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Lobeline for smoking cessation

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ABSTRACT

Background
Lobeline is a partial nicotine agonist, which has been used in a variety of commercially available preparations to help stop smoking.

Objectives
The objective of this review was to assess the effects of lobeline on long term smoking cessation.

Search strategy
We searched the Cochrane Tobacco Addiction Group trials register (most recent search January 2009).

Selection criteria
Randomized trials comparing lobeline to placebo or an alternative therapeutic control, which reported smoking cessation with at least six months follow-up.

Data collection and analysis
We extracted data in duplicate on the type of subjects, the dose and form of lobeline, the outcome measures, method of randomisation, and completeness of follow-up.

Main results
We identified no trials meeting the full inclusion criteria including long term follow-up.

Authors’ conclusions
There is no evidence available from long term trials that lobeline can aid smoking cessation.

PLAIN LANGUAGE SUMMARY

Can lobeline help people to quit smoking

Lobeline is an alkaloid derived from the leaves of an Indian tobacco plant, and has been widely used in commercial smoking remedies. Its adverse effects include dizziness, nausea, and vomiting, and tablets and pastilles containing Lobeline may lead to throat irritation.
The review found no adequate long-term trials which could provide evidence that Lobeline can help people stop smoking. Even short-term studies do not indicate a consistent effect on smoking behaviour.

**BACKGROUND**

Lobeline is an alkaloid derived from the leaves of an Indian tobacco plant (Lobelia inflata). It was synthesised in the early 1900s and classified as a partial nicotinic agonist. The first reported use in aiding smoking cessation was in the 1930s (Dorsey 1936). Since then it has been tested in a variety of doses and formulations, and has been quite widely used in proprietary smoking remedies.

Schwartz (Schwartz 1969) identified 16 studies or reviews of clinic success rates in which lobeline had been used. Few of these used placebo or other controls, or had follow up beyond the end of treatment. Davison (1972) also reviewed the evidence and concluded that poor methodological quality prevented any conclusions on efficacy being drawn. In 1993 the FDA banned all OTC smoking cessation products in the United States, including lobeline, due to a lack of acceptable clinical efficacy data (FDA 1993). This has led to renewed interest in investigating efficacy, and one short term trial has been recently reported with another planned (Schneider 1996).

The early use of high doses (8mg tablets) of lobeline sulphate gave rise to considerable side effects; Wright (Wright 1937) cautioned against the drug’s use because of the aversive gastric effects. Parenteral injection although reported as being particularly effective, caused dizziness, nausea and vomiting (Ejrup 1967). Even buffered tablets or flavoured pastilles may lead to local throat irritation, with the possibility that any short term efficacy could be due to a non-specific aversive effect.

**OBJECTIVES**

To assess the current evidence for the effectiveness of lobeline in assisting long term smoking cessation.

The hypothesis tested was that lobeline was more effective than placebo, or an alternative treatment, in achieving long term smoking cessation.

**METHODS**

Criteria for considering studies for this review

<table>
<thead>
<tr>
<th>Lobeline for smoking cessation (Review)</th>
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<tr>
<td>Copyright © 2009 The Cochrane Collaboration. Published by John Wiley &amp; Sons, Ltd.</td>
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</tbody>
</table>
Description of studies

See: Characteristics of excluded studies.
No studies were found which met all criteria for inclusion. A number of early reports of the use of lobeline did not use any control groups. Of those which used a placebo, a number employed a cross over design with smoking behaviour assessed over days rather than weeks. Percentage reduction in number of cigarettes smoked was more commonly used as an outcome than complete abstinence. Few trials followed up beyond the end of treatment, and none for the required 6 month period.

Risk of bias in included studies

Lack of long term follow-up was a reason for exclusion in all cases. A large number of the studies were not controlled. Where comparison was made with a placebo control or alternative treatment it was rarely clear that an appropriate method of randomization had been used.

Effects of interventions

On the basis of the trials which have been published in the past sixty years there is no evidence that lobeline has any long term effect on smoking cessation.

Discussion

Trials with long-term follow-up using validated sustained abstinence are the gold standard for evaluating smoking cessation methods. Trials with short term follow-up may overestimate both the overall abstinence rates and the size of any treatment effect.

