake inhibitors; SWS, slow-wave sleep; TCAs, tricyclic antidepressants.

Table 2 Comparing sleep parameters of depressed patients maintained on TCAs (group 1) versus depressed patients maintained on SSRIs (group 2) at the baseline pretreatment level

Sleep parameter	TCA group (mean ± SD)	SSRI group (mean ± SD)	*P* value
Sleep latency	42.53 ± 7.74	41.67 ± 10.71	0.774
Sleep efficiency	37.35 ± 5.08	40.58 ± 7.31	0.124
Arousal index	17.93 ± 1.31	17.47 ± 1.79	0.452
Stage 1	8.19 ± 1.2	10.18 ± 3.49	0.12
Stage 2	51.41 ± 0.92	19 ± 2.4	0.61
Stage 3	6.67 ± 10.07	3.87 ± 0.96	0.14
Stage 4	3.77 ± 0.71	2.76 ± 1.03	0.002
SWS%	7.87 ± 0.87	6.63 ± 1.41	0.003
PLMI	2.73 ± 0.65	2.29 ± 0.47	0.030
REM%	31.87 ± 3.25	30.65 ± 5.25	0.388
REM density	26.75 ± 0.74	26.03 ± 1.63	0.102
REM latency	44.40 ± 12.40	46.24 ± 13.03	0.57

Statistical significance level was set at a value ≤ 0.05, highly significant level at a value < 0.01, and very highly significant at a value < 0.001.
PLMI, periodic limb movement index; REM, rapid eye movement; SSRIs, selective serotonin reuptake inhibitors; SWS, slow-wave sleep; TCAs, tricyclic antidepressants.

On comparing the effect of TCAs and SSRIs on sleep parameters, TCAs led to a more statistically significant decrease in sleep latency, arousal index, sleep stage 1 as well as a more statistically significant increase in sleep efficiency, sleep stages 3 and 4, and SWS% than with SSRIs. In contrast, SSRIs led to a more significant decrease in REM% and a more statistically significant increase in sleep stage 2 than with TCAs. There was no statistically significant difference between the two drug groups regarding their effect on REM density, REM latency, and PLMI (Table 6).

Discussion

At pretreatment baseline, our depressed patients in the two treatment groups had sleep disturbance in the form of longer sleep latency, poorer sleep efficiency, higher arousal index, longer stage one, shorter stages three and four (SWS), higher REM percentage and density, and shorter REM latency than in controls. These findings are in accordance with most of the scientific studies regarding sleep disturbance in depression as those of Thase *et al.* [20], Rush *et al.* [21], Rechtschaffen *et al.* [22], and Doghramji [6] who found the same findings.

There were no statistically significant pretreatment differences between the two groups on nearly all the sleep measures, except for TCAs group that had significantly longer stage four and higher SWS%, which reflects better sleep and higher PLMI, which further reflects poorer sleep than the SSRIs group. These differences entirely occurred by chance as we selected patients already after prescription of the drug for the two groups randomly. Moreover, it may reflect the prescription habits in our practice, which differentiate between TCAs and SSRIs according to drug cost and/or severity of depression, with more TCAs being prescribed for severe depression [23,24]. To our knowledge, no research reflecting actual prescription habits of antidepressants in our culture is available.

Home sleep recording performed by Hicks *et al.* [25] could be comparable with our study, which provided valid data for sleep assessment on three successive nights as a period of adjustment to the unfamiliar surroundings reflecting the most comfort for the patient. They found higher SWS compared with most sleep laboratory studies in depression. This supports the use of home sleep than sleep center recordings as it reflects better sleep quality.

