

The effectiveness of acupuncture versus clonazepam in patients with burning mouth syndrome

A Jurisic Kvesic,¹ I Zavoreo,² V Basic Kes,² V Vucicevic Boras,³ D Ciliga,⁴ D Gabric,⁵ D V Vrdoljak⁶

¹Private Dental Practice, Zagreb, Croatia

²Clinic for Neurology, Clinical Hospital Centre Sisters of Mercy, Zagreb, Croatia

³Department of Oral Medicine, School of Dental Medicine and Clinical Hospital Centre, Zagreb, Croatia

⁴Faculty of Kinesiology, University of Zagreb, Zagreb, Croatia

⁵Department of Oral Surgery, School of Dental Medicine, University of Zagreb, Zagreb, Croatia

⁶Clinic for Tumours, Clinical Hospital Centre Sisters of Mercy, Zagreb, Croatia

Correspondence to

Dr V Vucicevic Boras, School of Dentistry, University of Zagreb, Gundulićeva 5, and Clinical Hospital Centre Zagreb, Kispaticeva 12, Zagreb 10 000, Croatia; boras@sfzg.hr

Accepted 29 April 2015

ABSTRACT

Objective Burning mouth syndrome (BMS) is a chronic oral condition, characterised by burning symptoms, which mainly affects perimenopausal and postmenopausal women. Neuropathy might be the underlying cause of the condition. There are still insufficient data regarding successful therapy. The aim of this study was to compare the effectiveness of acupuncture and clonazepam.

Methods Forty-two patients with BMS (38 women, 4 men) aged 66.7±12.0 years were randomly divided into two groups. Acupuncture was performed on 20 participants over 4 weeks, 3 times per week, on points ST8, GB2, TE21, SI19, SI18 and LI4 bilaterally as well as GV20 in the midline, each session lasting half an hour. Twenty-two patients took clonazepam once a day (0.5 mg in the morning) for 2 weeks and, after 2 weeks, two tablets (0.5 mg in the morning and in the evening) were taken for the next 2 weeks. Prior to and 1 month after either therapy, participants completed questionnaires: visual analogue scale, Beck Depression Inventory, Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) pain scale, 36-item Short Form Health Survey (SF-36) and Montreal Cognitive Assessment (MoCA).

Results There were significant improvements in the scores of all outcome measures after treatment with both acupuncture and clonazepam, except for MoCA. There were no significant differences between the two therapeutic regimens regarding the scores of the performed tests.

Conclusions Acupuncture and clonazepam are similarly effective for patients with BMS.

INTRODUCTION

Burning mouth syndrome (BMS) is a chronic condition characterised by burning symptoms in the oral cavity, which usually affects perimenopausal and

postmenopausal women. It seems that underlying neuropathy (either peripheral, central or both) might be the cause of the condition. Treatment of patients with BMS is mostly based on medication, although cognitive behavioural therapy certainly helps patients to cope better with the condition.¹ Drugs whose effectiveness in the management of BMS has been established in clinical trials are: α-lipoic acid, topical and systemic clonazepam, systemic capsaicin, trazodone, amisulpride, paroxetine and sertraline.²⁻³ However, some of these medications have side effects, such as drowsiness from clonazepam, gastric pain from systemic capsaicin, and drowsiness and dizziness from trazodone.² Topical clonazepam may be absorbed systemically and lead to benzodiazepine dependence if used for a prolonged period.³

Acupuncture is well known to be helpful in many other painful conditions such as low back pain, headaches and migraine, osteoarthritis and diabetic peripheral neuropathy.⁴ Although the literature published to date in Chinese supports the use of acupuncture in BMS, there are few published studies in the Western literature on the effect of acupuncture in patients with BMS.⁵⁻⁸

The aim of this study was to compare traditional Chinese acupuncture and clonazepam in the treatment of BMS.

MATERIALS AND METHODS

A randomised controlled trial was conducted comparing 4 weeks of treatment with acupuncture or clonazepam.