Because short term abstinence is not necessarily evidence of long term cessation this review has not systematically synthesized and evaluated the evidence from short term studies. However even these did not appear to provide consistent evidence that lobeline has an effect on smoking behaviour. A number of the controlled short term trials concluded that lobeline had no effect on smoking: (Merry 1963; BTA 1963; Edwards 1964 A; Edwards 1964 B; Ross 1967; Leone 1968; Davison 1972).

Schneider and colleagues (Schneider 1996) recently suggested that a formulation of lobeline with better bioavailability could be efficacious. They have conducted a clinical trial comparing 7.5mg sublingual lobeline 9 times/day with placebo for 6 weeks. Both groups received weekly individual counselling. The primary endpoint in this trial was abstinence during the last four weeks of the treatment period. Using an Intent to Treat analysis 10/34 lobeline treated subjects met this criterion of abstinence, compared to 8/ 47 receiving placebo (p=0.28). They plan further studies.

A multicentre study of sublingual lobeline with 750 subjects has been reported but not published in full (Dynagen 1997). Overall it found no statistically significant difference between placebo and lobeline sublingual tablets at 6 week follow-up, although one of the three sites did demonstrate significant efficacy. DynaGen has now discontinued its research programme, but formulations of lobeline for nasal, transdermal patch and transbuccal patch use may be further investigated by other companies.

Authors' Conclusions

Implications for practice

There are no well conducted trials with long term follow up. There is therefore no evidence that lobeline can aid smoking cessation.

Implications for research

Any other research should await the findings of further studies by Schneider.

Acknowledgements

JR Hughes is supported by a Research Scientist Development Award DA-00105 from the National Institute on Drug Abuse.
REFERENCES

References to studies excluded from this review

Bachman 1964 [published data only]
Bachman DS. Group smoking deterrent therapy. GP 1964; 30:86.

Bartlett 1957 [published data only]

BTA 1963 [published data only]

Davison 1972 [published data only]

Dorsey 1936 [published data only]

Dynagen 1997 [published and unpublished data]

Edwards 1964 A [published data only]
Edwards G. Double-Blind Trial of Lobeline in an Anti-Smoking Clinic. Medical Officer 1964;112:158–60.

Edwards 1964 B [published data only]
Edwards G. Hypnosis and lobeline in an Anti-Smoking Clinic. Medical Officer 1964;111:239–43.

Ejrup 1959 [published data only]
Ejrup B. Follow-up of the material of smokers difficult to treat. Sven Lakartidn 1959;56:2254–62.

Ejrup 1967 [published data only]

Farago 1968 [published data only]

Golledge 1965 [published data only]
Golledge AH. Influencing factors in ant-smoking clinics together with the results of a double blind trial of Lobidan. Medical Officer 1965;114:59–61.

Graf 1966 [published data only]

Hoffstaedt 1964 [published data only]

Hoffstaedt 1965 [published data only]

Jacobs 1971 [published data only]

Jochum 1961 [published data only]

Kalyuzhny 1968 [published data only]

Kaufman 1960 [published data only]

Leone 1968 [published data only]

London 1963 [published data only]

McChargue 2002 [published data only]

Merry 1963 [published data only]

Perlstein 1964 [published data only]

Rapp 1955 [published data only]
Rapp 1959  (published data only)

Rosenberg 1959  (published data only)

Rosnick 1965  (published data only)

Ross 1967  (published data only)

Schneider 1996  (published data only)

Scott 1962  (published data only)

Swartz 1964  (published data only)

Wright 1937  (published data only)

Additional references

FDA 1993

Schwartz 1969

 Yusuf 1985

* Indicates the major publication for the study
### Characteristics of excluded studies [ordered by study ID]

