Efficacy and safety of pharmacotherapy for smoking cessation among pregnant smokers: a meta-analysis

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CRD summary
The review concluded there may be clinical evidence to support use of pharmacotherapy for smoking cessation among pregnant women smokers but further randomised controlled trials were needed. The authors’ conclusion is cautious but the paucity of the evidence base and some limitations in the review process mean the reliability of the conclusions is unclear.

Authors' objectives
To evaluate the efficacy and safety of pharmacotherapy for smoking cessation among pregnant smokers.

Searching
PubMed, EMBASE and Cochrane Central Register of Controlled Trials (CENTRAL) were searched without language restriction to June 2011 for relevant published articles. Search terms were reported. Reference lists of relevant articles were searched.

Study selection
Controlled studies that evaluated the efficacy and safety of pharmacotherapy for smoking cessation among pregnant smokers were eligible for inclusion. Study designs could include randomised controlled trials (RCTs), quasi-RCTs and retrospective or prospective controlled studies. Outcomes of interest included point-prevalence abstinence and continuous abstinence (self-reported or validated with biochemical markers).

Most of the studies evaluated nicotine patch and/or gum; one study evaluated bupropion. Dosages varied between studies. The treatment period ranged from six to 12 weeks. Where reported the age of participants in the intervention group was 25 to 33 years and in the control group was 25 to 31 years. The number of cigarettes smoked per day ranged from 13 to 25 in the intervention group and from 14 to 24 in the control group, where reported. Studies were conducted in Denmark, USA, Canada and Australia. Follow-up ranged from 12 weeks to 26 weeks.

Two reviewers independently selected studies for inclusion. Disagreements were resolved through discussion.

Assessment of study quality
Quality was assessed using the Jadad scale of randomisation, blinding and follow-up. The maximum possible score was 5. Studies that scored 2 or less were considered low quality and studies that scored 3 to 5 points were considered high quality.

The authors did not state how many reviewers assessed quality.

Data extraction
Two reviewers extracted data on abstinence rates at the longest follow-up period and at the highest gestation point and used to calculate relative risk (RR) and 95% confidence intervals (CI). Where there was no event in one group 0.5 was added.

Methods of synthesis
Pooled relative risks and 95% confidence intervals were calculated. Where statistical heterogeneity was less than 50% a Mantel-Haenszel fixed-effect model was used for the meta-analyses. Where statistical heterogeneity was more than 50% a DerSimonian and Laird random-effects model was used. Statistical heterogeneity was assessed with $I^2$ and Cochran's Q. Subgroup analyses were conducted by study design, type of validation, pharmacotherapy, duration of follow-up, methodological quality and use of placebo. Publication bias was assessed using Begg and Egger tests and visual inspection of funnel plots.
Results of the review

Seven studies (1,386 participants, range 30 to 250) were included in the review: five RCTs, one quasi-RCT and one prospective controlled observational study. All five RCTs scored 3 or more on the Jadad quality scale and the two non-randomised studies scored zero.

The mean abstinence rate at late pregnancy was 13% (95% CI 10.9 to 15.25) for intervention and control groups.

Pharmacotherapy had a significant effect on smoking cessation at the longest follow-up (RR 1.80, 95% CI 1.32 to 2.44; seven studies; I²=41.5%).

Results remained significant when analysed by type of study design. Non-RCTs (RR 3.25, 95% CI 1.65 to 6.39; two studies) reported a larger effect than RCTs (RR 1.48, 95% CI 1.04 to 2.09; five RCTs). Results remained significant for studies that used nicotine patches or bupropion, studies that used validated measures, studies with short-term follow-up (<12 weeks) and those without placebo groups. No significant treatment effects were found in studies that used nicotine gum, studies that used self reported measures, studies with long-term follow-up (>24 weeks) and those that compared treatment with placebo. There was evidence of statistical heterogeneity (I²=52.9%) for the analysis of self reported abstinence.

Some minor adverse events in both intervention and control groups were reported in three studies. There were no significant differences between groups for serious adverse events including maternal hospitalisation, low birthweight, spontaneous abortion, preterm birth, neonatal intensive care unit admission, placental abruption and foetal demise (two studies). Birth outcome data was reported for individual studies. Three of five studies found no significant between-group differences for mean birthweight rate, low birthweight rate, mean gestational age and preterm delivery. One study found lower preterm delivery rates and low birthweight rate for intervention group (nicotine gum).

There was evidence of publication bias.

Authors' conclusions

The results indicated that there may be clinical evidence to support use of pharmacotherapy for smoking cessation among pregnant smokers.

CRD commentary

The review question was clear with defined inclusion criteria. Several relevant sources were searched. Publication bias was observed through formal assessment (difficult to interpret when the number of included studies is small). Study quality was assessed but the authors used a scale that was appropriate only for randomised controlled trials (other designs were included in the review). Appropriate methods were used to reduce reviewer error and bias in selecting studies; it was unclear whether similar methods were used for quality assessment and data extraction. Methods used to perform the meta-analysis appeared appropriate. Subgroup analyses were performed. Only seven studies were included and most only had short-term follow-up (26 weeks or less).

The authors' conclusion is cautious but the paucity of the evidence base and some limitations in the review process mean the reliability of the conclusions is unclear.

Implications of the review for practice and research

Practice: The authors did not state any implications for practice.

Research: The authors stated that further large randomised double-blind placebo-controlled trials were required to confirm the results of the review. Further trials were needed to investigate the effects of oral medication as well as nicotine replacement therapy and to investigate the difference in smoking cessation for pregnant smokers and those in the general population. An economic evaluation based on a cost-benefit analysis of smoking cessation versus adverse events for smoking cessation during pregnancy using pharmacotherapy was required.

Funding

None.

Bibliographic details

PubMedID
22780818

DOI
10.1111/j.1471-0528.2012.03408.x

Original Paper URL

Indexing Status
Subject indexing assigned by NLM

MeSH
Adult; Benzazepines /therapeutic use; Bupropion /therapeutic use; Controlled Clinical Trials as Topic; Dopamine Uptake Inhibitors /therapeutic use; Epidemiologic Methods; Female; Humans; Nicotinic Agonists /therapeutic use; Pregnancy; Pregnancy Complications /chemically induced /prevention & control; Pregnancy Outcome; Quinoxalines /therapeutic use; Smoking Cessation /methods; Tobacco Use Cessation Products; Varenicline; Young Adult

AccessionNumber
12012036930

Date bibliographic record published
11/10/2012

Date abstract record published
03/04/2013

Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.