Patients were randomised by the simple randomisation method of flipping a coin (heads: acupuncture; tails: clonazepam).

To cite: Jurisic Kvesic A, Zavoreo I, Basic Kes V, et al. *Acupunct Med* Published Online First: [please include Day Month Year] doi:10.1136/acupmed-2015-010759

Table 1 Baseline characteristics of study patients

	Acupuncture group	Clonazepam group
Age	66.7±12 years	63.2±14 years
Gender (male/female)	2/19	2/19
Sinusitis	2	2
Statoacoustic apparatus disturbances	4	2
Dysgeusia	3	3
Dry mouth	7	6
Cardiovascular disease	4	4
Cerebrovascular disease	1	0
Extrapyramidal symptoms	1	2
Thyroid disease	2	2
Diabetes mellitus	1	1
Smoking	2	1
Alcohol consumption	0	0
Stress in detailed medical history	14	15
Anxiodepressive symptoms	19	21

Forty-two patients with BMS (38 women and 4 men) of mean age 66.7±12.0 years were included in the study, which was the number eligible and giving consent from those referred to the Department of Oral Medicine in Zagreb during the study period from March to November 2014.

Inclusion criteria were symptoms of burning in the oral cavity with clinically healthy appearance of the oral mucosa. Burning symptoms had to be continuous throughout the day and to have lasted for more than 6 months. Some of the patients also had hyposalivation⁹ and disturbed taste.⁶ No other treatments for concomitant oral disturbances (such as hyposalivation or disturbed taste) were given to patients during the course of the study.

Prior to either therapy and 1 month after completion of the therapy, every participant completed the following questionnaires: visual analogue scale (VAS) scoring the severity of burning symptoms, Beck Depression Inventory (BDI), the Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) pain scale, 36-item Short Form Health Survey (SF-36) total sum score and Montreal Cognitive Assessment (MoCA).

Traditional Chinese acupuncture was performed on 20 participants three times per week for 4 weeks on points ST8 (*Tou Wei*), GB2, TE21, SI19 (*Ting Gong*), SI18 (*Quan Liao*), LI4 (*Yuan*) bilaterally as well as GV20 (*Bai Hui*), each session lasting half an hour. We used sterile acupuncture needles (Shenzhou, Shanghai, China) of surgical stainless steel, silicone coated, with a spring handle, 0.25 mm diameter and 30 mm length, inserted to a depth of 0.5–1 cun. Needles were not stimulated manually. The elicited *de qi* response was accompanied by redness and a feeling of numbness around the needles.

In the medication group, 22 patients took clonazepam once a day (0.5 mg in the morning) for the first 2 weeks and, after 2 weeks, one tablet (0.5 mg) in the morning and another tablet (0.5 mg) in the evening for a further 2 weeks.

Statistical analysis was performed with the Student t test and Pearson correlation test; p Values <0.05 were considered significant.

The study was approved by the Ethical Committee of the School of Dentistry in Zagreb. Prior to the study, each participant gave signed informed consent according to the Declaration of Helsinki II. All patients were recruited from the Department of Oral Medicine, School of Dentistry, Zagreb.

RESULTS

All patients completed the treatment and there were no dropouts. Five patients in the clonazepam group reported side effects (drowsiness, dizziness and nausea), but no adverse events were reported by the acupuncture group.

There were no significant differences in general health status (cardiovascular and cerebrovascular diseases, movement disorders, neuromuscular disorders, neoplasms, pathology of the paranasal sinuses, diabetes, arterial hypertension, hyperlipidaemia, thyroid disorders) compared with an age- and sex-standardised population, except for a history of *Helicobacter pylori*. However, increased anxiodepressive symptoms were identified in the detailed medical history of the patients as well as stress. According to these findings, the patients did not differ from the general population with regard to drug intake, except

Table 2 Test scores before and after treatment with acupuncture and clonazepam

	Before acupuncture	After acupuncture	Before clonazepam	After clonazepam
Visual analogue scale	7±3	4±3*	6±4	3±2*
Beck Depression Inventory	20±5.1	15±4.1*	21±4.8	14±3.7*
LANSS pain scale	15.5±2.8	9±2.2*	14.2±3.1	8±1.8*
SF-36	71.6±4.5	85.6±5.2*	73.4±5.2	86±4.7*
MoCA cognitive test	27±2	28±1	28±2	28±2

*p<0.05 within groups.

