

Short Communication**Effect of trazodone on sleep bruxism in children and adolescents 6-18 years of age, a pilot study***Fereshteh Shakibaei**, *Ali Gholamrezaei***, *Shahram Heidari******Abstract**

BACKGROUND: Sleep bruxism is a common sleep disorder with unclear etiology and no definitive treatment. Recent suggested medications are not often practically used due to their numerous limitations. Based on the fact that sleep bruxism occurs most often in the second stage of non-REM sleep, this study aimed to assess the effect of trazodone on sleep bruxism.

METHODS: This pilot study was conducted as a before-after design on 28 children and adolescents with 6-18 years of age suffering from sleep bruxism referring by children and adolescents mental health clinic, children dental specialists and pediatricians. The treatment started with 0.5mg/kg/day. In non-responders, it was weekly added by 0.5 mg/kg/day (with optimum of 2 mg/kg/day). Frequency of bruxism and related morning face/jaw pain were assessed daily from two weeks before (baseline) to four weeks after starting the intervention by the parents/roommate.

RESULTS: Findings showed a significant reduction in the frequency of both bruxism and related morning pain from baseline to the 2nd and the 4th weeks of the intervention ($P < 0.001$). Minor side effects such as drowsiness, nausea and dry mouth were seen among approximately one-third of the patients. These side effects were self-limited and tolerable.

CONCLUSIONS: Trazodone could be effective in reducing the frequency of sleep bruxism and its related morning face/jaw pain. Well-designed placebo-controlled trials are needed to confirm the results.

KEY WORDS: Sleep bruxism, trazodone, teeth clenching, teeth grinding.

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Sleep bruxism (SB) is a parasomnia stereotyped movement disorder characterized by grinding or clenching of teeth during sleep, usually associated with arousals from sleep¹. It can cause pain or tiredness in masseteric muscles, headache, oral infections and sleep disturbance in patients and their family members. In long term, SB may result in teeth decay, temporomandibular joint arthrosis and lower jaw dislocation². Since its etiology and pathophysiology remained unclear, there is no specific treatment for this disorder^{3,4}. The

medications suggested by previous studies are not efficient and appropriate due to unavailability and age contraindication (tiagabine), high costs and severe side effects (gabapentin), intolerance (bromocriptine) and no considerable clinical effect⁴⁻¹¹. There is evidence that SB episodes occur most often in the second stage of non-REM sleep³. Trazodone, a widely prescribed and effective medication for insomnia¹², is a serotonin reuptake inhibitor that can increase the third and fourth stages of the non-REM sleep, which results in decreasing the

*Assistant Professor of Psychiatry, Department of Psychiatry, Alzahra Hospital, Isfahan University of Medical Sciences (IUMS), Isfahan, Iran. e-mail: shakibaei@med.mui.ac.ir (Corresponding author).

**Medical Student, Medical Student Research Committee, IUMS, Isfahan, Iran.

***Clinical Resident of Psychiatry, Department of Psychiatry, Alzahra Hospital, IUMS, Isfahan, Iran.

first and second stages¹³⁻¹⁵ and as such is supposed to be effective in this disorder. To the best of our knowledge, there is no published data on the efficacy of trazodone in this case. Therefore, this pilot study was designed to investigate the effect of trazodone in the treatment of SB given its availability, good compliance, no age contraindication and no major side effects¹⁶.

Methods

This was a cross-sectional descriptive study performed as a pilot study based on a before-after design. The population of this study included children and adolescents aged 6-18 years referred by children and adolescents mental health clinic, children dental specialists and pediatricians (Isfahan University of Medical Sciences). The inclusion criteria were existence of SB, 6-18 years of age and patients (or their parents) interested in participating in the study. Those patients with SB after taking CNS stimulant medications (e.g., methylphenidate, dextroamphetamine, etc.), those not careful in filling the weekly charts or not cooperating with medication or follow up process and also those with cardiac dysrhythmias were all excluded from the study. The operational definition of SB was the complaint of the parents on frequent friction of their children's teeth in sleep so that it can wake up their roommates¹⁷. The frequency of the roommate's wake up was considered as the frequency of bruxism. For baseline evaluation, each participant was under supervision of his/her parents or roommate for two weeks before the intervention with a weekly chart to be evaluated regarding SB frequency and related morning face/jaw pain (which is selected as one of the complications of SB). Patients then received trazodone (desyrel) tablet for four weeks. The recommended dosage for children and adolescents is 0.5-2 mg/kg/day¹⁸. The treatment started with 0.5 mg/kg/day. In non-responders, it was weekly added by 0.5 mg/kg/day (with optimum of 2 mg/kg/day). The dosage was not added and the study went on with the constant dosage if bruxism disappeared or intoler-

able side effects occurred. During the intervention, a daily chart including SB frequency, existence of morning face/jaw pain and drug complications was given to subjects' parents/roommate to fill out based on their observations. The questionnaire face validity was obtained by three children and adolescent psychiatrists. Participants were explained about the goals of the research and the researcher obtained written consents to collect data. The researchers accepted all responsibility for treatment and possible complications already explained to the participants. The primary outcomes of this study were reduction in the frequency of SB and related morning pain. Changes in the frequency of SB and related morning pain from baseline to the 2nd and 4th weeks of intervention were analyzed by paired-samples t-test. Statistical analysis was performed using SPSS 16.0 for Windows software (SPSS Inc, Chicago, IL).

