Burning Issues in the Treatment of Burning Mouth Syndrome: An Evidence-Based Study of the Literature

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A b s t r a c t

Burning mouth syndrome (BMS) is defined as a chronic pain condition, characterized symptomatically by a generalized or localized burning sensation in the oral cavity. This review was based on evidence from electronic search engines, textbooks and independent interviews from experts in the field. A total of 8 relevant articles were analyzed, looking at the use of hormone replacement therapy, benzodiazepines/anti-convulsants, anti-depressants, analgesics, Capsaicin, alpha-lipoic acid and cognitive behavioural therapy, as treatment options. These articles were critically appraised using an "intervention checklist". The use of capsaicin, alpha-lipoic acid, cognitive behavioural therapy and clonazepam were shown to reduce the symptoms of BMS patients, while hormone replacement therapy, anti-depressants and analgesics were shown to be ineffective. Current knowledge of interventions for the treatment of BMS appears to be incomplete. Thus, future studies are required, in order to solidify the means in which clinicians diagnose, manage and treat patients suffering from this chronic and painful syndrome.

Burning mouth syndrome (BMS) is defined as a chronic pain condition, characterized symptomatically by burning pain localized to the tongue and lips or may involve the entire oral cavity. Alterations in taste and dryness may also be experienced by some patients (Grushka *et al.,* 2000). In clinical examinations, there are no oral manifestations observed, nor have any local or systemic factors been identified as contributing to the disease (Zakrzewska *et al.,* 2005).

Various synonyms are used interchangeably to describe BMS-such as stomatopyrosis, glossopyrosis, stomatodynia, glossodynia, sore mouth, sore tongue, and oral dysesthesia. These are used to emphasize the quality and the location of the pain (Scala *et al*., 2003). As a result of the variations in experienced symptoms, and despite the fact that numerous studies have been carried out, there is no universal consensus on the diagnosis, etiology and treatment of BMS (Grushka, 2002). This leads to patients being referred from one health care professional to another, causing an increased burden on both the health care system and the patient (Grushka, 2002).

Due to the lack in the consensus of diagnosing BMS, prevalence rates tend to vary across studies. The most commonly reported range has been 0.7% to 4.6% (Scala *et al*., 2003), however, rates as high as 14.8 % have also been estimated (Tammiala-Salonen *et*

Table 1: Search strategy and results

Treatment Intervention	*Search engine*	*Yield*	*Rejected at Title Stage*	*Rejected at Abstract Stage*	*Rejected at Full Text Stage*	*Accepted*
1) HRT						
a) Burning Mouth Syndrome AND Hormone Replacement Therapy	Ovid	17	11	5	1	0
b) Burning Mouth Syndrome AND Menopause	Ovid	42	37	3	1	1
c) Burning Mouth Syndrome, Hormone Therapy	PubMed	19	15	2	1	1
d) Burning Mouth Syndrome, Steroid Therapy	PubMed	9	6	1	1	1
2)Anti-Convulsants						
a) Burning Mouth Syndrome, anticonvulsants	PubMed	11	4	5	1	1*
3) Anti-Depressants						
a) Burning Mouth Syndrome, antidepressants	PubMed Limits: English	20	17	0	2	1
4) Capsaicin						
a) Burning, capsaicin	PubMed Limits: English	6	4	0	1	1
5) Benzodiazepines						
a) Burning Mouth Syndrome, benzodiazepines	PubMed Limits: English	11	6	2	2	1 *
6) Analgesic						
a) Burning Mouth Syndrome, analgesics	PubMed Limits: English	10	9	0	0	1
7) Cognitive Behavioural Therapy						
a) burning mouth syndrome, cognitive behavioural therapy	PubMed Limits: English	12	11	0	0	1
8) Alpha- lipoic acid						
a) Burning Mouth Sydrome, Alpha- lipoic-acid	PubMed	7	0	4	1	2**
b) BMS, Alpha-Lipoic Acid	Blackwell synergy	3	0	0	1	2**

Table 2: Search results for BMS synonyms

Key word: LIMITS: English and clinical trial	*Search engine*	*Yield*	*Rejected at Title Stage*	*Rejected at Abstract Stage*	*Rejected at Full Text Stage*	*Accepted*
Stomatopyrosis	Pubmed	24	13	4	3	6***
Glossopyrosis	Pubmed	3	2	1	0	0
Stomatodynia	Pubmed	3	1	0	1	1***
Glossodynia	Pubmed	3	2	1	0	0
Sore tongue	Pubmed	3	2	1	0	0
Sore mouth	Pubmed	24	24	0	0	0
Oral dysesthesia	Pubmed	36	36	0	0	0

*: same article **: same article ***: same articles found from chart #1

al., 1993). The syndrome typically affects middle-aged people, specifically pre- and post-menopausal women, however men should not be excluded (White *et a*l., 2004).

