Polyvalent mechanical bacterial lysate for the prevention of recurrent respiratory infections: a meta-analysis.
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CRD summary
The results suggested that polyvalent mechanical bacterial lysate was effective in both children and adults in preventing respiratory tract infections. Unclear quality of the included studies, statistical heterogeneity in some results and uncertainty surrounding the statistical methods raise serious questions about the reliability of the authors' conclusions.

Authors' objectives
To explore whether polyvalent mechanical bacterial lysate (PMBL) treatment is effective in preventing respiratory tract infection.

Searching
Reactions Database, PubMed and TOXLINE were searched without language restrictions. Google Scholar, the Institut de l'Information Scientifique et Technique (INIST) website and Scirus were searched for additional studies. Search terms were reported but search dates were not. The manufacturers of PMBL were contacted for further information on additional trials including unpublished data. The authors considered including data from abstracts of conference proceedings if the methods were clearly described and adequate data were reported.

Study selection
Randomised controlled trials (RCTs) that compared PMBL treatment with placebo or another convention bacterial lysate or no treatment in adults with chronic bronchitis and chronic obstructive pulmonary disease or tuberculosis were eligible for inclusion. Children with acute or recurrent respiratory tract infections were included. Studies on prevention of infections on healthy people or immunologic parameters were not considered.

The primary outcome measure was prevention of exacerbations or acute respiratory tract infection. Patient age ranged from 10 months to 82 years. In most studies the interventions lasted for three months. Patients in the trials took one PMBL tablet per day.

The authors did not report how many reviewers were involved in study selection.

Assessment of study quality
The quality of the selected trials was assessed according to the five-point validated Jadad scale of randomisation methods, blinding and description of withdrawals and drop-outs.

Trial quality was assessed independently by two reviewers and differences were resolved by consensus.

Data extraction
Mean effect sizes of treatment versus placebo and their corresponding 95% confidence intervals (CIs) were calculated using difference of means method for continuous variables.

It was unclear how many reviewers were involved in data extraction.

Methods of synthesis
The results of difference in means with their 95% CIs were pooled using both fixed-effect and random-effects models, depending on the presence of statistical heterogeneity. Statistical heterogeneity was assessed using I² and Cochran Q statistics statistic (I²>50% and p<0.10 indicated statistical heterogeneity). The authors stated that the results were calculated as mean differences and these were presented in the forest plots but relative risks were used in the main body of the review.

Subgroup analyses of patients with COPD (chronic obstructive pulmonary disease), bronchitis and tuberculosis were
planned.

**Results of the review**

Fifteen randomised controlled trials (2,557 participants) were included in the review. The authors did not report the findings of the quality assessment in the review but mentioned that they grouped studies into double-blind placebo-controlled randomised clinical trials.

PMBL induced a significant reduction of the number of recurrences of respiratory tract infections compared with placebo (mean difference -0.513, 95% CI -0.722 to -0.303; I²=67%, evidence of statistical heterogeneity; 15 RCTs). The number needed to treat for one year to avoid one infection was 1.15.

Subgroup analyses performed on adults and children with recurrent respiratory infections other than COPD, chronic bronchitis and tuberculosis found that PMBL significantly reduced the total number of infections in adults (mean difference -0.502, 95% CI -0.824 to -0.181; I²=68%, evidence of statistical heterogeneity; seven RCTs) and in children (mean difference -2.204, 95% CI -3.260 to -1.147; I²=0%; three RCTs). The finding was statistically significant in favour of PMBL in tuberculosis patients (mean difference -0.502, 95% CI -0.890 to -0.114; I²=13%; two RCTs) but not in COPD or chronic bronchitis patients (mean difference -0.404, 95% CI -0.864 to 0.057; I²=60% evidence of statistical heterogeneity; three RCTs).

None of the studies recorded or reported side effects of the interventions.

**Cost information**

One study reported the mean cost of the antibiotic therapy during the period from September to February prior to PMBL was €3,459.60 while during the PMBL trial (same period one year later) it was only €1,499.40 (-57%). Adding the latter amount to the cost (€1,295.04) of the prophylactic therapy with PMBL, the total cost of €2794.44 was significantly lower (-20%) than the cost for the same period of the previous year.

**Authors’ conclusions**

The results of the meta-analysis suggested that PMBL was effective in both children and adults in preventing respiratory tract infections but further trials were needed.

**CRD commentary**

The review addressed a clear question and was supported by appropriate inclusion criteria. Several relevant sources were searched without language restrictions and efforts were made to locate unpublished literature, which reduced potential for language and publication biases. The authors did not state whether study selection and data extraction were undertaken in duplicate, so reviewer error and bias could not be ruled out. The authors stated that they assessed the study quality but they did not report this in the review so it was difficult to assess overall study quality.

There was confusion regarding the statistical analysis and whether relative risks or mean differences were calculated. This made it unclear whether an appropriate synthesis was carried out using appropriate statistical methods. There were some errors in the study characteristics table and lack of labelling in the forest plots.

Small sample sizes, limited details of patient characteristics, unclear quality of the included studies, statistical heterogeneity in some results and uncertainty surrounding the statistical methods raised serious questions about the reliability of 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 a need for well-designed studies (in term of blinding and randomisation procedures) that should include a higher number of patients who were selected according to their disease and its severity.

**Funding**

Not stated.

**Bibliographic details**

**PubMedID**
22155205

**DOI**
10.1016/j.pupt.2011.11.002

**Original Paper URL**

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Adolescent; Adult; Aged; Aged, 80 and over; Bacteria /chemistry; Bacterial Vaccines /therapeutic use; Child; Child, Preschool; Data Interpretation, Statistical; Double-Blind Method; Female; Humans; Infant; Male; Middle Aged; Randomized Controlled Trials as Topic; Reproducibility of Results; Respiratory Tract Infections /prevention & control; Risk Assessment; Sample Size; Secondary Prevention; Treatment Outcome; Young Adult

**AccessionNumber**
12012010849

**Date bibliographic record published**
21/05/2012

**Date abstract record published**
01/11/2012

**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.