

THE EFFECTS OF THREE NOVEL NICOTINE REPLACEMENT THERAPIES ON THE RELIEF OF TOBACCO WITHDRAWAL SYMPTOMS.

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Background:

Nicotine replacement therapy (NRT) assists smokers to quit, primarily, by relieving tobacco withdrawal symptoms.

Products that deliver nicotine faster may provide greater withdrawal relief and increase abstinence rates.

Three novel NRTs – the Zonnic 4 mg oral nicotine pouch (4mg), Zonnic 1 mg/dose mouth spray and Zonic 2.5 mg lozenge have been designed for rapid delivery of nicotine.



Oral nicotine pouch

Objectives:

To compare the effects of the novel pouch, mouthspray and lozenge on withdrawal discomfort and craving after overnight abstinence from smoking with Nicorette® 4 mg nicotine chewing gum and placebo.

Method:

Design: Randomised, placebo controlled, single blind, repeated measures, cross over study.

Participants and procedure: a total of 77 dependent smokers aged 18–70 years were recruited (see Table 1 for participant characteristics).

The study was undertaken in two parts:

- Part 1 (n=30) compared the pouch with gum and placebo pouch
- Part 2 (n=47) compared lozenge, mouthspray, and placebo lozenge

Participants reported to the study site at 0730 on each study day, after overnight abstinence (carbon monoxide verified), provided baseline ratings, were randomly assigned to each NRT, then completed regular withdrawal ratings over 60 minutes on a 100mm visual analogue scale (VAS). Afterwards, they were asked to continue to abstain, use the product ad lib, leave the study centre, until returning at 1730 to report adverse effects and product satisfaction using a 5-item questionnaire adapted from Hajek et al 1989¹. Participants smoked as normal during the intervening 3 day period between study days.

Primary outcome: Mean change in craving score over 60 minutes (area under the curve/60 mins).

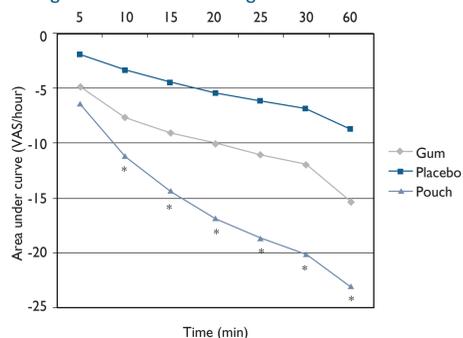
Other outcomes: Comparisons of VAS change from baseline at each time point; Satisfaction and helpfulness of the products – assessed using a 5-item questionnaire adapted from Hajek et al 1989².

Statistical Methods and Outcome measures: Analysis of covariance (ANCOVA) with individual participants included as random effects. The Tukey-Kramer method was used for multiple comparison adjustment.

Table 1. Participant characteristics

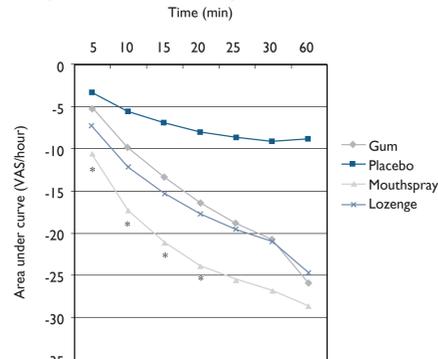
	Part 1 (n=30)	Part 2 (n=47)
% (n) male	57 (17)	49 (23)
Mean age (range)	50 (26-70)	49 (18-71)
% (n) living with a partner who smokes	20 (6)	28 (13)
Ethnicity		
% (n) Maori	20 (6)	11 (5)
% (n) New Zealand European	63 (19)	66 (31)
% (n) Other	17 (5)	11 (34)
Mean Fagerström test of nicotine dependence	6.0	5.7

Figure 1. Part 1 – Craving: Area under the curve



* Statistical significance ($p<0.05$) between pouch and placebo

Figure 2. Part 2: Craving: area under the curve.



- * Statistical significance ($p<0.05$) between mouthspray and gum.
- The difference between lozenge and placebo was significant at 10, 20, 25, 30 and 60 minutes. The difference between gum and placebo was significant at 20, 25, 30 and 60 minutes.
 - The difference between mouthspray and placebo was significant at all time periods. No significant differences were noted between lozenge and gum or mouthspray and lozenge.

Results:

Reduction in craving scores over time is shown in figures 1 and 2.

