## A Meta-Analysis Of Treatments For Burning Mouth Syndrome

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## **Background**

Burning mouth syndrome (BMS) is characterized by burning of the oral mucosa in the absence of underlying dental or medical causes. The results of previous systematic reviews have generally been equivocal. However, findings for most interventions are based on searches of 5-10 years ago and do not include meta-analyses. This study therefore updates previous searches of randomised controlled trials (RCTs) for pain as assessed by Visual Analogue Scales (VAS).

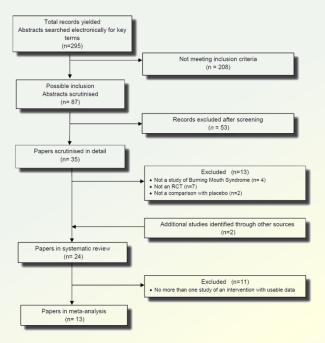
## **Methods**

A search of MEDLINE and Embase up to 2016. Where data were available for two or more studies, they were combined in a meta-analysis.

## Results

24 RCTs were identified, 13 of which (n=600) could be included in meta-analyses (Figure 1) The commonest interventions were alpha-lipoic acid (ALA) (8 comparisons), capsaicin, clonazepam (3 comparisons each) and psychotherapy (2 comparisons). ALA led to significant improvements in VAS (Risk Ratio (RR)=2.25; 95% CI=1.04-4.88; n=392; p=0.04) (Figure 2) while capsaicin significantly reduced pain at up to two months follow-up (standardised mean difference (SMD)=-0.60; 95%CI=-1.17 to -0.03; n=78; p=0.04), as did clonazepam (SMD=-1.44; 95%CI=-2.06 to -0.81; n=131; p<0.001) (Figure 3). However, capsaicin led to prominent dyspepsia. No significant improvements were found for psychotherapy (RR=14.28; 95%CI=0.42-44.0; n=74). In individual studies, capsaicin analogues, catauma and tongue-protectors showed promise.

Figure 1: PRISMA diagram



**Conclusions** 

ALA and capsaicin show modest benefit in the first two months. However, these conclusions are limited by short follow-up periods, high heterogeneity and low participant numbers in individual studies. For instance, Type 2 error may explain the disappointing results for psychotherapy. Further RCTs with follow-up of at least 12 months are indicated.



Figure 2: Outcomes as measured by improvement in pain intensity

	Experimental		Contr	Control		Risk Ratio	Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI	
1.1.1 ALA								
Carbone 2009	4	22	5	22	12.4%	0.80 [0.25, 2.59]		
Cavalcanti 2009	22	31	23	28	16.9%	0.86 [0.65, 1.15]		
Femanio 2000	16	21	3	21	13.0%	5.33 [1.82, 15.62]		
Femanio 2002a	18	20	0	20	5.4%	37.00 [2.38, 574.81]		
Femiano 2002	29	30	12	30	16.4%	2.42 [1.55, 3.76]	-	
Lopez-D'alessandro 2011	11	20	8	60	14.8%	4.13 [1.93, 8.80]		
Lopez-Jornet 2009	10	23	10	16	15.7%	0.70 [0.38, 1.27]		
Marino 2010	8	14	0	14	5.4%	17.00 [1.07, 268.84]		
Subtotal (95% CI)		181		211	100.0%	2.25 [1.04, 4.88]	•	
Total events	118		61					
Heterogeneity: Tau2 = 0.90;	Chi <sup>2</sup> = 61.6	6. df = 7	(P < 0.0	0001):	12 = 89%			
Test for overall effect: $Z = 2.0$	06 (P = 0.0	4)						
1.1.2 Clonazepam								
Gremeau-Richard 2004	11	22	3	23	41.0%	3.83 [1.23, 11.93]		
Rodriguez 2010	23	33	4	33	59.0%	5.75 [2.23, 14.81]		
Subtotal (95% CI)		55		56	100.0%	4.87 [2.35, 10.07]	•	
Total events	34		7					
Heterogeneity: Tau <sup>2</sup> = 0.00; Test for overall effect: Z = 4.			(P = 0.59)	$  \mathbf{l}   = 0$	%			
restror overall ellect. Z = 4	27 (F < 0.0	101)						
1.1.3 Psychotherapy								
Bergdahl 1995	14	15	1	15	42.7%	14.00 [2.10, 93.45]		
Miziara 2009	17	24	8	20	57.3%	1.77 [0.98, 3.21]	-	
Subtotal (95% CI)		39		35	100.0%	4.28 [0.42, 44.14]		
Total events	31		9					
Heterogeneity: Tau2 = 2.38;	Chi <sup>2</sup> = 5.62	df = 1	P = 0.02	); Iz = 8	2%			
Test for overall effect: $Z = 1$ .								
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Figure 3: Outcomes as measured by reductions in mean pain intensity

	Experimental			Control				Std. Mean Difference	Std. Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95%	CI
2.2.1 Capsaicin										
Marino 2010	2.9	2.6	14	5.3	2.2	14	38.8%	-0.97 [-1.76, -0.18]	<del></del>	
Petruzzi 2004 Subtotal (95% CI)	5.84	1.17	25 39	6.24	0.96	25 39	61.2% 100.0%	-0.37 [-0.93, 0.19] -0.60 [-1.17, -0.03]		
Heterogeneity: Tau2 = 0.0	6; Chi2=	1.47, 0	df = 1 (F	P = 0.22	$   ^2 = 3$	12%				
Test for overall effect: Z =	2.05 (P =	0.04)								
2.2.8 Clonazepam										
Gremeau-Richard 2004	3.5	3.3	22	5.5	1.92	23	34.7%	-0.73 [-1.34, -0.13]	-	
Heckmann 2012	3.9	2.9	10	4.6	2.4	10	16.4%	-0.25 [-1.13, 0.63]		
Rodriguez 2010 Subtotal (95% CI)	2.85	1.7	33 65	4.24	1.2	33 66	48.9% 100.0%	-0.93 [-1.44, -0.42] -0.75 [-1.11, -0.40]		
Heterogeneity: Tau2 = 0.0	0; Chi2=	1.73, 0	df = 2 (F	0.42	$  \cdot  ^2 = 0$	1%				
Test for overall effect: Z=	4.13 (P «	0.000	11)							
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