Reports of SSRI-Associated Bruxism in the Family Physician's Office

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A preliminary report of this study was presented at the Third International Congress on Orofacial Pain and Temporomandibular Disorders, May 13–14, 2000, Seoul, Korea.

Aims: *Recently, the use of selective serotonin reuptake inhibitors (SSRIs) has been associated with the occurrence or worsening of bruxism. The aim of this study was to obtain a first indication of the prevalence of SSRI-associated bruxism reported to family physicians, the main prescribers of SSRIs.* **Methods:** *A questionnaire, with questions about prescription rate, already registered adverse reactions, and bruxism-related side effects of 4 different types of SSRIs, was sent to all family physicians in greater Amsterdam (n = 391).* **Results:** *With a response rate of 42.5%, frequent observations of already registered side effects were found. In addition, 5 family physicians (3.2%) reported the occurrence of bruxism in relation to the use of SSRIs.* **Conclusion:** *The use of SSRIs might be associated with the occurrence of bruxism. A case report is provided that corroborates this suggestion.*
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Selective serotonin (5-hydroxytryptamine [5-HT]) reuptake inhibitors (SSRIs) are widely prescribed second- and third-generation antidepressants. Within this group of drugs, 4 types can be distinguished: fluoxetine, fluvoxamine, paroxetine, and sertraline. Unlike tricyclic (first-generation) antidepressants, which are both serotonin and norepinephrine uptake inhibitors, SSRIs have a high selectivity for serotonin reuptake.[1] Apparently, SSRIs enhance serotonin neurotransmission.

Besides effective treatment of depression (mood disorder),[2] a number of usually mild and transient adverse reactions have been reported with SSRIs.[3,4] Among others, the use of SSRIs has been associated with the occurrence or worsening of several so-called extrapyramidal reactions, such as akathisia, dystonia, and dyskinesia (for review, see Lane[5]), and movement disorders such as Parkinson's disease,[6–8] restless legs syndrome (RLS),[9,10] and bruxism (clenching or grinding of the teeth).[11–15] The cited papers that describe these adverse reactions concern mostly case reports and retrospective studies. With respect to bruxism, Ellison and Stanziani[11] described 4 cases in relation to the use of fluoxetine

and sertraline. In 3 of these cases, bruxism remitted with the administration of buspirone, a drug which, according to the authors, may counteract the SSRI-induced inhibition of extrapyramidal dopaminergic pathways; in the fourth case, bruxism remitted by SSRI dose reduction. Less clear cut are the cases reported by Fitzgerald and Healy.[12] These authors described the occurrence of bruxism in 6 patients who were also exposed to multiple other medicines besides SSRIs, including neuroleptic drugs, which hampers an unequivocal interpretation of their cases. Romanelli et al[13] described a single case of possible paroxetine-induced bruxism, in which buspirone caused a significant reduction in bruxism symptoms (eg, gritting, tooth pain, and jaw tenderness). In another case report, symptoms of bruxism declined after discontinuation of sertraline.[14] Finally, Stein et al[15] reported a case of a decrease rather than an increase in nocturnal bruxism in relation to paroxetine usage. So far, such a decrease has not been reported by others.

Because of the possible occurrence and/or worsening of RLS in association with the use of paroxetine, a warning was recently published in the *Dutch Drug and Therapeutics Bulletin (Gebu)*,[16] following reports of 7 cases of RLS in paroxetine users. The *Gebu* is a widely distributed publication that is readily accessible for most Dutch primary health care workers. Hence, all prescribers of SSRIs should be aware of this newly discovered adverse reaction. In contrast to RLS, the possibility of bruxism as a SSRI-associated side effect has never been published in readily accessible publications. Nevertheless, bruxism can be a major problem for the patient: Amongst others, its occurrence has been associated with tooth wear, "cracked teeth," increased dental mobility, and pain, stiffness, and fatigue in the masticatory muscles.[17] Therefore, an information letter was sent to all family physicians in greater Amsterdam to increase the awareness of the possibility of SSRI-associated bruxism among these main prescribers of SSRIs. The letter was followed by a short questionnaire. The aim of this study was to obtain a first indication of the prevalence of SSRI-associated bruxism (and other adverse reactions) reported to family physicians. It was hoped that the outcome of this study would yield a justification for the planning of further controlled postmarketing surveillance studies. A case report is included in this paper to illustrate the clinical implications of the findings.