LANSS, Leeds Assessment of Neuropathic Symptoms and Signs; MoCA, Montreal Cognitive Assessment; SF-36, 36-item Short Form Health Survey.

for triple *H pylori* therapy. Complete blood count, serum iron concentration, vitamin B12 and folic acid status were determined in all patients and all findings were within the normal range. There were no significant differences regarding concomitant oral symptoms such as dysgeusia and dry mouth. The baseline characteristics of the two groups are shown in [table 1](#).

There were significant changes in the scores of all outcome measures after treatment with both acupuncture and clonazepam compared with before treatment ($p < 0.05$), except for the MoCA cognitive test ([table 2](#)). However, there were no significant differences between the scores of the two groups receiving the different therapeutic regimens.

DISCUSSION

The results of this study show that acupuncture and clonazepam are similarly effective in the treatment of patients with BMS. Evidence published so far suggests that clonazepam taken either locally, systemically or both reduces the symptoms of BMS.^{10–12} Many of these studies are not randomised controlled trials, but two high-quality studies should be discussed. Gremeu-Richard *et al*¹³ randomised 48 patients with BMS to either 1 mg topical clonazepam three times a day or placebo for 14 weeks. Topical clonazepam decreased pain in the patients with BMS. A double-blind trial by Heckman *et al*⁹ in 20 patients found that oral clonazepam was superior to placebo for burning pain. The results of these studies^{9 13} support the effectiveness of clonazepam in patients with BMS.

Previous studies of acupuncture in patients with BMS mostly suggest beneficial effects. Sardella *et al*⁶ reported a slight but insignificant reduction in the VAS score after 8 weeks of acupuncture (20 sessions). There was no significant improvement in quality of life measured by SF-36, although patients with BMS coped better with their oral symptoms after acupuncture treatment. Yan *et al*,⁵ on the basis of the published literature in Chinese, reported that acupuncture was effective in 547 patients with BMS. Scardina *et al*⁷ showed that acupuncture increased oral microcirculation and decreased burning symptoms after 3 weeks of therapy. We have previously reported that low level laser acupuncture was effective in patients with BMS.⁸

This study therefore suggests that acupuncture for BMS has similar effects to a treatment that is known to be effective in the condition, although a placebo response to acupuncture cannot be entirely excluded.

The underlying mechanisms of acupuncture and clonazepam are different. It is thought that acupuncture increases oral microcirculation which in turn decreases burning mouth symptoms, which has been confirmed in the study by Scardina *et al*.⁷ Another possible explanation is that acupuncture-induced pain relief has physiological, anatomical and neurochemical

origins,¹⁴ although the exact mechanism is still unknown.¹⁵ It seems that acupuncture leads to the release of endogenous opioid-like substances that modulate pain signals within the central nervous system.¹⁵ One recent study suggested that acupuncture relieves pain via the local release of adenosine—that is, that local inflammation can result in the local release of adenosine with analgesic effects.¹⁶

In contrast to other Western studies of acupuncture in patients with BMS, our treatment was more intensive but of shorter duration.

Five patients on clonazepam had side effects while no side effects were reported in patients who received acupuncture. Therefore, we might conclude that acupuncture is safer with fewer side effects than clonazepam treatment. However, acupuncture is more time-consuming for healthcare providers and more painful to patients.

Summary points

- ▶ We compared acupuncture with oral clonazepam for patients with burning mouth syndrome.
- ▶ There was no difference in the effectiveness of the two treatments on severity of burning or a number of other outcomes.

