

The efficacy of paroxetine for oral psychosomatic diseases

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Abstract

In this investigation, we evaluated a population of patients (8 females) with glossodynia, depressive xerostomia, atypical facial pain, and abnormal sensation of the saliva who received treatment with oral administration of paroxetine at the department of dentistry, oral and maxillofacial surgery in our university.

The effect of paroxetine on pain in the tongue or in the face were measured using the visual analogue scales (VAS) in 6 patients. The Clinical Global Impression of Change scale (CGI-C) was recorded at each visit.

The final dose of paroxetine ranged from 10–20mg. The baseline values of pain on VAS were (mean) 76.7%. The mean percentage changes of VAS at endpoint were -87.7%.

Paroxetine was effective on CGI-C in all cases, consisting of Very much improved in 6 patients, Much improved in 2 patients.

Paroxetine has similar in efficacy to tricyclic antidepressants and lower incidence of side effects. However, the placebo often shows the effect for the patients with psychosomatic disease, further investigation is necessary to examine the efficacy.

(key words: oral psychosomatic disease, paroxetine, SSRI antidepressant)

I. Introduction

Glossodynia, depressive xerostomia, atypical facial pain, and abnormal sensation of the saliva as they say oral psychosomatic diseases are well-known chronic orolingual and orofacial pain or oral abnormal sensation.

Tricyclic antidepressants are effective in treating oral psychosomatic disease, but the side-effects, such as sleepiness, dry mouth, constipation and weight gain prevent such patients from taking sufficiently high doses.

Paroxetine is selective serotonin uptake inhibitors (SSRIs), which are being investigated as an antidepressant.

SSRIs are as effective as tricyclic antidepressants in the treatment of depression, but have distinct tolerability advantages; they are not associated with anticholinergic adverse effects, cardiotoxicity, sedation or weight gain.

The administration of paroxetine showed the effect exceeding the expectation.

This paper reports the favorable effect of paroxetine for patients with oral psychosomatic diseases.

II. Patients and methods

The subjects consisted of 8 patients with oral psychosomatic disease, and are classified 4 diseases such as glossodynia, depressive xerostomia, atypical facial pain, and abnormal sensation of the saliva who presented themselves at Jichi Medical School Hospital. No local or systemic disease was found. No organic lesions are noted in the oral and maxillofacial lesions. They had no history of significant psychiatric illness. The drug was given orally in a daily dose of 20mg for longer than 3 weeks. Some antianxiety drugs were used concurrently, when necessary.

The effect of paroxetine on pain in the tongue or in the face were measured using the visual analogue scales (VAS) in 6 patients. The VAS was evaluated at selection; at baseline; at weeks 1,2,4 and 8 ; and endpoint (week 12 or last visit). The VAS consists of 100-mm horizontal line with descriptors that range from "not at all" to "extreme".

The Clinical Global Impression of Change scale (CGI-C) was evaluated at selection; at baseline; at weeks 1,2,3,4 and 8 ; and at endpoint (week 12 or last visit). The CGI-C is a 7-point scale ranging from 1=Very much improved, through 4=neither better nor worse, to 7=Very much worse.

III. Results

Ages ranged from 37 to 84 (average: 61.5). All patients were female. The final dose of paroxetine ranged from 10-20mg. The baseline values of pain on VAS were (mean) 76.7% (Table 1).

Table 1 Patients characteristics

Case	Age	Sex	Clinical diagnosis	VAS (Baseline)	Dose (mg)	Combined medication
1	58	F	Glossodynia	100	20	clotiazepam
2	82	F	Glossodynia	80	20	
3	64	F	Glossodynia	80	20	
4	52	F	Glossodynia	60	20	
5	67	F	Glossodynia	80	10	
6	37	F	Atypical facial pain	60	20	
7	58	F	Xerostomia	—	20	
8	74	F	Abnormal sensation of the saliva	—	20	sulpiride
Mean	61.5	—	—	76.7	19.9	—