Table 3 Comparing HAMD score of depressed patients maintained on TCAs (group 1) versus depressed patients aintained on SSRIs (group 2) before and after treatment

Group 1 (before treatment)	Group 1 (after treatment)	*P* value
34.53 ± 3.72	15.93 ± 3.83	0.00
Group 2 (before treatment)	Group 2 (after treatment)	*P* value
32 ± 4.49	19.67 ± 6.16	0.00
Group 1 (after treatment)	Group 2 (after treatment)	*P* value
15.93 ± 3.83	19.67 ± 6.16	0.056

Statistical significance level was set at a value ≤ 0.05, highly significant level at a value < 0.01, and very highly significant at a value < 0.001.
HAMD, Hamilton Depression Rating Scale; SSRIs, selective serotonin reuptake inhibitors; TCAs, tricyclic antidepressants.

Table 4 Comparing sleep parameters in depressed patients maintained on TCAs (group 1) before and after receiving TCAs

Sleep parameter	Before (mean ± SD)	After (mean ± SD)	*P* value
Sleep latency	42.53 ± 7.74	20.27 ± 4.40	0.00
Sleep efficiency	37.35 ± 5.08	69.20 ± 7.43	0.00
Arousal index	17.93 ± 1.31	9.92 ± 1.50	0.00
Stage 1	8.19 ± 1.2	7.53 ± 1.21	0.07
Stage 2	51.41 ± 0.92	52.93 ± 1.03	0.00
Stage 3	6.67 ± 10.07	7.09 ± 0.97	0.01
Stage 4	3.77 ± 0.71	7.43 ± 1.40	0.00
SWS%	7.87 ± 0.87	14.51 ± 2.07	0.00
PLMI	2.73 ± 0.65	2.79 ± 0.64	0.52
REM%	31.87 ± 3.25	25.00 ± 2.78	0.00
REM density	26.75 ± 0.74	22.39 ± 1.49	0.00
REM latency	44.40 ± 12.40	62.80 ± 5.39	0.00

Statistical significance level was set at a value ≤ 0.05, highly significant level at a value < 0.01, and very highly significant at a value < 0.001.
PLMI, periodic limb movement index; REM, rapid eye movement; SWS, slow-wave sleep; TCAs, tricyclic antidepressants.

Table 5 Comparing sleep parameters in depressed patients maintained on SSRIs (group 2) before and after receiving SSRIs

Sleep parameter	Before (mean ± SD)	After (mean ± SD)	*P* value
Sleep latency	41.67 ± 10.71	27.80 ± 7.38	0.00
Sleep efficiency	40.58 ± 7.31	58.49 ± 8.59	0.00
Arousal index	17.47 ± 1.79	13.07 ± 2.18	0.00
Stage 1	10.18 ± 3.49	8.87 ± 1.94	0.08
Stage 2	52.55 ± 3.17	54.11 ± 13.32	0.01
Stage 3	3.87 ± 0.96	5.89 ± 1.05	0.00
Stage 4	2.76 ± 1.03	5.89 ± 1.05	0.00
SWS%	6.63 ± 1.41	11.76 ± 1.26	0.00
PLMI	2.29 ± 0.47	2.52 ± 0.50	0.03
REM%	30.65 ± 5.25	21.57 ± 2.77	0.00
REM density	26.03 ± 1.63	22.11 ± 1.63	0.00
REM latency	46.24 ± 13.03	62.40 ± 6.46	0.00

Statistical significance level was set at a value ≤ 0.05, highly significant level at a value < 0.01, and very highly significant at a value < 0.001.
PLMI, periodic limb movement index; REM, rapid eye movement; SSRIs, selective serotonin reuptake inhibitors; SWS, slow-wave sleep.