1. Do you ever prescribe 1 or more of the 4 types of SSRIs in your office? If yes, is this on a daily, weekly, monthly, or yearly basis?
2. Do your patients ever report 1 or more of the following already registered adverse reactions to you in association with the use of 1 or more of the 4 types of SSRIs? *(see Table 2 for the list of adverse reactions)*
3. Do your patients ever report 1 or more of the following bruxism-related symptoms (occurrence and/or deterioration) to you in association with the use of 1 or more of the 4 types of SSRIs? *(see Table 3 for the list of symptoms)*
4. If the answer to #3 was positive, have you ever noticed an improvement after discontinuation of the administration or lowering the dosage?
5. If the answer to #3 was negative, do you then qualify the causality of the SSRI-bruxism relationship as unknown, possible, likely, or very likely?

Fig 1 Questionnaire concerning the prevalence of reports of bruxism (and other adverse reactions) in association with the use of SSRIs. The answers can be specified for each of the 4 types of SSRIs: fluoxetine, fluvoxamine, paroxetine, and sertraline.

Materials and Methods

The target population of the present study was family physicians in greater Amsterdam. Addresses were obtained from the Amsterdam Society of Family Physicians. An information letter was mailed on July 1, 1998, to all 391 members of this society. In that letter, reference was made to the RLS-paroxetine publication.[16] Furthermore, the phenomenon of bruxism was explained, including possible etiologic similarities between bruxism and RLS (eg, central dopaminergic imbalance).[18] In addition, information was given regarding the possibility of the occurrence of SSRI-associated bruxism, with reference to the case reports in the international literature (see above). Finally, the forthcoming mailing of a short questionnaire on this matter was announced.

On August 4, 1998, a questionnaire with 5 closed-ended questions about prescription rate, already registered adverse reactions, and bruxism-related side effects of the 4 types of SSRIs was mailed to all 391 family physicians in greater Amsterdam together with a cover letter in which the questionnaire was introduced and its relevance was stressed. The questions (Fig 1; translated from Dutch) were formulated according to suggestions by Spilker,[19] so that the adverse reactions could be categorized in several ways (eg, degree of

Table 1 Percentage of Family Physicians in Greater Amsterdam (n = 160) Who Prescribe 1 or More of the 4 Types of SSRIs on a Daily, Weekly, Monthly, or Yearly Basis

Frequency	Fluoxetine (n = 129)	Fluvoxamine (n = 128)	Paroxetine (n = 150)	Sertraline (n = 40)	χ^2	*P*
Daily	0.8	0.0	0.7	0.0	1.228	.746
Weekly	27.9	21.9	35.3	5.0	16.986	.001*
Monthly	51.9	52.3	52.7	37.5	3.222	.359
Yearly	19.4	25.8	11.3	57.5	41.005	.000†

n = 160; missing = 3; total prescription rate = 98.2%.
*Paroxetine was prescribed more frequently than the average weekly prescription rate; sertraline was prescribed less frequently than the average weekly prescription rate.
†Paroxetine was prescribed less frequently than the average yearly prescription rate; sertraline was prescribed more frequently than the average yearly prescription rate.

association with the medicine). Unfortunately, an already validated questionnaire of this kind was not available. Therefore, and in the absence of a readily accessible "gold standard," the authors followed the approach described in Hulley and Cummings[20] to validate the instrument more or less subjectively; with the expert judgment of 2 colleagues (a specialist in temporomandibular disorders/orofacial pain and a physician), a satisfactory level of content validity was achieved. To ascertain satisfactory levels of accuracy and reliability, the questionnaire was pretested, revised (ie, shortened), and again pretested for clarity of the questions and instructions with the help of 2 respondents who were not included in the "final" study, again following the procedures described in Hulley and Cummings.[20] No follow-up questionnaire was planned so as to keep the interval between receipt of the information letter and delivery of the questionnaire the same for all respondents, thus making the answers as comparable as possible.

