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Leukotriene receptor antagonists for non-cystic fibrosis bronchiectasis (Review)

Corless JA, Warburton CJ

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Leukotriene receptor antagonists for non-cystic fibrosis bronchiectasis.
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TABLE OF CONTENTS

[Intervention Review]

Leukotriene receptor antagonists for non-cystic fibrosis bronchiectasis

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ABSTRACT

Background

Leukotriene receptor antagonists are a new class of drug that were initially identified for use in asthma. As they have an effect on neutrophil mediated inflammation, they may be of benefit in bronchiectasis.

Objectives

To determine whether leukotriene receptor antagonists have any additive benefit over and above conventional treatment for bronchiectasis (usually consisting of antibiotics and postural drainage).

Search methods

The Cochrane Airways Group Specialised Regsiter of trials and CENTRAL were searched up to May 2011.

Selection criteria

Only randomised, controlled trials were considered

Data collection and analysis

The results of searches were analysed by both authors

Main results

No randomised, controlled trials were identified. The latest search was in May 2011.

Authors' conclusions

Further research is required to establish any benefit from the use of leukotriene antagonists in bronchiectasis.

PLAIN LANGUAGE SUMMARY

Leukotriene receptor antagonists for non-cystic fibrosis bronchiectasis

Leukotriene receptor antagonists are a new class of drug which may have an anti-inflammatory action in some patients with asthma. In theory they may also be of benefit in bronchiectasis, but no randomised controlled trials have yet been reported so it is not possible to make a recommendation about their use in this condition.

BACKGROUND

Leukotriene receptor antagonists (LRAs) have recently been identified as a useful drug in bronchial asthma. In an acute asthma attack, numerous inflammatory mediators including leukotrienes are released by mast cells. Leukotrienes in particular are potent bronchoconstrictor agents and act as a chemo-attractant for eosinophils. They also have a role in neutrophil mediated inflammation, for example in cystic fibrosis. LRAs inhibit specific receptors for leukotrienes in the bronchiolar tissues so they may reduce bronchoconstriction, oedema, mucus secretion and eosinophil or neutrophil - mediated airway damage.

This review aimed to identify all clinical trials of LRAs in bronchiectasis and synthesize the findings into an overall conclusion regarding the effect of LRAs in bronchiectasis.

OBJECTIVES

The objective of the review was to determine whether LRAs have any additive benefit over and above conventional treatment for bronchiectasis (usually consisting of antibiotics and postural drainage).
The specific purpose of the review was to assess whether the use of LRAs has any benefit on symptoms, pulmonary function, exacerbation rate, quality of life and mortality.

METHODS

Criteria for considering studies for this review

Types of studies

To be selected, studies will be randomised against either placebo or other active treatment ,and may be parallel group or cross-over design.

Types of participants

Adults with a diagnosis of bronchiectasis based on clinical symptoms and imaging techniques (either high resolution CT scanning or bronchography). Patients with cystic fibrosis would be excluded.
Other therapy used for bronchiectasis during the study must be stable and well documented. Subgroup analysis by co-intervention would be carried out to investigate use in differing grades of severity of bronchiectasis.

Types of interventions

Participants randomised to use LRAs such as Montelukast or zafirlukast or matching placebo.

Types of outcome measures

All outcome measures of bronchiectasis severity were to be considered, but specifically:

- bronchiectasis symptom scores
- clinic measurements of airway function, mainly FEV1 and FVC
- quality of life score
- bronchiectasis exacerbation rates
- mortality data

Search methods for identification of studies

Trials were identified using the Cochrane Airways Group Specialised Register of trials, which is derived from systematic searches of bibliographic databases including the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE and CINAHL, and handsearching of respiratory journals and meeting abstracts (please see the Airways Group Module for further details). All records in the Specialised Register coded as 'bronchiectasis' were searched using the following terms:

leukotriene* or leucotriene* or anti-leuk* or "anti leuk*" or anti-leuc* or "anti leuc*" or *lukast or lukast* or cysteinyl OR montelukast or zafirlukast or pranlukast

An additional search of CENTRAL was carried out using the same search terms. The most recent searches were run in May 2011.

