Fusidic acid and erythromycin in the treatment of skin and soft tissue infection: a double blind study

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The use of fusidic acid and erythromycin in the treatment of skin and soft tissue infections. Fusidic acid was given as a 250-mg tablet, twice daily, while erythromycin was given as a 1.0-g tablet, twice daily. Patients took the treatment for 5 days, followed by a further 5 days if the condition remained uncured.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised individuals aged 18 years and over, with skin and soft tissue infections for which oral antibacterial therapy was indicated. The types of infections included were boils, carbuncles, acute paroncyhia, impetigo and acute folliculitis. Patients with cellulitis without a focal centre of infection, chronic or recurrent furunculosis, postoperative wound infection, leg ulcer, or a deep tissue abscess such as a pilonodal or breast abscess, were excluded from the study. Also excluded were patients with pre-existing infected dermatoses (e.g. eczema, diabetes or immunosuppression), a history of liver disease, or known hypersensitivity to the study treatments. Other exclusions were patients who had received systematic or topical therapy in the 7 days prior to entry, and those who had received an investigational drug in the last 3 months. Pregnant and nursing females, females of child-bearing potential using inadequate contraception, and uncooperative patients were also excluded.

Setting
The setting was primary care. The economic study was conducted in the UK.

Dates to which data relate
The effectiveness and cost data were gathered in 1994/95. The price year was 1999.

Source of effectiveness data
The effectiveness evidence was derived from a single study.

Link between effectiveness and cost data
The costing was undertaken prospectively on the same patient sample as that used for the effectiveness study.

Study sample
Power calculations were reported. A sample size of 240 patients in each group was required to achieve a relative clinical difference of 10% at a power of 80% (alpha 5%). A total of 467 patients were included in the study and were randomly allocated to receive either fusidic acid (n=230) or erythromycin (n=237). The patients in the fusidic acid group had a mean age of 43.3 years and 103 were male. The patients in the erythromycin group had a mean age of 44.4 years and 114 were male. The stratification was carried out according to whether the lesion was "open" or "closed".

**Study design**

This was a multi-centre, prospective, randomised, double-blind, control group study. Blinding was achieved using a double-dummy technique using a placebo that matched fusidic acid and another placebo that matched erythromycin. Assessments were undertaken on day 1, day 6 and on day 11 for those who continued treatment. The final follow-up assessment was carried out 14 days after the end of the treatment. One patient in the erythromycin group did not take medication and another patient in this group was lost to follow-up.

**Analysis of effectiveness**

The first analysis of the clinical study was conducted on an "intention to treat" basis. This population consisted of all patients who took the study medication and provided efficacy data. Efficacy data were unavailable for 4 patients in the fusidic acid group and 5 patients in the erythromycin group. Therefore, the intention to treat population comprised 226 fusidic acid-treated patients and 230 erythromycin-treated patients.

A second analysis was conducted on the bacteriological efficacy population. This population comprised patients with an infection due to Staphylococcus aureus, which was found to be susceptible to the treatment allocated. Bacteriological efficacy data were obtained from 53 patients treated with fusidic acid and 58 patients treated with erythromycin.

The primary health outcomes considered in this study were:

- the physicians’ assessment of the clinical efficacy of treatment,
- the bacteriological efficacy,
- the patients’ satisfaction with the treatment,
- the adverse events, and
- the duration of treatment and concomitant medications.

On day 6, overall effectiveness was rated as cured, improved or failed. On day 11, overall effectiveness was rated as either cured or failed. At the follow-up visit, overall effectiveness was rated as either cure maintained or relapsed.

The two groups were well matched at baseline in terms of age, gender and characteristics of the lesion. The baseline characteristics of the bacteriological efficacy population were also similar in each treatment group.

**Effectiveness results**

A high proportion of patients in each treatment group were cured or improved at the end of the treatment (intention to treat basis: fusidic acid 85%, erythromycin 87%; bacteriological efficacy basis: fusidic acid 85%, erythromycin 90%). The difference between the treatment groups was not statistically significant for the intention to treat population or the bacteriological efficacy population.

At the follow-up visit, cure was maintained for 95% (n=159) in the fusidic acid group and for 97% (n=177) in the erythromycin group in the intention to treat population. The difference was not statistically significant. In the bacteriological efficacy population, cure was maintained for 98% (n=39) in the fusidic acid group and for 96% (n=45) in the erythromycin group. No statistics were reported.

Both treatments had good bacteriological efficacy, with no statistically significant difference between treatments. The
success rate was 96% (50 out of 52) in the fusidic acid group and 97% (56 out of 58) in the erythromycin group. Both treatments were similarly effective in "open" (fusidic acid 94%; erythromycin 97%) and "closed" (fusidic acid 100%; erythromycin 96%) lesions.

At the end of the treatment, 87% (n=193) patients in the fusidic acid group and 90% (n=207) in the erythromycin group rated treatment as very satisfactory or satisfactory in the intention to treat population. There was no significant difference between the treatments. Patient satisfaction was similar between the groups for the bacteriological efficacy population (fusidic acid 92%; erythromycin 86%).

The total number of patients reporting adverse events was similar in the fusidic acid group (30%; 69 out of 230) and erythromycin group (32%; 74 out of 235). There was a greater number of moderate or severe adverse events in the erythromycin group (58 events, 6 severe) compared with the fusidic acid group (39 events, 10 severe). One adverse event led to hospitalisation in the fusidic acid group. No statistics were reported.