Part 1:

- Overall there was a 23, 15, and 9 unit reduction in craving over 60 minutes in the pouch, gum and placebo groups respectively.
- The pouch produced significantly greater reduction in craving compared to placebo (see table 2).
- The pouch was preferred over the gum (figure 3) of product preference were significantly higher for the pouch than gum in the domains of helpfulness as a cessation aid (mean difference 21, 95% CI 2 to 39), pleasant to use (mean difference 17, 95% CI 3 to 33), likely to use to stop smoking (mean difference 22, 95% CI 0.3 to 43), and recommend to a friend (mean difference 28, 95% CI 8 to 48).

Table 2. Between product comparisons of mean reduction in craving over 60 minutes

Comparison	Mean difference (95% CI)	P-value*
Active Pouch – Gum	-7.7 (-17.3 to 1.9)	0.1387
Active Pouch – Placebo Pouch	-14.4 (-24.1 to -4.8)	0.002
Gum – Placebo Pouch	-6.7 (-16.4 to 3.0)	0.2245
Active Lozenge – Gum	1.1 (-6.8 to 9.1)	0.9821
Active Lozenge – Mouth Spray	3.9 (-4.1 to 11.8)	0.5835
Active Lozenge – Placebo Lozenge	-15.8 (-23.7 to -7.9)	<.0001
Gum -Mouth Spray	2.7 (-5.2 to 10.7)	0.8046
Gum – Placebo Lozenge	-16.9 (-24.8 to -9.0)	<.0001
Mouth Spray -Placebo Lozenge	-19.7 (-27.6 to -11.7)	<.0001

CI – Confidence interval

* Adjusted for multiple comparison and baseline craving

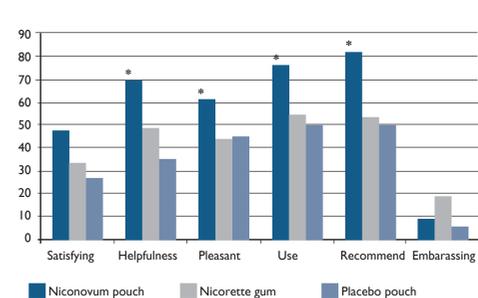
Part 2:

- Over 60 minutes the mouth spray showed the greatest reduction in craving (29 units) followed by the gum (26 units), lozenge (25 units) and placebo lozenge (9 units) (table 2).
- Compared to placebo, active NRTs had significantly greater craving relief (see table 2). Area under the curve comparisons between active products (lozenge, mouthspray and gum) showed no statistical differences at 60 minutes, but mouthspray showed superior craving relief than the gum throughout the first 20 minutes (see figure 2).
- Mouthspray was preferred over gum in helpfulness as a cessation aid (figure 4; mean difference 15, 95% CI: 27 to 2).

Conclusions and recommendations:

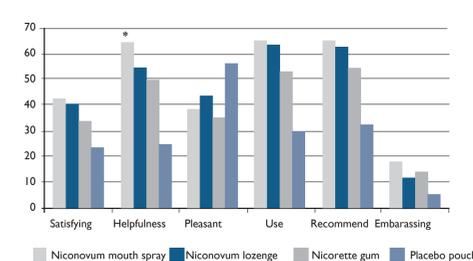
- Three novel nicotine treatments have shown equivalent efficacy in reducing craving after overnight abstinence, compared to gum and are likely to show similar efficacy in assisting smokers to quit.
- The pouch and mouthspray groups show a trend for faster and greater craving relief than gum, which may result in increased efficacy as a quitting aid, although not significant.
- The pouch and the mouthspray hold promise of superior user compliance, and may be acceptable to a broader range of smokers attempting to quit, indicated by ratings of user efficacy.

Figure 3. Part 1: mean ratings of product preference



* Statistical significance ($p<0.05$) between pouch and gum

Figure 4. Part 2: mean ratings of product preference



* Statistical significance ($p<0.05$) between mouth spray test group and gum

References:

- Hughes J, Hatsukami DK. Errors in using tobacco withdrawal scale. Tob Control 1998;7(1):92-3.
- Hughes JR, Hatsukami D. Signs and symptoms of tobacco withdrawal. Arch Gen Psychiatry 1986;43(3):289-94.
- Hajek P, Jarvis MJ, Belcher M, Sutherland G, Feyerabend C. Effect of smoke-free cigarettes on 24 h cigarette withdrawal: a double-blind placebo-controlled study. Psychopharmacology (Berl) 1989;97(1):99-102.

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