This literature review was carried out in an attempt to identify the best treatment for burning mouth syndrome, using the strongest sources of evidence in the field.

Methods

Several searches were carried out using a systematic method, in order to identify relevant published articles on BMS. Search criteria were divided based on the most common treatment interventions currently used by clinicians. Search strategy and results are presented in Table 1 and search results using alternate synonyms are presented in Table 2.

In addition to the literature search, opinions of expert authorities on BMS were also reported. The opinions of Dr. C. Kilmartin (B.D.S, M.Sc., D.D.S, FRCD(C)), Dr. R.J McComb, Dr. I. Leong (B.Sc. Hons., B.D.S., F.R.C.D.C. Oral Pathology, M.Sc., F.R.C.D.C Oral Medicine) and Dr. M. Grushka (M.Sc., D.D.S., Ph.D.) were gathered through independent interviews.

Results

Since the current review is attempting to identify the best treatment for BMS, only randomized controlled trials were identified as offering the best level of evidence**.** From the systematic search of literature, only 8 studies were found to satisfy the above criteria. Each study was then critiqued using the checklist developed by Leake (2005) (Refer to Table 3 for checklist criteria).

When analyzed against the checklist criteria, all relevant studies achieved a score greater than 10 out of a possible 18. This indicates that the results of these studies provide strong evidence in regards to the treatment of BMS (Refer to Appendix 1 for detailed analysis of relevant studies).

Pisanty *et al*. (1975) found that the use of topical steroid hormones had no effect on relieving dryness and burning sensations as experienced by 22 female BMS patients. Similarly, anti-depressants, such as Trazodone, did not effectively relieve BMS associated symptoms, as studied by Tammialia-Salonen *et al*. (1999). Lastly, topical benzydamine hydrochloride rinse was not shown to be effective in managing pain of BMS patients (Sardella *et al*., 1999).

In contrast, patients who received systemic Capsaicin, did report a decrease in pain symptoms, however, as reported by Petruzzi *et al*.(2003), side effects such as gastric pain were also experienced, thus questioning the potential benefit of this treatment.

When alpha-lipoic acid was used alone or in conjuction with psychotherapy, patients reported a significant decrease in pain symptoms (Femiano et al. 2002, 2004). In addition, in trials testing the effectiveness of Clonazepam in alleviating BMS symptoms, Gremeau-Richard *et al*. (2004) reported a significant improvement in pain alleviation in those treated. Finally, Bergdahl *et al*. (1995) demonstrated a decrease in the intensity of BMS symptoms as a result of cognitive behavioural therapy.

Discussion

According to the review of the literature, it appears that current knowledge of interventions for the treatment of BMS is incomplete. Thus, further studies are required in order to solidify the means by which clinicians diagnose, manage and treat patients suffering from this chronic and painful syndrome.

Research on steroid hormones as a means of treating BMS is insufficient, primarily due to the lack of current studies. The most recent randomized controlled trial was carried out in 1975 by Pisanty et al., and no differences were found between the 3 treatment groups. However, it was unclear whether the patients who participated in the study actually suffered form BMS, or suffered from oral manifestations related to menopause. Moreover, this study precludes males, who also suffer from this syndrome, and thus results can not be generalized clinically.

Tammiala-Salonen (1999) came to inconclusive results in studying the effectiveness of Trazodone, due to the high drop-out rate as a result of side-effects experienced by participants, primarily dizziness. At the start of the study, 18 patients were assigned to receive Trazodone, but by the end of the 8 week trial only 4 remained. As well, the Trazodone trial, similar to the Pisanty et al. (1975) study, included only female participants and thus also prevents the extrapolation of experimental findings to the male population.