Table 2 Efficacy of paroxetine

Case	VAS at endpoint (% change)	Change from baseline CGI-C at endpoint (Improvement)	Side effects
1	-95	Very much improved	
2	-99	Very much improved	
3	-100	Very much improved	headache, vomiting
4	-60	Much improved	
5	-100	Very much improved	
6	-72	Very much improved	drowsiness
7	—	Much improved	
8	—	Very much improved	

The efficacy of paroxetine is as in Table 2. Six patients were available for analysis at the end of the study. Paroxetine was effective in 6 cases, consisting of 6 patients who showed a marked reduction (decrease in VAS > 50%) of pain. The mean percentage change of VAS at endpoint was -87.7%.

Paroxetine was effective on CGI-C in all cases, consisting of Very much improved in 6 patients, Much improved in 2 patients.

In two patients side effects were revealed as follows: all being slightly, headache and vomiting in one patient, drowsiness in one patient. Eighty-eight percent of the patients complained of no severe side effects even when it was administered for a prolonged period.

IV. Case reports

Case1

A-58-year-old female was gone to our hospital because of severe tongue pain.

The patient was consulted to this hospital since no accurate diagnosis was made by several dentists whom she had consulted. No organic lesions are noted in her tongue. Clinical diagnosis was glossodynia. Amitriptyline hydrochloride was given orally in a daily dose of 50mg in 1 divided portion for 9 consecutive months. Resistance is appeared by the continuous administration of this drug.

The increased amount was given in a daily dose of 75mg for 6 months. However, the problem of drug-resistance and side effects such as dry mouth and weight gain in long-term administration has arisen. Amitriptyline hydrochloride was switched over to paroxetine that was given orally in a daily dose of 20mg and concomitantly treated with clonazepam that was given orally in a daily dose of 15mg in 3 divided portion for two weeks.

Three days after administration of them showed the effect exceedingly. No side effects were recognized even when it was administered for 6 consecutive months. There is no sign of recurrence.

Case2

A-82-year-old female was referred to the department of dentistry oral and maxillofacial surgery of our university by her dentist as she had complained of severe tongue pain for a long period.

The patient's previous history has nothing to be described in particular. No organic lesions are noted in her tongue. Paroxetine was given orally in a daily dose of 20mg in 1 divided portion. Seven days after administration of this drug showed the effect exceedingly. No side effects were recognized even when it was administered for 9 consecutive months. Favorable progress has been made after administration.

Case3

A-64-year-old female was referred to the department of dentistry oral and maxillofacial surgery of our university by her otorhinolaryngologist as she had complained of severe tongue pain. A significant local white lesion is noted in the dorsum of the tongue where steroidal ointment is administered for 3 months by her otorhinolaryngologist. Clinical diagnosis was candidiasis initially. She was underwent local application of miconazol gel initially. Persistent pain continues although white lesion has disappeared. No organic lesions are noted in her tongue. The patient was diagnosed as glossodynia. Paroxetine was given orally in a daily dose of 20mg in 1 divided portion. Three days after administration of this drug she complained headache and vomiting. The patient revealed spontaneous recovery without discontinuity its administration within 3 days after she has suffered side effects. Seven days after administration of this drug showed the effect exceedingly. There is no sign of recurrence.

Case4

A-52-year-old female was referred to the department of dentistry oral and maxillofacial surgery of our university by her dentist as she had complained of severe tongue pain for 3-4 months. No organic lesions are noted in her tongue. The patient was diagnosed as glossodynia. Paroxetine was given orally in a daily dose of 20mg in 1 divided portion. Tongue pain were reduced by half 7 days after it was administered. No side effects were recognized even when it was administered for 3 consecutive months. Being administered with this medicine, tongue pain took a favorable turn.

Case5

A-67-year-old female who was treated by a dentist in his neighborhood was referred to the department of dentistry oral and maxillofacial surgery of our university hospital as she had pain in the tip of the tongue.

