EFFICACY E-CIGS: RANDOMIZED CONTROL TRIALS

KU LEUVEN

THOMAS MORE

EFFICACY: RCTs

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RESEARCH ARTICLE Open Access

Effect of an electronic nicotine delivery device (*e*-Cigarette) on smoking reduction and cessation: a prospective 6-month pilot study

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Source*:* Effect of an electronic nicotine delivery device (e-Cigarette) on smoking reduction and cessation: A prospective 6-month pilot study. *BMC Public Health,* 2011, 11:786.

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Table 2 Subject Parameter Outcomes Following 24 Weeks of Electronic Cigarette Use

Parameter	AT BASELINE	AT 24-Weeks Post E-Cigarette	*p value‡*
Sustained 50% (excluding quitters) reduction in cigarette smoking (n = 13)			
Age	40.1 (± 7.7)†	6 (5, 6)*	< 0.001
Sex	8M; 5F	8 (6, 11)*	0.001
Smoking Years	24.5 (± 8.7)†		
Cigarettes/day	25 (20, 30)*		
eCO	18 (14, 33)*		
Sustained 80% (excluding quitters) reduction in cigarette smoking (n = 5)			
Age	40.6 (± 10.4)†	3 (3, 6)*	0.043
Sex	4M; 1F	6 (4, 10)*	0.042
Smoking Years	25.4 (± 11.8)†		
Cigarettes/day	30(25, 35)*		
eCO	15 (14, 44)*		
Sustained 100% (quitters) reduction in cigarette smoking (n = 9)			
Age	44.7 (± 9.3)†	0 (0, 0)*	0.008
Sex	8M; 1F	3 (2, 3)*	0.008
Smoking Years	29 (± 9.6)†		
Cigarettes/day	25 (23, 30)*		
eCO	31 (23, 41)*		
Sustained > 50% (including quitters) reduction in cigarette smoking (n = 22)			
Age	42 (± 8.5)†	3 (0, 6)*	< 0.001
Sex	16M; 6F	5.5 (3, 9.5)*	< 0.001
Smoking Years	26.3 (± 9.1)†		
Cigarettes/day	25 (20, 30)*		
eCO	27 (15.5, 37.5)*		
Smoking Failure (< 50% smoking reduction) (n = 5)			
Age	45.6 (± 7.9)†	20 (20, 20)*	0.157
Sex	2M; 3F	28 (17, 31)*	0.892
Smoking Years	31.2 (± 7)†		
Cigarettes/day	25 (20, 25)*		
eCO	18 (16, 32)*		

Abbreviations: SD - Standard Deviation; M - Male; F - Female; eCO - exhaled carbon monoxide.
‡p value - within group Wilcoxon Signed Rank Test.
† Parametric data expressed as mean (± SD).
*Non-parametric data expressed as median (interquartile range(IQR)).

Source*:* Effect of an electronic nicotine delivery device (e-Cigarette) on smoking reduction and cessation: A prospective 6-month pilot study. *BMC Public Health,* 2011, 11:786.

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PLOS ONE

EffiCiency and Safety of an eLectronic cigAreTte (ECLAT) as Tobacco Cigarettes Substitute: A Prospective 12-Month Randomized Control Design Study

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Source*:* EffiCiency and safety of an eLectronic cigAreTte (ECLAT) as tobacco cigarettes substitute: A prospective 12-month randomized control design study. *PLOSONE,* 2013, 8, e66317.

EFFICACY: RCTs

Abstract

Background: Electronic cigarettes (e-cigarettes) are becoming increasingly popular with smokers worldwide. Users report buying them to help quit smoking, to reduce cigarette consumption, to relieve tobacco withdrawal symptoms, and to continue having a 'smoking' experience, but with reduced health risks. Research on e-cigarettes is urgently needed in order to ensure that the decisions of regulators, healthcare providers and consumers are based on science. *Methods* ECLAT is a prospective 12-month randomized, controlled trial that evaluates smoking reduction/abstinence in 300 smokers not intending to quit experimenting two different nicotine strengths of a popular e-cigarette model ('Categoria'; Arbi Group Srl, Italy) compared to its non-nicotine choice. GroupA (n = 100) received 7.2 mg nicotine cartridges for 12 weeks; GroupB (n = 100), a 6-week 7.2 mg nicotine cartridges followed by a further 6-week 5.4 mg nicotine cartridges; GroupC (n = 100) received no-nicotine cartridges for 12 weeks. The study consisted of nine visits during which cig/day use and exhaled carbon monoxide (eCO) levels were measured. Smoking reduction and abstinence rates were calculated. Adverse events and product preferences were also reviewed.

