Efficacy of selected treatments of HIV wasting: a systematic review and meta-analysis


CRD summary
This review evaluated the efficacy of recombinant human growth hormone (rhGH), testosterone and anabolic steroids in the treatment of HIV wasting. The authors concluded that there were no significant differences between the treatments in their efficacy for increasing lean body mass, but an approved dose of rhGH may be advantageous in terms of functional capacity and quality of life. Given the methodology of the review, the reliability of the results and conclusions is uncertain.

Authors' objectives
To assess the efficacy of recombinant human growth hormone (rhGH), testosterone and anabolic steroids in the treatment of human immunodeficiency virus (HIV) wasting.

Searching
PubMed (from 1996 to April 2004) and Current Contents were searched; the search terms were reported. In addition, the reference lists of included studies and reviews published in the previous two years were checked. Abstracts of meetings (2002 and 2003) were also searched: the Infectious Diseases Society of America, International AIDS Society, Interscience Conference on Antimicrobial Agents and Chemotherapy, and the Conference on Retroviruses and Opportunistic Infections. The search was restricted to studies published in English.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs), non-randomised controlled trials and uncontrolled case series were eligible for inclusion.

Specific interventions included in the review
Studies of rhGH, testosterone or anabolic steroids, with a minimum treatment duration of 2 weeks, were eligible for inclusion. The duration of treatment in the included studies varied from 8 to 24 weeks. The interventions evaluated were nandrolone, testosterone, oxandrolone, oxymetholone and rhGH, while the comparators included megestrol, dietary counselling, exercise and placebo.

Participants included in the review
Studies involving more than 10 people with HIV or acquired immune deficiency syndrome (AIDS) wasting, who were over 18 years of age, were eligible for inclusion. Studies of people with lipodystrophy only were excluded. The authors used the definition of wasting reported in the studies. The included studies defined wasting as a weight loss of over 5% or over 10% over various periods of time, or a body weight less than 90% of ideal. Four studies were restricted to hypogonadal patients, 10 studies included only men, and one was restricted to women with serum androgen levels CDC deficiency below the mean for premenopausal women. The age of the participants ranged from 35 to 46 years (mean 39.8).

Outcomes assessed in the review
Studies reporting a body composition measure, an assessment of physical function, or quality of life, were eligible for inclusion.

How were decisions on the relevance of primary studies made?
The authors did not state how the studies were selected for full paper assessment, or how many reviewers performed the initial selection. Two reviewers screened the full papers. However, it was unclear whether this was undertaken independently and how any disagreements were resolved.
Assessment of study quality
The quality of included RCTs was assessed using the Jadad score. The authors did not state how the papers were assessed for quality, or how many reviewers performed the quality assessment.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

The mean difference (MD), and range, of change in lean body mass (LBM), fat-free mass (FFM) and body cell mass, and the percentage of deaths, withdrawals and adverse events, were calculated across studies for each intervention type.

Methods of synthesis
How were the studies combined?
Pooled mean changes in LBM and FFM between treatment and placebo groups were also calculated. The results for physical function and quality of life were combined in a narrative.

How were differences between studies investigated?
The authors presented P-values for a statistical test of heterogeneity, however, the method used was not reported.

Results of the review
Eighteen studies (n=1,792) were included in the review: 15 RCTs (one a crossover design) and 3 uncontrolled case series.

Ten of the included RCTs scored 3 or more on the Jadad scale out of a possible 5.

Body composition.
There was a statistically significant pre-post increase in LBM or FFM in people treated with rhGH (6 comparisons; MD 2.75, 95% CI: 1.44, 3.71), testosterone (5 comparisons; MD 1.93, 95% CI: 0.42, 3.45), testosterone/exercise (3 comparisons; MD 3.57, 95% CI: 2.30, 4.85), anabolic steroids (5 comparisons; MD 2.68, 95% CI: 2.06, 3.30), and combinations of oxandrolone with megestrol or testosterone/exercise (2 comparisons; MD 6.20, 95% CI: 4.93, 7.48).

There was statistically significant heterogeneity in all but the anabolic steroids meta-analysis (P<0.10).

There was a statistically significant increase in LBM or FFM in people treated with rhGH (3 comparisons; MD 3.15, 95% CI: 2.68, 3.61), testosterone (2 comparisons; MD 2.91, 95% CI: 0.91, 4.92) or anabolic steroids (2 comparisons; MD 1.95, 95% CI: 0.52, 3.39), compared with placebo. There was no statistically significant heterogeneity in the meta-analysis of rhGH or anabolic steroid studies.

Safety.
There was no significant difference in mortality, the number of withdrawals, total adverse events, treatment-related adverse events, or hepatotoxicity withdrawals for patients treated with rhGH, testosterone, or anabolic steroids. There was a statistically significant increase in hepatotoxicity with anabolic steroids (OR 5.12, 95% CI: 1.68, 15.58) in comparison with placebo.

Physical function.
Two studies reported an improvement in work output in patients treated with rhGH. Two studies reported improved strength in some muscle groups when treated with testosterone or testosterone/exercise, compared with placebo. One study reported a significant increase in shoulder strength in patients treated with oxandrolone than in those given placebo. One study reported a significant increase in upper body strength and power, and knee power with rhGH, but a
decrease in strength in patients receiving a combination of rhGH and insulin-like growth factor.

Quality of life.

Two of 3 studies evaluating rhGH, two of 6 studies evaluating testosterone, and all 5 studies evaluating anabolic steroids reported statistically significant improvements in some aspects of quality of life with treatment. Two studies reported significant improvements in quality of life with rhGH after 12 weeks. Another study reported a significant improvement in quality of life for patients treated with rhGH when compared with placebo. One study reported significant improvements in the Beck Depression Inventory and the Oster's scale in patients treated with testosterone.

Authors' conclusions
The authors concluded that there was no suggestion of any statistically significant differences between rhGH, testosterone and anabolic steroids in the degree of efficacy for increasing LBM in people with HIV wasting. The Food and Drug Administration-approved dose of rhGH may have advantages over the other two therapies in terms of improvements in functional capacity and quality of life.

CRD commentary
The review question and inclusion criteria were clearly stated. The authors searched relevant sources for studies, although the search was restricted to English language studies and publication bias was not investigated. The authors did not describe the methods used to select the studies, assess quality, or extract the data, thus error and bias cannot be ruled out. Only the quality scores for 13 RCTs were given, with a validity test for the other 2 RCTs and the 3 uncontrolled case-series being deemed not applicable. The authors pooled statistically and clinically heterogeneous studies, which might not have been appropriate. The combining of data for physical functioning and quality of life in a narrative seems appropriate. Given the lack of review methodology, the reliability of the results and conclusions is uncertain.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors suggested that the use of additional agents as primary and concomitant therapy should be investigated more in women, and covariates such as androgen deficiency need to be addressed. They went on to suggest that the roles of prescribed resistance exercise and appetite stimulants as concomitant therapy should also be investigated.

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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.