Bibliographies from included studies, reviews and texts were checked for further references to trials.

Data collection and analysis

SELECTION OF TRIALS

Initially the titles, abstracts and citations were independently reviewed by the two reviewers (JC and CW) to assess potential relevance for full review. Subsequently from the full text, both reviewers independently assessed studies for inclusion based on the criteria for population, intervention, study design and outcomes.

QUALITY ASSESSMENT
Studies to be included were subjected to quality assessment by both reviewers, using two the Cochrane approach and the method of Jadad.

DATA EXTRACTION
Data were to be extracted from published selected studies by both reviewers JAC and CJW and entered into the Cochrane Collaboration software programme.

STATISTICAL CONSIDERATIONS
Where possible, all included trials were to be combined using the Review Manager. For continuous variables the results of individual studies were to be calculated as fixed effects weighted mean difference (WMD) or standardised mean difference (SMD), with 95% Confidence Intervals (CI). For similar studies the pooled WMD or SMD and 95%CI were to be calculated. The SMD was to be used only used to pool the same type of variable (e.g. PEFR) when expressed in different units e.g. L/min and percent of predicted normal. It would not have been used to pool different variables such as clinic FEV1 and home PEFR measurements. For pooled effects a Breslow-Day test of heterogeneity was to have been carried out and a p value <0.05 would have been considered significant.

Planned subgroup comparisons were:

1. Concurrent use of corticosteroids (none, inhaled, oral)
2. Concurrent use of salmeterol (which may have effects on neutrophils)

Planned sensitivity analyses were:

1. Methodological quality - Cochrane criteria A versus B & C and Jadad score 3-5 versus <3
2. Random effects versus fixed effects modelling.

RESULTS

Description of studies

A total of 38 references have been identified from the database searches up to May 2011. No randomised or controlled clinical trials were identified.

Risk of bias in included studies

No trials could be assessed.

Effects of interventions

No data could be analysed.

DISCUSSION

Leukotriene antagonists have only recently been licensed for use in asthma, for which they were originally designed. The absence of reported trials in bronchiectasis is more likely due to prioritisation of trials than failure to publish negative studies. The number of patients with asthma (and therefore the market for this type of drug) is much larger than for bronchiectasis. There are theoretical grounds for studies using these drugs in bronchiectasis, however.

AUTHORS' CONCLUSIONS

Implications for practice

No relevant trials appear to have been published so this review concludes that there is no evidence of effect of leukotriene antagonists in bronchiectasis rather than evidence of no effect.

Implications for research

Clinical trials of the use of leukotriene antagonists in bronchiectasis are required.

ACKNOWLEDGEMENTS

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Additional references

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Peters-Golden 1999

Peters-Golden M. Pulmonary diseases other than asthma as potential targets for antileukotriene therapy. *Clinical Reviews in Allergy & Immunology* 1999;**17**(1-2):247-60.

WHAT'S NEW

Date	Event	Description
5 May 2011	New search has been performed	New literature search run, no new eligible studies found.

HISTORY

Protocol first published: Issue 4, 1999
Review first published: Issue 2, 2001

Date	Event	Description
21 April 2009	New search has been performed	Literature search re-run; no new studies identified
1 August 2008	Amended	Converted to new review format.
3 April 2007	New search has been performed	New studies sought but none found: 03/04/07
24 January 2000	New citation required and conclusions have changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

JC: Protocol initiation, study assessment, review development & write-up
CW: Protocol development, study assessment, write-up of review

DECLARATIONS OF INTEREST

None

SOURCES OF SUPPORT

Internal sources

- NHS Research and Development, UK.

External sources

- No sources of support supplied

INDEX TERMS

Medical Subject Headings (MeSH)

Acetates [therapeutic use]; Bronchiectasis [*drug therapy] [etiology]; Clinical Trials as Topic; Leukotriene Antagonists [*therapeutic use]; Placebos; Quinolines [therapeutic use]; Tosyl Compounds [therapeutic use]

MeSH check words

Humans