Table 6 Comparing sleep parameters of depressed patients maintained on TCAs (group 1) versus depressed patients maintained on SSRIs (group 2) at the post-treatment level

Sleep parameter	After TCAs (mean ± SD)	After SSRIs (mean ± SD)	*P* value
Sleep latency	20.27 ± 4.40	27.80 ± 7.38	0.00
Sleep efficiency	69.20 ± 7.43	58.49 ± 8.59	0.00
Arousal index	9.92 ± 1.50	13.07 ± 2.18	0.00
Stage 1	7.53 ± 1.21	8.87 ± 1.94	0.02
Stage 2	52.93 ± 1.03	54.11 ± 13.32	0.00
Stage 3	7.09 ± 0.97	5.89 ± 1.05	0.00
Stage 4	7.43 ± 1.40	5.89 ± 1.05	0.00
SWS%	14.51 ± 2.07	11.76 ± 1.26	0.00
PLMI	2.79 ± 0.64	2.52 ± 0.50	0.21
REM%	25.00 ± 2.78	21.57 ± 2.77	0.00
REM density	22.39 ± 1.49	22.11 ± 1.63	0.62
REM latency	62.80 ± 5.39	62.40 ± 6.46	0.86

Statistical significance level was set at a value ≤ 0.05, highly significant level at a value < 0.01, and very highly significant at a value < 0.001.
PLMI, periodic limb movement index; REM, rapid eye movement; SSRIs, selective serotonin reuptake inhibitors; SWS, slow-wave sleep; TCAs, tricyclic antidepressants.

The linkage between sleep disturbance and depression in a clinical setting has long been recognized; however, many points are not much discussed. One of these points is compliance and its relation to sleep improvement by antidepressant. In our study, 25% of patients (five out of 20) in each group stopped their antidepressant secondary to intolerable side effects of drugs and/or severe sleep complaint that needs rapid intervention. This confirmed the unmet need of considering sleep effect and/or side effect as a key factor in tailoring antidepressant treatment in order to decrease the ratio of noncompliance on antidepressant with a high rate of early dropout in the course of treatment.

No difference in the dropout ratio in both TCAs and SSRIs groups was found in this study, which supports the findings of the meta-analyses carried out on SSRIs versus TCAs antidepressants that there were no significant differences in crude indices of compliance between fluoxetine and dothiepin, despite marked differences in side effect profile and dose regimen. This could be explained by the fact that studies that have examined compliance with antidepressants as a primary objective have usually been carried out in hospital outpatients, whereas the majority of prescriptions for antidepressants are made in primary care. However, most studies conducted in this setting have been small and almost all have relied on self-reports of tablet consumption by patients or on tablet counts by doctors. TCAs prescriptions in primary care are often at subtherapeutic doses, which will favor their compliance [7,26].

Assessment in this study was conducted 1 month after antidepressant start, which represented the midpoint in the duration needed (2–6 weeks) for antidepressant therapeutic action and was considered as a suitable time for assessing the drug effects on sleep, apart from either the effect of pretreatment depressive disorder or post-treatment recovery. If it was less than 4 weeks, it might have reflected the sleep disturbance of depression itself as the antidepressant did not yet exert its effect, and the symptoms are at their peak. If it was more than 4 weeks, it may have reflected the sleep improvement as a part of depression' remission [24].

SSRIs and TCAs are the antidepressants widely used in clinical practice [9,27] including ours. SSRIs have become a first-line treatment of depression over the past decade [28]. They offer significant advantages compared with the old compounds including TCAs and monoamine oxidase inhibitors (MAOI), such as fewer side effects and nonlethality in overdose [29]. However, some useful properties of the TCA, such as the promotion of sleep, do not apply to SSRIs. Indeed, the SSRIs can increase wakefulness, reduce TST, and sleep efficiency, having an alerting effect in acute treatment, although sleep disruption can ease with long-term treatment [30]. Further sleep disruption by antidepressant can lead either to disaffection with the treatment and early dropout or poor compliance, negatively affecting the overall outcome, or it could require additional treatment with a hypnotic [24].

The main TCA in our sample was amitriptyline (11 out of 15 patients) and the main SSRI was paroxetine (12 out of 15 patients). This practice appears similar to that of Netherlands where paroxetine is the most prescribed antidepressant, followed by amitriptyline, citalopram, and venlafaxine [24].