Results: Declines in cig/day use and eCO levels were observed at each study visits in all three study groups ($p<0.001$ vs baseline), with no consistent differences among study groups. Smoking reduction was documented in 22.3% and 10.3% at week-12 and week-52 respectively. Complete abstinence from tobacco smoking was documented in 10.7% and 8.7% at week-12 and week-52 respectively. A substantial decrease in adverse events from baseline was observed and withdrawal symptoms were infrequently reported during the study. Participants' perception and acceptance of the product under investigation was satisfactory.

Conclusion: In smokers not intending to quit, the use of e-cigarettes, with or without nicotine, decreased cigarette consumption and elicited enduring tobacco abstinence without causing significant side effects.

Source: EffiCiency and safety of an eLectronic cigAreTte (ECLAT) as tobacco cigarettes substitute: A prospective 12-month randomized control design study. *PLOSONE,* 2013, 8, e66317.

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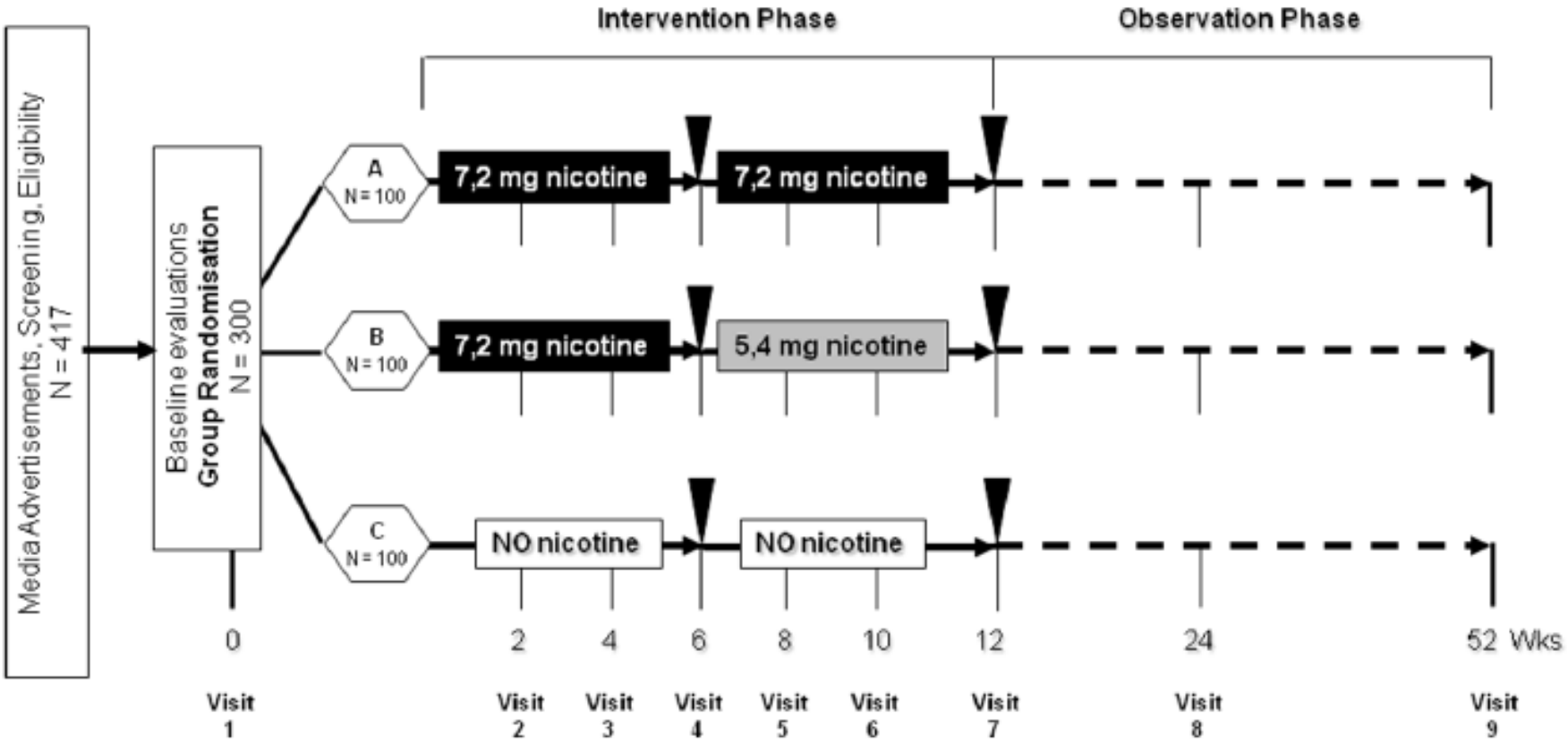

