Effect of an E-Cigarette on Cravings and Withdrawal, Acceptability and Nicotine Delivery: Randomised Cross-Over Trial.

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Aim

To measure the effects of the Ruyan e-cigarette (EC) on craving relief and withdrawal and explore its acceptability and pharmacokinetic properties in comparison to placebo EC (i.e. with cartridges containing no nicotine), Nicorette® nicotine inhalator and factory made cigarettes.

Methods

Prospective, single blind randomised cross-over trial of the EC. Participants were 40 adult New Zealand tobacco smokers randomised to a day's use of each of the following products with 3-days smoking their usual cigarette between: EC containing either nicotine or placebo capsules, Nicorette® nicotine inhalator, or their own brand cigarette. After overnight abstinence, measures were taken before and for one hour after first use, and again after 8 hours further use on each day. The primary outcome was craving relief rated on a 0-10 visual analogue scale measured as 'area under the curve'. Secondary outcomes included withdrawal symptoms and acceptability. Nine of the participants also had serum nicotine levels measured over one hour after first use of each product.

Results

Over 60 minutes participants using the 16mg EC experienced significantly less craving than when using the placebo EC (mean difference 0.82; 95% C.I. 0.25–1.38; p=0.0061). Cigarette use reduced craving more than the 16mg (difference 1.44; 95% CI 0.39 to 2.48) and 0mg (difference 2.23; 95% CI 1.17 to 3.30). ECs and Nicorette® inhalator (difference 1.54 95% CI 0.48 to 2.59) over the same period. Compared to the 0mg EC and Nicorette® inhalator, the 16mg EC rated lowest for irritability, restlessness, poor concentration and need for a cigarette but these differences were not significant. The EC was well-tolerated, acceptable and had fewer adverse effects than the inhalator. The 16mg EC delivered nicotine more rapidly (mean tmax 19.4 minutes) than Nicorette® inhalator (30 minutes) but not as rapidly as cigarettes (14.3 min), which also gave the highest cmax of nicotine (13.4 ng/ml), almost ten-fold that of the 16mg EC (0.9 ng/ml), and Nicorette® inhalator (1.8 ng/ml).

Table 2 shows that use of the EC 0mg and EC 16mg was less likely to be associated with mouth and throat irritation (the most commonly reported adverse effects) than with use of the inhalator. Other differences in adverse effects reported between the products were small and not significant.

Figure 1. Comparison of change in VAS score from baseline for craving during the first hour after each product use.

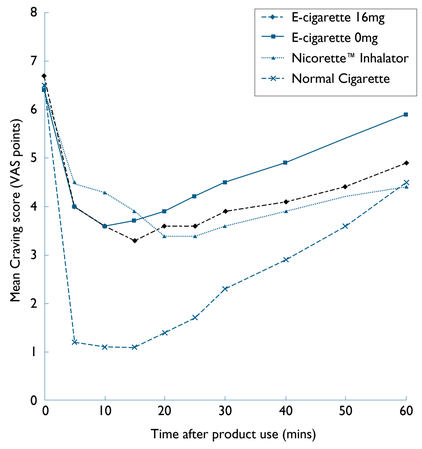

Figure 2. Participant Ratings of Product preference.

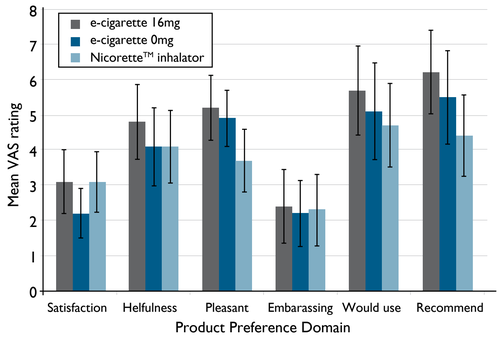

Table 1. Comparison of summary pharmacokinetic properties of own brand cigarette, Nicorette® inhalator and 16mg e-cigarette .

Product	tmax (mins) (95% CI)	Cmax (ng/mL) (95% CI)
Own brand cigarette	14.3 (8.8 to 19.9)	13.4 (6.5 to 20.3)
16 mg E-cigarette	19.6 (4.9 to 34.2)	1.3 (0.0 to 2.6)
Nicorette® inhalator (10mg)	32.0 (18.7 to 45.3)	2.1 (1.0 to 3.1)

Table 2. Adverse events

	E-cigarette 0mg		E-cigarette 16mg		Nicorette® inhalator	
	N	(%)	N	(%)	N	(%)
Mouth irritation	5	13%	9	23%	13	33%
Throat irritation	9	23%	13	33%	23	58%
Aching jaws	3	8%	3	8%	2	5%
Feeling sick	6	15%	9	23%	6	15%
Vomiting	0	0%	0	0%	0	0%
Flatulence/Belching	3	8%	4	10%	6	15%
Stomach ache	1	3%	1	3%	3	8%
Heartburn	2	5%	1	3%	0	0%
Diarrhoea	0	0%	0	0%	0	0%
Hiccups	0	0%	0	0%	1	3%
Feeling high	2	5%	5	13%	3	8%
Feeling Dizzy	7	18%	9	23%	8	20%
Headache	7	18%	6	15%	6	15%
Sweatiness	3	8%	2	5%	2	5%
Cold hands/feet	0	0%	1	3%	0	0%
Palpitations	0	0%	2	5%	0	0%

Conclusion

The EC shows promise as a device that might aid cessation. Trials to assess long-term cessation outcome and safety are needed.

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