In our study, both TCAs and SSRIs were well tolerated and equally effective in treating depression. Both were effective in lowering the HAMD score; however, there was a statistically insignificant bias toward TCAs over SSRIs, which reached the sufficient response level defined as at least a 50% reduction in self-reported or observed symptoms. This difference in potential therapeutic effects of both groups could be explained by the severity of depression in our patients (all were moderate or severe scored > 14 on HAMD), and pretreatment difference between both groups on sleep parameters, which reflect to some extent better sleep quality in the TCA group.

All sleep parameters in our study were improved by both TCAs and SSRIs, except for sleep microstructure, which was not affected by both, where shortening of light sleep (stages 1 and 2) and prolongation of deep sleep (stages 2 and 4 and SWS%) showed either nonsignificant difference or significant difference but were still below the normal values. This highlighted an observation that sleep staging restoration may be a part of the remission or the recovery of the depression itself and not merely the sleep effects of antidepressant. This goes with Hicks *et al.* [25] who stated that significant drug effects on sleep, such as TST, sleep efficiency, and wakefulness after sleep onset, occurred early in treatment but stage 1 sleep and number of awakenings showed significant treatment effects more obviously at 8 weeks when the difference between different antidepressants on sleep quality disappeared. In addition, sleep microstructure may need the neuroadaptive changes that occur in the brain with prolonged administration and depression improves [31].

This observation confirmed the explanation postulated by Wilson *et al.* [30] who stated a postantidepressant treatment discrepancy between subjective and objective sleep findings, where subjective complaints about poor sleep were decreased when patients improved, in spite of lack of significant changes in objective measures of sleep as measured by PSG.

In contrast, nonimprovement of sleep microstructure found in this study could be considered as residual symptoms as reported by Nierenberg *et al.* [32] and Menza *et al.* [33], who found 44% of individuals who had achieved remission of depression, and yet had persistent sleep abnormalities.

In this study, TCAs were accompanied by more desirable sleep effects in comparison with SSRIs. All desirable sleep effects as represented in good sleep efficiency (decrease sleep latency and arousal index), shortening of light sleep (decrease in sleep stages 1 and 2), prolongation of deep sleep (increase in sleep stages 3 and 4, and SWS%) were more statistically significant in TCAs than in SSRIs group. This was not expected as our SSRIs group mainly used paroxetine, which is known as the most common SSRIs having sedative properties [34].

This weak sedative property of SSRIs in comparison with TCAs could be explained by the consequence of increased serotonin function, which leads to sleep disturbance early in treatment [35] as well as by the weak anticholinergic effects as reported by Rush *et al.* [21]. Furthermore, this finding accords Wilson and Nutt [36] findings of increased sleep disturbance after paroxetine, and Wilson *et al.* [30] who stated that TCAs tend to improve sleep fragmentation acutely, whereas SSRIs decrease sleep continuity, until there is resolution because of improvement of the depressive illness.

However, REM suppression as evident only in a decrease in REM% was more statistically significantly increased in SSRIs than in TCAs group. This finding egress the findings of Sharpley *et al.* [37] who found that REM sleep suppression remained marked throughout treatment with paroxetine in comparison with nefazodone, which had a small nonsignificant promoting effect on REM. There was no statistically significant difference between the two drug groups regarding their effect on both REM density and latency, a finding that contradicts other studies, which showed early changes of REM sleep latency and percentage and considered it as predictors of treatment outcome [38]. This contradiction may be related to the difference in time of assessment found in-between studies.

Antidepressants that increase serotonin function by blocking reuptake or by inhibiting metabolism have the greatest effect on REM sleep. The decrease in the amount of REM sleep appears to be greatest early in treatment, and gradually diminishes during long-term treatment, except after MAOIs when REM sleep is often absent for many months [39].

REM suppression occurred with all major antidepressant drugs, except trimipramine, mirtazapine, and nefazodone [40]. The MAOIs almost completely suppress REM sleep, whereas the TCAs and SSRIs have been shown to produce immediate (40–85%) and sustained (30–50%) reductions in REM sleep [41]. The clinical efficacy of antidepressant largely derives from their suppressant effects on REM sleep [42], Even though REM sleep time may be decreased, the density of REM periods may increase during antidepressant therapy [43].