For data analysis, descriptive statistics were obtained (counts and percentages). Differences in proportions between types of SSRIs were analyzed with chi-square tests. Significance was set at the .05 probability level. For all statistical procedures, the SPSS 9.0 package (1998) was used.

Results

Questionnaire Response Data

Of the 391 questionnaires that were sent out, 166 were returned, for a response rate of 42.5%.

The results of the questions 1 to 3 are given in Tables 1 to 3. Table 1 shows the SSRI prescription rates. The percentages are given for each type of SSRI and are specified for prescriptions on a daily, weekly, monthly, and yearly basis. It can be seen that paroxetine is prescribed more frequently on a weekly basis, but less frequently on a yearly basis than the average weekly and yearly prescription rates. For sertraline, findings were the opposite: This type of SSRI is prescribed less frequently on a weekly basis, but more frequently on a yearly basis than the respective average rates.

The percentages of reported and already registered adverse reactions associated with the use of the 4 types of SSRIs are given in Table 2. Six types of adverse reactions (ie, agitation, sweating, dry mouth, sexual disturbances, sleep disturbances, and gastrointestinal disturbances) were reported less frequently in association with sertraline than with the other types of SSRIs. However, following the classical Bonferroni correction for multiple comparisons, only the lower percentage of reported sexual disturbances remained statistically significant.

In Table 3, it can be seen that reports of bruxism-related symptoms associated with the use of the 4 types of SSRIs were relatively rare; the total reporting rate was only 3.2%. While increases in tooth wear were never reported to the family physicians, 5 physicians reported clenching and/or grinding as well as masticatory muscle pain, stiffness, and/or fatigue among their patients in association with the use of fluoxetine and paroxetine. No differences in percentages of reported symptoms were found between the 4 types of SSRIs.

One of 5 positive responders to the questionnaire item about bruxism observed an improvement of bruxism-related symptoms in their patient after discontinuation of the administration of the drug. A similar observation will be described in the subsequent case report. The 5 positive responders qualified the causality of the SSRI-bruxism rela-

Table 2 Percentage of Family Physicians in Greater Amsterdam (n = 149) to Whom Adverse Reactions Associated with the Use of the 4 Types of SSRIs Were Reported

Adverse reaction	Fluoxetine (n = 120)	Fluvoxamine (n = 118)	Paroxetine (n = 140)	Sertraline (n = 35)	χ^2	*P*
Agitation	33.3	22.0	27.9	8.6	10.053	.018*
Anxiety	25.8	20.5	19.3	8.6	5.262	.154
Confusion	15.0	14.4	14.3	5.7	2.133	.545
Headache	23.3	22.0	19.3	8.6	3.960	.266
Tremor	9.2	7.6	10.7	0.0	4.330	.228
Sweating	24.2	24.6	31.4	5.7	10.029	.018*
Dry mouth	37.5	36.4	40.7	11.4	10.638	.014*
Sexual disturbances	42.5	29.7	43.6	8.6	17.166	.001*
Sleep disturbances	35.0	27.1	40.0	11.4	12.584	.006*
Movement disorders	3.3	1.7	7.9	2.9	6.611	.085
Extrapyramidal reactions	1.7	3.4	5.7	0.0	4.626	.201
Gastrointestinal disturbances	50.0	55.1	49.3	20.0	13.566	.004*
Other reactions	6.7	5.1	7.1	0.0	2.887	.409

n = 149; missing = 17; total reporting rate = 100%.
*Sertraline showed fewer reports of agitation, sweating, dry mouth, and sexual, sleep, and gastrointestinal disturbances than the average percentage of reporting these adverse reactions. After the classical Bonferroni correction for multiple comparisons, only the reaction "sexual disturbances" remained statistically significant.

