

Efficacy of nicotine inhaler in smoking reduction

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Background

Smoking and/or exposure reduction may be achieved by reducing the daily number of cigarettes or by switching to low tar/nicotine cigarettes. However, since smokers tend to compensate and self-titrate their smoking to provide the brain with adequate nicotine, switching to 'light' cigarettes has been shown to lead to a higher intake of toxic constituents of cigarette smoke such as carbon monoxide (CO) and carcinogens. For example, changes in inhalation practice with low tar cigarettes appear to be increasing the incidence of certain types of lung cancer¹. A less hazardous alternative would be to reduce the daily number of cigarettes smoked through concomitant use of nicotine replacement therapy (NRT). Many smokers are unable or unwilling to quit, but would like to reduce smoking. There is evidence that reduced exposure to tobacco smoke benefits health and NRT can be used to achieve and maintain reduced smoking, which may motivate smokers to completely quit.

It has previously been shown that smoking reduction over 24 months could be achieved effectively and safely with the aid of a nicotine inhaler².

Objective

The primary objective with this study was to show the efficacy of a nicotine inhaler in *smoking reduction*, defined as self-reported reduction in daily cigarettes smoked by $\geq 50\%$ compared to baseline from week 6 to month 4 (with a 15-month follow-up). Smoking reduction was biochemically verified by a decrease in exhaled CO. The effect of smoking reduction on cardiovascular risk factors and smoking cessation was also evaluated.

Study design

This double-blind, placebo-controlled study recruited 429 healthy adult smokers who smoked ≥ 20 cigarettes/day and who had smoked for ≥ 3 years. Eligible subjects had to have an exhaled CO ≥ 15 ppm after 15 smoke-free minutes, and had failed at least one serious quit attempt within the previous 2 years. All subjects wanted to reduce smoking. Individuals who intended to quit smoking within the next 4 weeks were excluded. Eligible subjects were randomised to receive either nicotine 10 mg inhaler or placebo inhaler to be used *ad libitum* (up to 12 cartridges/day) for up to 12 months. Participants could use the inhaler whenever they felt the urge to smoke, with the aim of reducing smoking as much as possible.

Table 1. Effect of smoking reduction on certain cardiovascular risk markers. * The slightly lower n's are due to missing data. Abbreviations: WBC; White Blood cell Count, HDL, LDL; High and Low Density Lipoprotein, CRP; C-Reactive Protein.

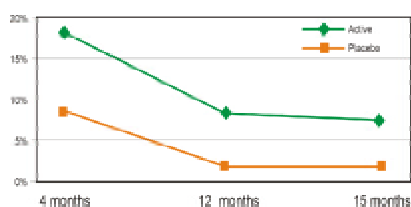
Variable	Unit	N*	Baseline		Change from baseline to month 4						
			MEAN	SD	MEAN	95% CL of mean		SD	Median	MIN	MAX
WBC	10 ⁹ /L	54	7.78	1.85	-0.34	-0.73	0.04	1.42	-0.45	-3.0	4.6
HDL	mg/dL	56	43.8	14.5	+2.11	0.71	3.50	5.20	3.00	-12.0	10.0
LDL	mg/dL	55	133.6	41.3	-5.76	-14.5	2.97	32.3	-5.00	-164	60.0
Fibrinogen	mg/dL	52	319.1	76.3	-18.6	-38.4	1.12	71.0	-4.00	-191	130
CRP	mg/dL	56	0.53	0.43	-0.09	-0.20	0.01	0.39	0.00	-2.66	0.32

Results

Smoking reduction:

This study showed that treating subjects unwilling or unable to quit smoking with the nicotine inhaler was superior to placebo up to month 4, 12 and 15. See **figure 1**.

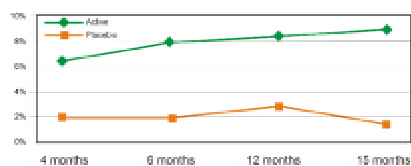
Figure 1. Sustained smoking reduction by at least 50% from week 6. P-value from $\chi^2 < 0.001$ at all time points.



Smoking cessation:

Active treatment promoted smoking cessation as measured by point prevalence self reported non smoking verified by a CO of less than 10 ppm to a higher degree compared to placebo. There is a slight increase in point prevalence quit rates over time in the active group. See **figure 2**.

Figure 2. Point prevalence complete abstinence (verified by a CO of less than 10 ppm) at 4, 12 and 15 months. P-value from $\chi^2 < 0.001$ at all time points.



Cardiovascular risk markers:

Among successful reducers (59 subjects; 40 in active and 19 in placebo) WBC was decreased by 4.4% up to 4 months (ns), HDL was increased by 4.8% ($p < 0.05$). LDL was decreased by 4.3% (ns). Fibrinogen decreased with 5.8% (ns) and CRP decreased with 17% (ns). See **table 1**.

Safety

The study did not reveal any unexpected adverse drug effects. Adverse events related to possible nicotine overdose (nausea, vomiting and palpitations) were evenly distributed between the treatment groups (7 events in active vs 6 events in placebo). Only dizziness was statistically significantly different between active and placebo groups (2 in active and 9 in placebo $p = 0.036$). Throat irritation was reported by 15 subjects among active and 6 among placebo treated subjects (ns). Cough was reported by 12 and 5 subjects respectively (ns). None of the reported serious adverse events was related to the investigational treatment.

Discussion

This study showed that a sustained substantial reduction of cigarettes per day, with the help of the nicotine inhaler, over a period of 15 months is achievable and may lead to smoking cessation (19 subjects in active and 4 in placebo at month 15). Our arbitrary suggestion to reduce daily cigarette consumption with at least 50% seems to be a good aim. The subjects in the control group that did not reach the success definition of at least a 50% reduction still reduced their number of cigarettes. It is noteworthy that "insufficient" cigarette reduction in the control group also resulted in reduction of certain risk markers for illness (not presented here).

Cessation remains the ultimate goal but it might be that some smokers need a longer period to sufficiently reduce their smoking, take control over their smoking, and eventually quit.

Health benefits

The assessed parameters were improved among the successful reducers, but, probably because of the relatively small sample of successful reducers, the difference between the groups was statistically significant only for HDL. Excluding the 5 subjects who managed to quit smoking did not have a significant impact on any of the comparisons. The clinical relevance of our findings needs to be further elucidated.

Conclusion

This study showed that smokers were able to reduce the daily cigarette consumption by at least 50% for a period of 15 months with the nicotine inhaler and that they achieved a positive effect on certain cardiovascular risk markers.

Although *smoking cessation is the ultimate goal* of treatment with NRT, smoking reduction is a promising alternative approach for smokers who are not willing or not able to quit at the present time. This study shows that the nicotine inhaler is well tolerated also when used concomitantly with smoking.

References

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