A systematic review of commonly used medical treatments for hirsutism in women

Koulouri O, Conway GS

CRD summary
This review assessed drugs to treat hirsutism in women and concluded that seven drug groups (including oral contraceptives and metformin) showed beneficial results. Weight loss was an important aspect of treatment. Due to limitations in the review methods, an inappropriate method of meta-analysis and lack of detail of individual study results, these conclusions may not be reliable.

Authors' objectives
To evaluate the efficacy of drug treatments for hirsutism in women.

Searching
MEDLINE and EMBASE (from inception to 2006) and Cochrane Central Register of Controlled Trials (CENTRAL) were searched. Full details of search terms were not reported (other than all trials were identified from the term hirsutism).

Study selection
Randomised controlled trials (RCTs) of drug therapy for women with idiopathic hirsutism or polycystic ovary syndrome were eligible for the review. Studies that included women with congenital adrenal hyperplasia or of drugs outside routine treatment (ketoconazole, analogues of gonadotrophin-releasing hormone, cimetidine, dexamethasone and cyproterone not in combination with an oral contraceptive pill) were excluded. Eligible studies had to measure outcomes with the mean Ferriman-Gallwey (F-G) score over six months of treatment.

Included trials were of women with mean body mass index (BMI) in the range 20.8kg/m² to 37.8kg/m². Baseline F-G scores ranged from nine to 28.4. Studies compared two or more drugs to each other or to placebo. Some studies assessed drugs in combination. Included treatments were: metabolism moderators (metformin, thiazolidinediones, acarbose and sibutramine); oral contraceptive pills (ethinyl oestradiol with progestogens, cyproterone acetate, desogestrel, levonorgestrel, gestodene); antiandrogens (ethinyl oestradiol with cyproterone acetate, spironolactone, finasteride, flutamide); and combinations of these treatments. Doses varied between studies. Study duration ranged from six to 12 months.

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

Assessment of study quality
The authors did not state that they assessed validity. Details of whether the trial was single- or double-blinded were reported.

Data extraction
Details of the statistical comparison in each trial (whether between or within groups) and the absolute and percentage change in mean F-G score from zero to six months for the drug groups (but not placebo groups) were extracted. Data extraction was performed by two reviewers.

Methods of synthesis
It appeared that the authors pooled the baseline F-G scores and the six-month scores separately using fixed-effect meta-analyses weighted by sample size for each treatment group. They considered that there was a statistically significant difference between treatments if the 95% confidence intervals (CI) did not overlap. The percentage decrease from baseline for each drug was calculated. The relationship between obesity and treatment was assessed using correlation coefficients (Spearman's rank correlation coefficient) to compare baseline body mass index and baseline F-G score with the absolute and percentage change in F-G score.
Results of the review

Twenty eight studies (n=1,226) were included in the review. Six were double-blind and seven were single-blind RCTs.

Significant improvements in mean F-G score were seen for all treatment groups. Baseline F-G score showed a positive correlation with change in F-G score after six months (r=0.46, p<0.001) across all studies, but not in the analyses of individual treatments. A negative correlation between body mass index and change in F-G score was observed for the analysis of all studies (r=-0.38, p=0.004) and for oral contraceptive pill alone (r=-0.67, p=0.05).

Authors’ conclusions

The evidence showed that seven different drug groups showed improvements in hirsutism. Creative use of these could provide greater benefits for women with this condition. Obesity had a negative impact on treatment efficacy and appropriate lifestyle advice should be given to women to enable a successful treatment programme.

CRD commentary

This review had a clearly stated aim and reported the inclusion and exclusion criteria. Limiting the criteria to studies that reported a specific outcome measure at a specific time point may have resulted in the loss of potentially useful data. A number of relevant databases were searched. It was unclear whether efforts were made to locate unpublished material and whether there were any language restrictions (the authors highlighted potential publication bias as a limitation of the review). Data were abstracted by two reviewers, but it was not reported that studies were selected in the same way (which increased the risk of error and bias). There did not appear to be any discussion or evaluation of clinical or statistical heterogeneity between the studies and no validity assessment was made, which made it unclear whether pooling data in a meta-analysis was appropriate. The main problem with this review was the presentation of study results and the method of meta-analysis. Neither results for the placebo arms nor the between-treatment comparisons for each study were reported. The meta-analysis appeared to have pooled the pre-treatment scores separately from the post-treatment scores, thus ignoring the randomisations of the original trials. Due to some limitations with the review methods and the reporting of the study and meta-analysis results, the conclusions of this review may not be reliable.

Implications of the review for practice and research

**Practice:** The authors stated that weight loss should be an integral part of any treatment programme for hirsutism.

**Research:** Future research should consider outcome measures for hirsutism that could provide quality of life data that would be of value in health economic analyses.

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