Table 3 Percentage of Family Physicians in Greater Amsterdam (n = 5) to Whom Bruxism-Related Symptoms (Occurrence and/or Deterioration Associated with the Use of the 4 Types of SSRIs) Were Reported

Adverse reaction	Fluoxetine (n = 120)	Fluvoxamine (n = 128)	Paroxetine (n = 150)	Sertraline (n = 35)	χ^2	*P*
Clenching and/or grinding	1.7	0.0	2.1	0.0	3.101	.376
Masticatory muscle pain/stiffness/fatigue	0.8	0.0	1.4	0.0	2.096	.553
Increase of tooth wear	0.0	0.0	0.0	0.0	—	—

n = 5; missing = 10; total reporting rate = 3.2%.

tionship as unknown (n = 1), possible (n = 2), likely (n = 1), and very likely (n = 1).

Case Report

On November 30, 1998, a 43-year-old woman was examined in the authors' clinic for temporomandibular disorders and orofacial pain for a complaint of intense clenching. She had been diagnosed by her family physician with depression, for which she took paroxetine. Between March and August 1998, the dosage was 20 mg per day, followed by a medication-free period in September. In October 1998, she took 10 mg per day, after which the dosage was increased to 20 mg per day, starting November 1, 1998, and maintained until the day of her visit to the authors' clinic.

The patient perceived positive changes in her depression by about 3 weeks after the start of the paroxetine administration, suggesting a good effectiveness of the medicine. At the start of the therapy, she noted some adverse reactions: agitation, headache, and restless legs. These reactions were temporary and disappeared in a couple of days. In addition, she experienced tremors, sexual disturbances, sleep disturbances, and obstipation. These reactions persisted throughout the therapy. The presence of sleep disturbances was corroborated

by the patient's high score on the sleep disturbances scale of the Dutch version of the Symptom Checklist 90 (SCL-90).[21]

At an unspecified point during the treatment, the patient herself noted the occurrence of bruxism-related symptoms in association with the use of paroxetine. She was aware of intense clenching, both while awake and during sleep, every day of the week for almost 24 hours per day. Episodes of bruxism activity were of moderate to severe intensity and lasted for several minutes. She also reported some masticatory muscle problems (stiffness and fatigue), although these symptoms were not among her main complaints. During the clinical examination of the masticatory system, the findings from the oral history were confirmed: No pain could be provoked in the muscles and joints, nor were there any functional disturbances such as joint sounds or a limited mouth opening. Intraorally, very pronounced hyperkeratotic lesions were observed on the mucosa of the cheeks, tongue, and lips. Mild to moderate attrition was present in the anterior part of the dental arches.

In September 1999, when the paroxetine administration was temporarily discontinued, the patient noted a marked decrease in the bruxism-related symptoms, while her depression deteriorated. After the paroxetine therapy was resumed, the depression improved slightly and the clenching behavior began again, even with the initially lower dosage of only 10 mg per day. According to the patient, the bruxism-related symptoms were practically nonexistent before the start of the paroxetine administration. She qualified the causality of the paroxetine-bruxism relationship as very likely.

Discussion

The results of the present questionnaire study suggest that at least the SSRI types paroxetine and fluoxetine might be associated with the occurrence of bruxism. The described case report corroborates this suggestion. Clenching and/or grinding and masticatory muscle symptoms were especially reported; the total reporting rate, 3.2%, is only slightly lower than that of the already registered adverse reactions "movement disorders" and "extrapyramidal reactions." The mechanism behind this suggestion is still unclear, but one might speculate that the many interactions between the serotonergic and the dopaminergic neurotransmitter systems are somehow involved.[5,22] At least for the dopmaninergic system, an involvement in the etiology of bruxism has been demonstrated.[18,23,24]

The case report in this paper is of special interest because of the variations in the dosage of paroxetine that the patient took between March and November 1998. The clenching and masticatory muscle symptoms became apparent during the first period of her treatment, disappeared when she refrained from paroxetine for 1 month, and reappeared as soon as the paroxetine regimen was reinstated. An improvement in bruxism-related symptoms after the discontinuation of SSRI therapy was observed by 1 of the positive responders to the third question of the questionnaire as well. Taken together, this supports a possible causal relationship between paroxetine and bruxism.