Results

A total of 28 patients with SB (mean age = 13.07, SD = 2.96) participated in the current study and all of them completed the study. Seventeen (61%) patients were male and eleven (39%) were female. The history of SB was less than six months in 50% of the subjects. About 18.6% of the subjects were on psychiatric drugs for a psychiatric background disorder. There was a significant reduction in the frequency of both SB and related morning face/jaw pain from baseline to the 2nd week of intervention ($P < 0.001$). This reduction continued to the 4th week ($P < 0.001$, table 1). Side effects were seen in 36% (10/28) of patients. Four subjects suffered from dry mouth, three from drowsiness, one from nausea and two from dry mouth plus drowsiness. All of the side effects were reported as tolerable by patients.

Discussion

As SB episodes occurs most often in the second stage of the non-REM sleep³ and considering the effect of trazodone in decreasing the first and second stages of the non-REM sleep¹³⁻¹⁵ this pilot study was done to evaluate the

Table 1. Comparison of SB and morning face/jaw pain before and after the intervention.

Evaluation times	Frequency of SB	Frequency of morning face/jaw pain
Baseline	5.57 (1.79)	2.17 (3.52)
2 nd week	3.64 (2.26)	1.39 (2.69)
4 th week	1.21 (2.23)	0.25 (1.32)
	P<0.001*	P<0.001*
	P<0.001**	P<0.001**

Data are shown as mean (S.D).

* $P<0.001$, Paired-samples t-test from baseline to the 2nd week.

** $P<0.001$, Paired-samples t-test from baseline to the 4th week.

effects of trazodone on treating SB in children and adolescents. According to the results, the frequency of SB and related morning face/jaw pain were significantly reduced by two and four weeks intervention. There have been numerous studies conducted on the treatment of SB with different medications in recent years. But, they did not seem appropriate considering the expensive costs, unavailability, lack of noticeable clinical effects and tolerance and severe side effects ^{3,4}. Botulinum toxin injection in masseter muscle has been suggested as an effective treatment method for severe bruxism ¹⁰. However, the results are controversial and it is an invasive treatment that requires frequent injections to be effective. Moreover, it is unavailable and expensive. Another study has shown that tiagabine could be effective in decreasing SB frequency and its proceeding morning pain but it is contraindicated in children <12 years ⁶. This medication is also an anticonvulsant, which increases the risk of convulsion in those without the previous history of convulsion. In addition, it is expensive and unavailable with severe side effects such as dangerous rashes, visual disorders and muscle weakness ⁶. Saletu et al observed that clonazepam is effective in treatment of SB if taken in short term. But, that can be accompanied with mental and physical dependency, treatment tolerance and drowsiness in day time ⁹. Other investigators reported that bruxism resulted

from taking antidepressant drugs is well managed with gabapentin ⁵. However, besides expensive cost of gabapentin, it causes numerous side effects such as diplopia, dizziness, ataxia, nausea, vomiting, drowsiness, aggression and higher chance of viral infections; also in long term, pancreas adenocarcinoma is reported ¹⁹. Trazodone is an available and cost-effective medication with considerable treatment effects, in all stages of sleep. There is no tolerance to its treatment effects and it has no mental and physical dependency ¹². More over, it has no serious side effects and its side effects are tolerable ¹⁶. Considering the efficacy of trazodone in treatment of insomnia, some investigators ²⁰ have suggested it as a treatment for SB, but its direct effect on SB was not investigated previously. There is evidence that selective serotonin reuptake inhibitors (SSRIs) are effective in treatment of SB. Stein et al ¹⁷ reported successful treatments of two patients with SB and a comorbid psychiatric illness using SSRIs (paroxetine, citalopram). This is in contrast to beliefs that SSRIs can exacerbate bruxism ²¹⁻²³. However, there is also evidence that stereotypic movement disorder may respond well to SSRIs ^{24,25}. Although Stein et al ¹⁷ recommended antidepressants for patients with bruxism particularly when there is comorbid psychiatric illness, only 18% of patients in our study had background psychiatric disorders. More analysis of our data showed that

the results remained the same after excluding patients with comorbid psychiatric illness. Nevertheless, according to the results of this study, we concluded that trazodone can decrease the frequency of SB and related morning face/jaw pain regardless of the presence or absence of psychiatric disorders. Although, side effects such as drowsiness, nausea and dry mouth were seen among approximately one-third of the patients, these side effects were self-limited and tolerable. There were several limitations to this study, which needs to be improved before any definite conclusion. There was not a placebo-controlled group and investigators and participants were not blinded to the intervention, which could affect the results. The frequency of SB and related morning pain reported by parents/roommate is not as reliable as an objective data collection method like polysomnographic analysis, which could better record SB episodes³. Also, the treatment period (four weeks) was not long enough and the patients were not followed up. It is also recommended that future studies

select patients with a narrower age. However, this pilot study is the first reported data on the effect of trazodone on SB. We hope that future well-designed trials help to better understand the efficacy of trazodone in treatment of SB.

Conclusion

Trazodone could be effective in reducing the frequency of sleep bruxism and its related morning face/jaw pain. Well-designed double blind randomized placebo-controlled trials are warranted to confirm the results.

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