No organic lesions were noted without slightly flared in the tip of the tongue. The patient's previous history has nothing to be described in particular. A patient could not get sufficient sleep and often awakened in the night. The patient was diagnosed as glossodynia. Paroxetine was given orally in a daily dose of 10mg in 1 divided portion. All the symptoms have disappeared after 2 months. There is no sign of recurrence.

Case6

A-37-year-old female was referred to the department of dentistry oral and maxillofacial surgery of our university by her physician as she had complained of facial pain for 6 months. No organic lesions were noted in her oral and maxillofacial region. She moved from the west

city to the east city one year ago.

Environmental changes caused psychic tension since then. The following symptoms were observed.

The patient could not get sufficient sleep and often awakens in the night. The patient feels sick whenever she was jostled in a crowd of people. On these bases, the patient was diagnosed as atypical facial pain.

Paroxetine was given orally in a daily dose of 20mg in 1 divided portion. Seven days after administration of it showed the effect exceedingly. Presently, local unpleasantness is subjectively felt under weather change.

No severe side effects were recognized without minimal drowsiness even when it was administered for 8 consecutive months. There is no sign of recurrence. We will reduce the dose of it as the progress is made toward recovery

Case7

A-58-year-old female was referred to the department of dentistry oral and maxillofacial surgery of our university by her dentist as she had complained of xerostomia for 8 months. No definite diagnosis was made although the patient was examined at different institutions. There were no grounds for supporting a diagnosis of Sjogren's syndrome. She was notified that there were no specifically effective therapies for this disease by a dentist. The patient felt very tired at all times for a long-time. The patient often awakened in the night as his sleep was not deep enough. On these bases, the patient was diagnosed depressive xerostomia. Paroxetine was given orally in a daily dose of 20mg in 1 divided portion. Reduction of subjective symptoms were noted 7 days after paroxetine was administered. No side effects were recognized even when it was administered for 4 consecutive months.

Case8

A-74-year-old female was referred to the department of dentistry oral and maxillofacial surgery of our university by her physician as she had complained of abnormal sensation of the saliva. The patient complains of sticky in her saliva and the saliva overflows from her oral cavity. The patient noted the mild anorexia and the insomnia. The patient periodically became irritated. As a course of therapy, we decided that psychosomatic therapy was absolutely necessary for this patient. Paroxetine was given orally in a daily dose of 20mg in 1 divided portion. Paroxetine was given orally in a daily dose of 20mg and concomitantly treated with sulpiride that was given orally in a daily dose of 150mg in 3 divided portion for three weeks. All the symptoms reduced 5 days after those drugs were administered. No side effects were recognized even when it was administered for 5 consecutive months.

V. Discussion

The oral cavity is location for different conditions of local and systemic origin ; many of them with controverted and or multifactorial etiology, where the psychogenic factors constitute an important variable to be considered.

In the patients complain of only tongue pain, facial pain, xerostomia, or abnormal sensation of the saliva slightly, in general, clinicians have the tendency to diagnose patients with an oral

psychosomatic disease, according to the traditional criteria for psychosomatic disease¹⁾. Some patients with such symptoms could be diagnosed as borderline cases between psychiatric disease and psychosomatic disease.

A considerable number of clinical cases have been reported on the efficacy of tricyclic antidepressants, including amitriptyline, to treat chronic orolingual and orofacial pain.^{2),3)}

Glossodynia is thought to be a disorder with a wide range of possible causes.

As for the pathophysiology of glossodynia, Toyofuku et al.⁴⁾ suggested two aspects;

- 1) Biochemical dysfunction of noradrenergic and serotonin neurotransmission in the trigeminal nerve pathway.
- 2) False connection between teeth and an undefined tongue pain due to cognitive processes in the association cortex.

Secretion of saliva is evidently varied by the degree of psychological stresses. Salivary gland strongly governed by the autonomic nervous system. Xerostomia can lead to dysgeusia, glossodynia, sialadenitis, cracking and fissuring of the oral mucosa, and halitosis⁵⁾. Our results suggest that serotonin may play an important role in the pathophysiology of depressive xerostomia and abnormal sensation of the saliva.