The suggestion that the depression, for which the SSRI was prescribed, was itself the cause of the bruxism-related symptoms is refuted by the fact that during the paroxetine-free month, the patient's symptoms of bruxism more or less disappeared, while the depressive symptoms reappeared. Unfortunately, this case was not documented with polysomnography (the current "gold standard" for a bruxism diagnosis),[17] so that the presence of clenching was determined solely on the basis of the oral history. However, the patient was a health care worker herself, which increases the reliability of her report.

The fact that in the questionnaire, increases in tooth wear were never reported in association with the use of SSRIs is not surprising, because as long as the severity of the attrition is only mild to moderate, this phenomenon is seldom recognized by bruxers themselves, let alone their family physician. Moreover, the average "physiologic" attrition rate is about 50 to 65 μm per year,[25] and this might increase only slightly with bruxism, which makes it even less likely that a patient would notice an acceleration of such a slow process during the usually restricted period of SSRI therapy.

No bruxism-related symptoms were reported in association with fluvoxamine and sertraline. While sertraline was prescribed less frequently than the other types of SSRIs (Table 1) and is therefore less likely to be associated with symptoms of bruxism for reasons of limited statistical power, fluvoxamine had only a slightly lower prescription rate than fluoxetine and paroxetine. Since the pharmacologic mechanisms of the 4 types of SSRIs, ie, enhancement of serotonin neurotransmission, are similar, the different finding for fluvoxamine may be the result of differences in pharmacokinetic properties. However, it should be noted that no statistically significant differences in the percentage of reported bruxism-related symptoms between the 4 types of SSRIs could be detected.

At first glance, the 42.5% response rate of the questionnaire seems low, and it is unclear how this rate might have affected the results. However, since the target population consisted of family physicians, a group of health care workers whose professional interest is not primarily focused on a mainly dental problem such as bruxism, the response rate may be considered acceptable. The information letter that was sent about 5 weeks before the questionnaire would have helped draw the recipients' attention to the possibility of bruxism-related symptoms as side effects of SSRIs. This increases the reliability of the answers given in the returned questionnaires. As mentioned in the Materials and Methods section, we decided against sending a follow-up questionnaire to increase the response rate, because we wanted to keep the duration of the interval between receipt of the information letter and delivery of the questionnaire the same for all respondents so as to make the answers as comparable as possible.

The percentages of reports of already registered adverse reactions to SSRIs (Table 2) are comparable to those reported in other studies.[3,4] This increases the validity of the percentage of bruxism-related symptoms that was reported in the present study. The lower percentage of reported sexual disturbances in the present study for sertraline with respect to the other types of SSRIs may be a result of the relatively low prescription rate of this type of SSRI (Table 1), which reduces the chance that side effects will be reported.

Although this study cannot be considered conclusive due to its design (eg, no objective measures of bruxism were recorded), its results justify further polysomnographic and placebo-controlled research (postmarketing surveillance studies). For instance, the effects of the start of the administration of an SSRI/placebo (or an increase in dosage) on the occurrence of bruxism-like behavior could be studied in the controlled environment of a sleep laboratory. Similarly, the effects of discontinuation or a decrease in dosage could be evaluated, although the so-called discontinuation syndrome might complicate this particular avenue.[26] Finally, the effects of the appropriate antidote for SSRIs, buspirone,[27,28] an anxiolytic drug that is suggested to restore the central dopaminergic imbalance, could be studied polysomnographically. If a bruxism-SSRI relationship can be demonstrated in such studies, their outcome should be published in a journal that is readily accessible for most primary health care workers, family physicians, and dentists alike.

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