Appetite stimulants in cystic fibrosis: a systematic review

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CRD summary
This review aimed to assess the benefits of appetite stimulants in cystic fibrosis-related anorexia and concluded that megesterol acetate may be a useful adjunct for treatment for cystic fibrosis patients who had difficulty maintaining their weight. This conclusion may not be reliable given the overall poor quality of the included studies.

Authors' objectives
To assess the benefits of appetite stimulants in cystic fibrosis-related anorexia.

Searching
MEDLINE, AMED (from 1966), British Nursing Index (from 1985), CINAHL (from 1982), EMBASE (from 1996), The Cochrane Library, National Research Register databases were searched to January 2007. A Google search was made. The citations and references of included studies were handsearched and reviewed for further relevant studies. The reviewers also consulted experts, suppliers, authors and/or poster abstracts for unpublished and negative studies. Authors of conference abstracts were contacted for publications in press. Search terms were reported. The search was restricted to articles in English.

Study selection
Eligible studies involved cystic fibrosis patients of any age or disease severity where the principal aim was to study appetite stimulants. Inclusion criteria for the outcomes were not specified. Included studies assessed megesterol acetate, dronabinol, mirtazapine and cyproheptadine. Doses varied. Duration of active intervention ranged between one and 28 months. Megesterol acetate was used in children and young adults, dronabinol in teenagers and adults, mirtazapine in teenagers and cyproheptadine in adults and children. Age, where reported, ranged between 1.75 and 44 years. Outcomes included weight gain, lung function, appetite, body composition, quality of life and oral intake.

The authors stated neither how the papers were selected for review nor how many reviewers performed the selection.

Assessment of study quality
Each study was given a score between 1 (lowest) and 7 (highest) on the basis of whether seven prespecified measures had been assessed: pulmonary function measured as forced expiratory volume in 1 s as a percentage of the predicted value (FEV1 % predicted); anorexia and/or weight loss; body weight; body composition; quality of life; dietary energy and protein intake; and side-effects.

Studies were also classified according to levels of evidence for treatment, with Level I best and Level V poorest (Chalmers & Altman, 1995).

Two reviewers conducted the validity assessment. Disagreements were resolved by consensus.

Data extraction
Study characteristics were reported in a table and in the text. Two reviewers independently conducted the data extraction. Disagreements were resolved by consensus.

Methods of synthesis
A narrative synthesis was carried out. Differences in outcomes were presented in a table.

Results of the review
Fifteen studies were included (n=139). Three studies were randomised and double-blind. Ten did not use a control. The sample sizes ranged from one to 18.
The median number of measures included in the studies was 4 (range 1 to 7). Levels of evidence ranged from levels II to V.

**Megesterol acetate**: Two randomised double-blind placebo-controlled studies reported statistically significant improvements in weight and lung function. Four found improvement in body composition, two of which were statistically significant. A statistically significant improvement in oral energy and protein intake was reported in one study.

**Mirtazapine and dronabinol**: Two non-randomised trials reported statistically significant weight gain, as did a cyproheptadine study.

**Adverse effects**: Adverse effects for megesterol acetate included adrenal suppression, abnormalities of glycaemic control, mood changes and testicular failure. Mood changes were reported with cyproheptadine and dronabinol.

**Authors’ conclusions**
Megesterol acetate may be a useful adjunct for treatment for cystic fibrosis patients who had difficulty maintaining their weight. Insufficient data existed for the other appetite stimulants.

**CRD commentary**
The review addressed a clear question and undertook a comprehensive search for studies. Efforts were made to search for unpublished literature, which may have reduced the chance of publication bias affecting the review (no formal assessment was performed). The restriction to literature in the English language may have made the review prone to language bias. Appropriate steps were taken to minimise reviewer error and bias in the review process. But, it was unclear how the papers were selected for review, which might mean that selection bias occurred. A narrative synthesis was appropriate given that the studies comprised small samples, were generally of poor quality and very few were randomised. Although generally a well-conducted review, the reliability of the authors’ conclusions is unclear given the small number, size and heterogeneity of the included studies; their recommendations for future research seem reasonable.

**Implications of the review for practice and research**

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

**Research**: More evidence was required on the role of appetite stimulants acting as adjuncts to natural supplements, high calorie/fat diet and tube feeding. There was also a requirement for an adequately powered randomised controlled trial of megesterol acetate in cystic fibrosis. Studies that incorporated relevant clinical measures and monitoring of compliance, frequency of unwanted effects and maintenance of results following the cessation of megesterol acetate should be undertaken.

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