However, REM suppression makes a conflict for the concept of ideal antidepressant [44] as, despite being responsible for the clinical efficacy of antidepressant, it often causes increased fatigue in patients who take large doses of antidepressants for extended periods of time. Such fatigue can occasionally interfere with a patient's everyday activities [38].

In conclusion, commonly used antidepressants in clinical practice have a positive effect on objective sleep parameters, except for sleep microstructure. TCAs significantly improved objective sleep quality away from its antidepressant therapeutic effect compared with SSRIs.

We hoped this study to be a cornerstone in future serials concerned with the effect of the new antidepressants on sleep quality early in the treatment, in order to enhance compliance with antidepressant, and to provide descriptive guidelines for effective treatment for sleep problems in depression. Selecting proper antidepressant for depression with profound sleep problems is an art that needs future research considering properties of an ideal antidepressant regarding its effect on sleep disturbances, including improving both subjective and objective sleep complaints, not causing either further sleep disruption or marked REM suppression, and rapidly improving the distribution of sleep symptoms of depression.

Limitations of this study include the small number of our sample, no comparison between subjective and objective sleep complaints for both groups, the absence of placebo group (used for comparison), and the nonseparation of the pretreatment baseline difference from the sleep effects.

There is no conflict of interest to declare.

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الملخص العربي

تأثير عقاقير الاكتئاب الأكثر استخداما علي صورة النوم فى مرضى الاكتئاب: دراسة مع عينة ضابطة

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هدف البحث: من متطلبات علاج الاكتئاب الأمثل أن يكون له تأ ثير مرغوب فيه علي النوم, لكن الدراسات التى تقارن تأثير المجموعات الدوائية بعضها ببعض مازالت قليلة في هذا المجال. و تهدف هذه الدراسة إلي مقارنة تأثير مجموعات أدوية الاكتئاب الأكثر استعمالا علي شكل النوم باستخدام معمل النوم في نسق إكلينيكي. **طريقة البحث:** و قد شملت عينة البحث 30 حالة اكتئاب جسيم جديدة مشخصة تبعا للتقسيم العالمى العاشر, لم يتعاط أفرادها أدوية كما سجل جميعهم أكثر من 14 على مقياس هاملتون. وقد خضع جميع أفراد العينة لعمل: فحص جسمانى شامل, الاختبارات المعملية الروتينية, رسم مخ, بالإضافة إلي فحص الحالة العقلية باستخدام نموذج مستشفى جامعة عين شمس. و قد تم تقسيم العينة الي مجموعتين: 1) مجموعة تعالج بمضادات الاكتئاب ثلاثية الحلقات (15 مريضا), 2) مجموعة تعالج بأدوية السيروتونين (15 مريضا). و تم اختيار 10 من الأصحاء متلائمين فى الجنس والعمر مع عينة البحث يمثلون العينة الضابطة. و خضع أفراد العينتين إلى: -استبيان مقنن لاضطرابات النوم, - مقياس هاملتون للاكتئاب, - معمل قياسات النوم. و تم تطبيق هذه الفحوص علي العينتين قبل استعمال الدواء ثم أعيد تطبيقها مرة ثانية علي أفراد عينة البحث فقط بعد شهر من العلاج. **نتائج البحث:** و قد أظهرت النتائج تحسنا عاما في صورة النوم باستعمال كلا المجموعتين- فيما عدا بعض التراكيب الدقيقة للنوم- مع بعض الفروق الطفيفة لصالح الأدوية ثلاثية الحلقات و خاصة في احساس المريض بالتحسن في النوم. **الاستنتاج:** و قد أكد البحث علي أهمية اختيار العقار المناسب في وجود مشاكل شديدة في النوم مما يجعلها نوعا من الفن (الحرفية) التي تحتاج إلى دراسات أكثر في المستقبل.