Contributors VBK and IZ are neurologists who treated the patients. DG and AJK screened the patients in the Department of Oral Medicine. DVV performed statistical analysis. VVB, DG and DC wrote the article.

Competing interests None declared.

Ethics approval Ethics approval was obtained from the Ethical Committee of the School of Dentistry in Zagreb, Croatia.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Bergdahl J, Anneroth G, Perris H. Cognitive therapy in the treatment of patients with resistant burning mouth syndrome: a controlled study. *J Oral Pathol Med* 1995;24:213–15.
- 2 Woda A, Grushka M. Burning mouth syndrome. In: Zakrzewska JM, eds. *Orofacial pain*. 1st edn. Oxford: Oxford University Press, 2009.
- 3 Buchanan JA, Zakrzewska JM. Burning mouth syndrome. *BMJ Clin Evid* 2010;2010:pii: 1301.
- 4 en.wikipedia.org/wiki/Acupuncture
- 5 Yan Z, Ding N, Hua H. A systematic review of acupuncture or acupoint injection for management of burning mouth syndrome. *Quintessence Int* 2012;43:695–701.
- 6 Sardella A, Lodi G, Tarozzi M, *et al*. Acupuncture and burning mouth syndrome: a pilot study. *Pain Pract* 2012;13:627–32.
- 7 Scardina GA, Ruggieri A, Provenzano F, *et al*. Burning mouth syndrome: is acupuncture a therapeutic possibility? *Br Dent J* 2010;209:E2.
- 8 Brailo V, Bosnjak A, Boras VV, *et al*. Laser acupuncture in the treatment of burning mouth syndrome: a pilot study. *Acupunct Med* 2013;31:453–4.

- 9 Heckmann SM, Kirchner E, Grushka M, *et al.* A double blind study on clonazepam in patients with burning mouth syndrome. *Laryngoscope* 2012;122:813–16.
- 10 Amos K, Yeoh SC, Farah CS. Combined topical and systemic clonazepam therapy for the management of burning mouth syndrome: a retrospective pilot study. *J Orofac Pain* 2011;25:125–30.
- 11 De Moraes M, do Amaral Bezerra BA, da Rocha Neto PC, *et al.* Randomized trials for the treatment of burning mouth syndrome: an evidence based review of the literature. *J Oral Pathol Med* 2012;41:281–7.
- 12 De Castro LA, Ribeiro-Rotta RF. The effect of clonazepam mouthwash on the symptomatology of burning mouth syndrome: an open pilot study. *Pain Med* 2014;15:2164–5.
- 13 Gremeu-Richard C, Woda A, Navez ML, *et al.* Topical clonazepam in stomatodynia: a randomized placebo controlled study. *Pain* 2004;108:51–7.
- 14 Zhao ZQ. Neural mechanism underlying acupuncture analgesia. *Prog Neurobiol* 2008;85:355–75.
- 15 Wang SM, Kain ZN, White P. Acupuncture analgesia: I. The scientific basis. *Anaesth Analg* 2008;106:602–10.
- 16 Gorski DH. Integrative oncology: really the best of both worlds? *Nat Rev Cancer* 2014;14.



The effectiveness of acupuncture versus clonazepam in patients with burning mouth syndrome

A Jurisic Kvesic, I Zavoreo, V Basic Kes, V Vucicevic Boras, D Ciliga, D Gabric and D V Vrdoljak

Acupunct Med published online May 18, 2015

Updated information and services can be found at:

<http://aim.bmj.com/content/early/2015/05/17/acupmed-2015-010759>

These include:

References

This article cites 13 articles, 1 of which you can access for free at:
<http://aim.bmj.com/content/early/2015/05/17/acupmed-2015-010759>
#BIBL

Email alerting service

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:

<http://group.bmj.com/group/rights-licensing/permissions>

To order reprints go to:

<http://journals.bmj.com/cgi/reprintform>

To subscribe to BMJ go to:

<http://group.bmj.com/subscribe/>