Source*:* EffiCiency and safety of an eLectronic cigAreTte (ECLAT) as tobacco cigarettes substitute: A prospective 12-month randomized control design study. *PLOSONE,* 2013, 8, e66317.

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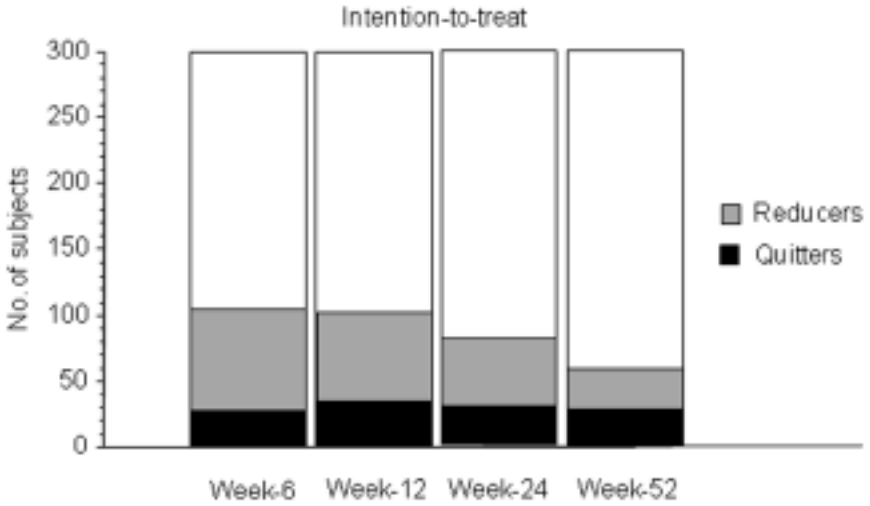

Figure 6. Time-course (at Week-6, -12, -24, and -52) of changes in the number of reducers and quitters in the ECLAT study (intention-to-treat analysis; all three study groups combined together).

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Source*:* EffiCiency and safety of an eLectronic cigAreTte (ECLAT) as tobacco cigarettes substitute: A prospective 12-month randomized control design study. *PLOSONE,* 2013, 8, e66317.

EFFICACY: RCTs

Electronic cigarettes for smoking cessation: a randomised controlled trial

Christopher Bullen, Colin Howe, Murray Laugesen, Hayden McRobbie, Varsha Parag, Jonathan Williman, Natalie Walker

Summary

Background Electronic cigarettes (e-cigarettes) can deliver nicotine and mitigate tobacco withdrawal and are used by many smokers to assist quit attempts. We investigated whether e-cigarettes are more effective than nicotine patches at helping smokers to quit.