Benzydamine hydrochloride oral rinses were shown to have no effect in alleviating symptoms of BMS, by Sardella *et al*. (1999). Although the study was well conducted, future RCTs on this type of intervention are recommended in order to completely exclude these rinses as potential treatment options.

Capsaicin was shown to provide patients with symptomatic relief, however Petruzzi *et al*. (2004) found that systemic administration of this drug was also associated with significant gastric pain. Thus, Capsaicin should only be administered for a short term basis in order to avoid this side effect. This potential intervention raises the question as to whether the potential benefits of the drug outweigh the negative effects.

In both RCTs concerning alpha lipoic acid, it was concluded that there was a significant improvement of symptoms between the treatment and placebo groups (Femiano *et al*., 2002, 2004). More specifically, the greatest improvement was reported among the group who received both lipoic acid and cognitive behavioural therapy (Femiano *et al*., 2004). These results support the theory that BMS has a neuropathic origin. However, both studies were conducted by the same research group which limits the reliability of the results. In order to confirm the effectiveness and reproducibility of alpha lipoic acid as a treatment option for those suffering from BMS, more independent research needs to be carried out. Cognitive behavioural therapy was shown to be effective even when used independently (Bergdahl *et al*., 1995), thus reinforcing its potential as a treatment option for BMS patients.

Research by Gremeau *et al*. (2004) on the anti-convulsant, Clonazepam (used topically), provided the most clinically reliable evidence based on the strength of the research design. Clonazepam was shown to effectively reduce the pain associated with BMS and thus more research can be carried out to validate these promising results. In summary, the limitations of the 8 studies that were analyzed indicate that practitioners need to be cautious when interpreting outcomes of published studies.

The independent interviews with the experts yielded conflicting beliefs in regards to the best treatment option for BMS. Specifically, Dr. Leong suggested that showing empathy and reassuring the patient that the disorder is real can significantly lower the perception of pain. She also stated the importance of confirming with the patient that BMS is not fatal nor is it cancerous and will eventually resolve.

In contrast, Dr. Grushka, one of the leading researchers on BMS,

believes that the best treatment for the syndrome consists of a combination of drugs, such as Clonazepam, Gabapentin and Baclofen (Grushka, 2006). She believes that these drugs alleviate the symptoms of BMS through a neuropathic mechanism, which she hypothesizes to consist of a close link between cranial nerves V, VII, IX, X. It is hypothesized that a loss in taste, specifically a defect in CN VII leads to hyperexcitability of CN V, which is responsible for pain, thus leading to increased sensations of pain (Grushka et al., 2000 & 2003) The very contrasting opinions from these practicing clinicians, reinforces the lack of uniformity in the management of BMS patients.

In conclusion, although much research has been geared towards studying BMS, it is evident that there is a lack of understanding within the field. While examining the literature, it became apparent that no consensus exists in defining, diagnosing and treating BMS. Furthermore, the lack of understanding the cause and mechanism behind the syndrome adds to the difficulty in finding a therapeutic management program. If an intervention is to be found, researchers need to first agree upon a universal definition, which would improve the diagnosis of the syndrome, and only then can an attempt be made to formulate treatment guidelines for the management of BMS patients.

Table 1 Checklist to Assess Evidence of Efficacy of Therapy

1. Was the study ethical?
2. Was a strong design used to assess efficacy?
3. Were outcomes (benefits and harms) validly and reliably measured?
4. Were interventions validly and reliably measured?
5. What were the results?
   - Was the treatment effect large enough to be clinically important?
   - Was the estimate of the treatment effect beyond chance and relatively precise?
   - If the findings were “no difference” was the power of the study 80% or better?
6. Are the results of the study valid?
   - Was the assignment of patients to treatments randomized?
   - Were all patients who entered the trial properly accounted for and attributed to its conclusion?
     i) Was loss to follow-up less than 20% and balanced between test and controls?
     ii) Were patients analysed in the groups to which they were randomized?
   - Was the study of sufficient duration?
   - Were patients, healthworkers, and study personnel “blind” to treatment?
   - Were the groups similar at the start of the trial?
   - Aside from the experimental intervention, were the groups treated equally?
   - Was care received outside the study identified and controlled for?
7. Will the results help in caring for your patients?
   - Were all clinically important outcomes considered?
   - Are the likely benefits of treatment worth the potential harms and costs?

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APPENDIX 1
Detailed analysis of relevant studies