Chronic orofacial pain patients frequently undergo numerous dental procedures that fail to the oral and maxillofacial surgeon for evaluation and treatment⁶⁾. Depression is a common serious disorder that has a high comorbidity with chronic atypical facial pain⁷⁾. This fact enables us to explain the effect of paroxetine qualitatively.

The clinical pharmacology, adverse event profiles, and clinical efficacy of several serotonin reuptake inhibitors are summarized and compared with those of the classic tricyclic antidepressants⁸⁾. Serotonin reuptake inhibitors discussed are sertraline, zimelidine, fluoxetine, fluvoxamine, and paroxetine. While they do not differ from tricyclics in efficacy or onset of action, the serotonin reuptake inhibitors clearly have a different side effect potential. Unlike tricyclics, serotonin reuptake inhibitors provide effective antidepressant activity without sedating, anticholinergic, or cardiotoxic reactions.

It is important to choose antidepressant therapy on the basis of a patient's ability to tolerate the specific adverse reactions that may occur with a given agent.

Paroxetine is a second generation antidepressant that selectively inhibits neuronal reuptake of serotonin (5-hydroxytryptamine; 5-HT). Paroxetine exhibits antidepressant activity similar to that of the tricyclic antidepressants, but has a somewhat improved tolerability profile, particularly with respect to a lower incidence of anticholinergic effects and reduced cardiotoxic potential. However, gastrointestinal adverse effects, especially nausea, are seen more frequently with paroxetine than with the tricyclic antidepressants.

In most patients, the onset of drug efficacy was observed within 1 week. No side effects were recognized even when it was administered for a prolonged period.

Depression is often an important component of the psychological profile of the oral psychosomatic diseases. Not only functional psychosomatic symptoms are expression of depressive experience, also organic detectable disorders and diseases often show depressive backgrounds which are based on inner or general isolation. Recently, we often find combina-

tions and changes of the different pathological symptoms: depressives who predominantly suffer from somatic symptoms—masked depressions—states of pain, which manifest themselves in somatic symptoms often without organic cause. There are some patients that have been initially diagnosed with a psychosomatic disease but whose diseases progressed to psychiatric diseases such as depression and schizophrenia^{9,10,11}). In this study, depression was suspected in Case 5,6,7, and 8. Mukai reported that DSM-IV is very useful for diagnosing borderline patients between psychosomatic disease and psychiatric disease¹⁰).

Our results suggest that paroxetine has similar in efficacy to tricyclic antidepressants and lower incidence of side effects. However, the placebo often shows the effect for the patients with psychosomatic disease. Further investigation is necessary to examine the efficacy, incidence and degree of side effects as accurately as possible for patients with oral psychosomatic disease.

VI. References

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口腔心身症に対する paroxetine の効果

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要 約

従来、口腔心身症に対する治療においては、その高い効果から三環系抗うつ薬が用いられてきたが、抗コリン作用による口渇や眠気などの副作用のため十分な投与量が得られない症例をしばしば経験してきた。今回われわれは、口腔心身症の症例に対して三環系抗うつ薬と作用機序が異なる選択的セロトニン再吸収阻害薬である paroxetine を投与し、その効果について検討した。

対象は、当科を受診した口腔心身症と診断された8例（全て女性）で、内訳は舌痛症5例、口腔乾燥症、唾液異常感症と非定型顔面痛が各1例であった。

効果判定は、疼痛を主訴とした6例に対しては visual analogue scales (VAS) を用い、全例にたいして Clinical Global Impression score (CGI) を用いた。8例全てに症状の改善を認めた。副作用は、重篤なものはなく、2例に軽度の頭痛、嘔吐、眠気が認められたがいずれも特に処置を必要とせず回復した。Paroxetine は口腔心身症に対して効果的であることが示唆されたが、心身症はプラセボが効きやすい疾患でもあるため、今後さらに症例を増やし検討を続ける必要があるものと思われた。

（キーワード：口腔心身症，パロキセチン，SSRI）