Effectiveness of pharmacologic therapy for smoking cessation in adolescent smokers: meta-analysis of randomized controlled trials

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CRD summary
The review concluded that pharmacological therapy in adolescent smokers did not statistically significantly effect smoking cessation with up to 26 weeks follow-up. There were few adverse events. The results may have been affected by small sample sizes. The review had some methodological problems and the limitations of the included studies should be borne in mind when interpreting the authors' conclusions.

Authors' objectives
To determine the effectiveness and safety of pharmacological smoking cessation interventions in adolescent smokers.

Searching
PubMed, EMBASE and Cochrane Central Register of Controlled Trials (CENTRAL) were searched for articles in any language. Search terms were reported. Reference lists of relevant studies were searched.

Study selection
Randomised controlled trials (RCTs) of pharmacological smoking cessation interventions aimed at adolescent smokers (20 years or younger) that reported on rates of smoking cessation were eligible for inclusion. The primary outcome (abstinence rates) was validated by expired-air carbon monoxide or levels of saliva cotinine. Secondary outcomes were adverse events. Trials that did not report on smoking cessation as an outcome were excluded.

The included trials studied nicotine patch, nicotine nasal spray, nicotine gum and bupropion in combination with smoking cessation counselling versus placebo or placebo plus counselling or counselling alone. Participant ages were reported to range from 12 to 20 years. Trials were conducted between 1991 and 2009. Most trials were conducted in USA. England was also represented. Duration of therapy ranged from six to 12 weeks, where reported.

Two reviewers independently performed study selection. Disagreements were resolved by discussion.

Assessment of study quality
Trial quality was assessed using the Jadad scale of randomisation, blinding, allocation concealment and withdrawals/drop-outs to give a maximum score of 5. Trials that scored at least 4 were considered high quality.

The authors did not state how many reviewers performed quality assessment.

Data extraction
Data were extracted on smoking cessation and adverse events and were used to calculate relative risks (RRs) and 95% confidence intervals (CIs).

The authors did not state how many reviewers performed data extraction. Trial authors were contacted for missing information.

Methods of synthesis
A fixed-effect or random-effects meta-analysis, using intention-to-treat, was used to calculate pooled relative risks and 95% CIs. Statistical heterogeneity was assessed using $I^2$. Subgroup analyses were conducted for type of pharmacological therapy, follow-up period and statistical analysis. Sensitivity analysis excluded a poor quality trial. Publication bias was assessed using funnel plots and Egger's test.
Results of the review
Six RCTs were included in the review (n=816 participants reported in the text). Sample size ranged from 40 to 211 participants. Follow-up ranged from eight to 26 weeks. Two trials scored 5 on the Jadad scale, three trials scored 4 and one trial scored 3. Attrition rates ranged from 17.4% to 93.9% for the intervention group and 23.5% to 89.8% for the control group.

Compared with control, pharmacological smoking cessation interventions did not statistically significantly differ in rates of smoking cessation (RR 1.38, 95% CI 0.92 to 2.07, I²=0%; six RCTs). Subgroup analysis indicated that the results were not significant on the basis of follow-up and using per protocol analysis. Results were not significant when assessing subgroups of patients according to type of pharmacological intervention. Sensitivity analysis that excluded the one low quality trial did not change the results. There was no evidence of publication bias according to Egger’s test.

Safety data indicated that common adverse events with patches (two studies) were itching (33% to 62%) and redness at patch site (12% to 52%). Common adverse events with bupropion (two studies) were headache (3% to 44%) and nausea (7% to 10%). No treatment-related serious adverse events were noted.

Authors’ conclusions
Pharmacological therapy for smoking cessation in adolescent smokers did not have a statistically significant effect on smoking cessation up to 26 weeks follow-up. There were few adverse events. The results may have been affected by the small sample sizes.

CRD commentary
Inclusion criteria for the review were broadly defined. Three relevant data sources were searched without language restrictions. No search dates were reported. Publication bias was assessed and was not detected; the meaningfulness of the assessment with fewer than 10 trials was limited. Attempts were made to reduce reviewer error and bias during study selection; it was unclear whether similar attempts were made for data extraction and quality assessment. Quality assessment indicated the generally good quality of the included trials, although none of the trials appeared to be adequately powered to detect a significant difference in smoking cessation rates. Trials were combined using meta-analysis and statistical heterogeneity was assessed and explored in sensitivity analysis, which was appropriate. The authors acknowledged a number of limitations with the included studies, notably the small sample sizes, small number of studies, high attrition rates, short duration of follow-up and heterogeneity.

Overall, this review had some methodological problems and the limitations of the included studies should be borne in mind when interpreting the authors’ conclusions.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that further trials needed adequate sample sizes. A sample size of at least 2,920 participants was needed to show a statistical difference in rates of smoking cessation. Studies with longer follow-up periods were needed.

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