Methods We did this pragmatic randomised-controlled superiority trial in Auckland, New Zealand, between Sept 6, 2011, and July 5, 2013. Adult (≥18 years) smokers wanting to quit were randomised (with computerised block randomisation, block size nine, stratified by ethnicity [Māori; Pacific; or non-Māori, non-Pacific], sex [men or women], and level of nicotine dependence [>5 or ≤5 Fagerström test for nicotine dependence]) in a 4:4:1 ratio to 16 mg nicotine e-cigarettes, nicotine patches (21 mg patch, one daily), placebo e-cigarettes (no nicotine), from 1 week before until 12 weeks after quit day, with low intensity behavioural support via voluntary telephone counselling. The primary outcome was biochemically verified continuous abstinence at 6 months (exhaled breath carbon monoxide measurement <10 ppm). Primary analysis was by intention to treat. This trial is registered with the Australian New Zealand Clinical Trials Registry, number ACTRN12610000866000.

Findings 657 people were randomised (289 to nicotine e-cigarette, 295 to patches, and 73 to placebo e-cigarette) and were included in the intention-to-treat analysis. At 6 months, verified abstinence was 7·3% (21 of 289) with nicotine e-cigarettes, 5·8% (17 of 295) with patches, and 4·1% (three of 73) with placebo e-cigarettes (risk difference for nicotine e-cigarette *vs* patches 1·51 [95% CI −2·49 to 5·51]; for nicotine e-cigarettes *vs* placebo e-cigarettes 3·16 [95% CI −2·29 to 8·61]). Achievement of abstinence was substantially lower than we anticipated for the power calculation, thus we had insufficient statistical power to conclude superiority of nicotine e-cigarettes to patches or to placebo e-cigarette. We identified no significant differences in adverse events, with 137 events in the nicotine e-cigarettes group, 119 events in the patches group, and 36 events in the placebo e-cigarettes group. We noted no evidence of an association between adverse events and study product.

Interpretation E-cigarettes, with or without nicotine, were modestly effective at helping smokers to quit, with similar achievement of abstinence as with nicotine patches, and few adverse events. Uncertainty exists about the place of e-cigarettes in tobacco control, and more research is urgently needed to clearly establish their overall benefits and harms at both individual and population levels.

Source*:* Electronic cigarettes for smoking cessation: A randomised controlled trial. *Lancet*, 2013, 382: 1629-1637.

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	Nicotine e-cigarettes (n=289)	Patches (n=295)	Difference χ^2 p value	Relative risk (95% CI)	Risk difference (95% CI)
Continuous abstinence					
1 month	67 (23·2%)	47 (15·9%)	0·03	1·46 (1·04 to 2·04)	7·25 (0·84 to 13·66)
3 months	38 (13·1%)	27 (9·2%)	0·12	1·44 (0·90 to 2·33)	4·00 (–1·10 to 9·10)
6 months (primary outcome)	21 (7·3%)	17 (5·8%)	0·46	1·26 (0·68 to 2·34)	1·51 (–2·49 to 5·51)

	Nicotine e-cigarette		Patches		Difference (nicotine e-cigarette–patches)		
	Mean	SE	Mean	SE	Mean	SE	p value
Overall	11·1	0·4	9·1	0·4	2·0	0·5	<0·0001
1 month	12·9	0·4	10·5	0·4	2·4	0·6	<0·0001
3 months	10·8	0·4	9·1	0·4	1·7	0·6	0·006
6 months	9·7	0·4	7·7	0·4	1·9	0·6	0·002

*For those reporting smoking at least one cigarette in past 7 days.

Table 4: **Change from baseline in cigarettes consumed per day during follow-up period, nicotine e-cigarettes and patches***

Source*:* Electronic cigarettes for smoking cessation: A randomised controlled trial. *Lancet*, 2013, 382: 1629-1637.

SUMMARY EFFICACY RCTs

- limited # so far
- most (R)CT's in smokers without intention to quit
- first generation (inefficient) e-cigs
- "medicine approach" (>< "consumer" choice approach)

- weak to moderate effects on reduction/quitting
- as least as good as NRT

- read 2014 Cochrane Review