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
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<tbody>
<tr>
<td>Bachman 1964</td>
<td>Double blind crossover evaluation of Nikoban.</td>
</tr>
<tr>
<td>Bartlett 1957</td>
<td>Crossover trial comparing lobeline, meprobamate and placebo. Smokers not attempting to cut down.</td>
</tr>
<tr>
<td>BTA 1963</td>
<td>Only six week follow-up</td>
</tr>
<tr>
<td>Davison 1972</td>
<td>No follow-up after 4 weeks treatment.</td>
</tr>
<tr>
<td>Dorsey 1936</td>
<td>Not controlled</td>
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<tr>
<td>Dynagen 1997</td>
<td>Follow-up for main study only 6 weeks.</td>
</tr>
<tr>
<td>Edwards 1964 A</td>
<td>Double blind trial, follow up only 3 months after 4 weeks of treatment</td>
</tr>
<tr>
<td>Edwards 1964 B</td>
<td>Subjects alternated to lobeline or hypnosis. Only 3 month follow-up after treatment.</td>
</tr>
<tr>
<td>Ejrup 1959</td>
<td>Not controlled. Used lobeline injections in a smoking clinic.</td>
</tr>
<tr>
<td>Ejrup 1967</td>
<td>Not controlled. Used lobeline injections in smoking clinics.</td>
</tr>
<tr>
<td>Golledge 1965</td>
<td>Only 28 day follow-up</td>
</tr>
<tr>
<td>Graff 1966</td>
<td>Only 3 month follow-up</td>
</tr>
<tr>
<td>Hoffstaedt 1964</td>
<td>No control group. Lobeline, hydroxyzine and discussion in a smoking clinic.</td>
</tr>
<tr>
<td>Hoffstaedt 1965</td>
<td>No control group. Lobeline, hydroxyzine and discussion in a smoking clinic.</td>
</tr>
<tr>
<td>Jacobs 1971</td>
<td>Only 10 week follow up</td>
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<tr>
<td>Jochum 1961</td>
<td>Lobeline compared with psychotherapy. No follow up.</td>
</tr>
<tr>
<td>Kaufman 1960</td>
<td>Not controlled.</td>
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<tr>
<td>Leone 1968</td>
<td>Describes a number of clinics. Outcomes not reported for lobeline and placebo separately. 6 week follow up.</td>
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<tr>
<td>London 1963</td>
<td>Controlled trial of 0.5mg pastilles. No follow-up after 4 weeks treatment</td>
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<tr>
<td>Reference</td>
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<td>--------------</td>
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<tr>
<td>McChargue 2002</td>
<td>Controlled trial of lobeline and moist snuff replacement with placebos over four weeks (one week for each condition). Follow up for each measured 48 hours later.</td>
</tr>
<tr>
<td>Merry 1963</td>
<td>Controlled trial of lobeline or placebo after failure to quit with one week without medication and one week on placebo. No post treatment follow-up</td>
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<tr>
<td>Perlstein 1964</td>
<td>No post-treatment follow-up reported</td>
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<tr>
<td>Rapp 1955</td>
<td>Crossover trial of lobeline and placebo. Smoking behaviour recorded for one week on each.</td>
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<tr>
<td>Rapp 1959</td>
<td>Crossover study of lobeline sulphate in capsules, Bantron in capsules or starch placebo.</td>
</tr>
<tr>
<td>Rosenberg 1959</td>
<td>Controlled trial, no long term follow-up data reported</td>
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<tr>
<td>Rosnick 1965</td>
<td>No long term follow-up</td>
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<tr>
<td>Ross 1967</td>
<td>Long term quit rates not reported by treatment group</td>
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<tr>
<td>Schneider 1996</td>
<td>No follow up reported after 6 weeks of treatment</td>
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<tr>
<td>Scott 1962</td>
<td>Crossover study with no long term follow up</td>
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<tr>
<td>Swartz 1964</td>
<td>Not controlled</td>
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<tr>
<td>Wright 1937</td>
<td>Not controlled</td>
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DATA AND ANALYSES

This review has no analyses.

WHAT’S NEW

Last assessed as up-to-date: 7 January 2009.

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<td>8 January 2009</td>
<td>New search has been performed</td>
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<td>28 October 2008</td>
<td>Amended</td>
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HISTORY


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<td>27 April 2006</td>
<td>New search has been performed</td>
<td>Searches rerun, no new studies</td>
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<tr>
<td>19 May 2003</td>
<td>New search has been performed</td>
<td>One reference added to excluded studies list</td>
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</table>

CONTRIBUTIONS OF AUTHORS

LS and JH conceived the review; both extracted data, and collaborated on text and subsequent updates

DECLARATIONS OF INTEREST

None
SOURCES OF SUPPORT

Internal sources

- Department of Primary Health Care, University of Oxford, UK.
- National School for Health Research School for Primary Care Research, UK.

External sources

- National Institute on Drug Abuse (NIDA), USA.
- NHS Research and Development National Cancer Programme, England, UK.

INDEX TERMS

Medical Subject Headings (MeSH)

*Smoking Cessation; Lobeline [*therapeutic use]; Nicotinic Antagonists [*therapeutic use]; Smoking [*prevention & control]

MeSH check words

Humans