More gastrointestinal adverse events were reported for patients who received erythromycin (22%) than for those who took fusidic acid (16%), (p=0.098).

More patients in the erythromycin group experienced diarrhoea (19 versus 9), flatulence (7 versus 3), dyspepsia (8 versus 4), vomiting (4 versus 2) and rash (3 versus 0). Nausea was experienced by 7% (n=17) of the fusidic acid group and 12% (n=29) of the erythromycin group. Unacceptable adverse events led to premature withdrawal of 10 patients in the fusidic acid group versus 6 in the erythromycin group. No statistics were reported.

In the fusidic acid group, 52% of patients (versus 57% in the erythromycin group) received 5 days' treatment and 48% (versus 43%) of patients received 10 days' treatment.

Approximately half of the patients recruited in each group took no other medications during the study (fusidic acid 56%; erythromycin 55%).

Clinical conclusions

Both fusidic acid and erythromycin were effective in the treatment of skin lesions and soft tissue infections.

Measure of benefits used in the economic analysis

No summary benefit measure was used in the economic evaluation. This was therefore a cost-consequences analysis.

Direct costs

The perspective was not reported, but it was likely to have been that of the heath care system. Only the drug costs of the two systemic antibiotics at basic National Health Service prices in the UK June 1999 were considered. The unit costs and the quantities of resources used were not presented separately. The resource use data were derived using actual data coming from the sample of patients involved in the effectiveness study. Discounting was not relevant as all the costs were incurred during less than one year.

Statistical analysis of costs

A statistical analysis of the costs was not carried out.

Indirect Costs

The indirect costs were not included.

Currency

UK pounds sterling (£).
Sensitivity analysis
Sensitivity analyses were not performed.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
The costs of achieving acceptable, good and excellent responses to treatment for the intention to treat population were similar for both groups. The costs were 11.84 (acceptable), 25.50 (good) and 31.87 (excellent), respectively, for fusidic acid, and 11.70, 25.15 and 33.15 for erythromycin.

The costs of achieving good and excellent responses to treatment for the bacteriological efficacy population were less for fusidic acid (22.11 and 27.93, respectively) than for erythromycin (28.88 and 42.20, respectively).

Synthesis of costs and benefits
A synthesis of the costs and benefits was not relevant as a cost-consequences analysis was carried out.

Authors' conclusions
Fusidic acid, given at a dose of 250 mg twice daily, is safe and effective in the treatment of skin and soft tissue infections. The cost analysis stressed no conclusive evidence that either treatment offers significant cost-advantages.

CRD COMMENTARY - Selection of comparators
The choice of the comparator (erythromycin) was justified as it represented a widely used antibiotic in the treatment of skin and soft tissue infections. However, the authors could have compared fusidic acid treatment with flucloxacillin, a commonly used treatment of skin and soft tissue. You should decide whether erythromycin represents a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
A multi-centre prospective randomised double-blind study was performed, which was appropriate for the study question. Power calculations were carried out and these justified the size of the sample used in the study. The study groups were comparable at baseline and, therefore, confounding factors are probably low. The investigators were blinded to the allocation of patients to the study groups, therefore no assessment biases occurred. Data came from multiple centres and this may enhance the generalisability of the results to other settings. Appropriate statistical analyses were undertaken to compare health outcomes between the groups. Although the compliance of each patient in taking medication was checked, the authors did not draw any conclusions on it.

Validity of estimate of measure of benefit
No summary benefit measure was used in the analysis because a cost-consequences analysis was carried out. Please refer to the comments in the 'Validity of estimate of measure of effectiveness' field (above).

Validity of estimate of costs
The perspective of the study was not stated, thus it is not possible to assess whether all the relevant categories of costs were included in the analysis. The unit costs and the quantities of resources were not reported separately, which limits the transferability of the economic analysis to other settings. The price year was reported and this enhances reflation exercises. Discounting was not relevant and was not performed. The cost estimates were not specific to the authors' setting. Therefore, the generalisability of the results to other settings was facilitated. However, statistical and sensitivity analyses were not performed on the costs. Consequently, the internal and external validity of the study may be low.
Other issues

The authors compared their results with a published study, showing consistent effectiveness results. The authors did not address the issue of the generalisability of the study results to other settings. The results were not reported selectively and the effectiveness conclusions reflected the scope of the study. The authors did not report any limitations of their study.

A main drawback of the study was the lack of a measure of benefits. This will make it difficult to perform comparisons with other studies and technologies necessary to help decision-makers in the allocation of resources. A second drawback was the limited cost analysis. A further drawback was the absence of sensitivity analyses to account for uncertainty in the cost or effectiveness data. Consequently, caution should be exercised when extrapolating the study results to different contexts. Finally, the reader should be aware of the potential conflict of interest with the financial support provided by Leo Pharmaceuticals (the manufacturers of fusidic acid).

Implications of the study

The authors did not make any recommendations or suggestions for further research.

Source of funding

Sponsored by Leo Pharmaceuticals.

Bibliographic details


Other publications of related interest


Indexing Status

Subject indexing assigned by CRD

MeSH

Costs and Cost Analysis; Double-Blind Method; Economics, Pharmaceutical; Erythromycin /administration & dosage /therapeutic use /adverse effects /economics; Fusidic Acid /administration & dosage /therapeutic use /adverse effects /economics; Patient Satisfaction; Skin Diseases, Infectious /therapy; Soft Tissue Infections /therapy

AccessionNumber

22003007646

Date bibliographic record published

31/07/2005

Date abstract record published

31/07/2005