A comparison of fusidic acid tablets and flucloxacillin capsules in skin and soft tissue infection

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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 health technologies considered were fusidic acid (250mg tablets, twice daily) and flucloxacillin (250 mg capsules, four times daily) in the treatment of skin and soft tissue infections. Treatment was taken for five days and for a further five 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 type of infections included boils, carbuncles, acute paronychia, impetigo and acute folliculitis. Patients with cellulitis without a focal centre of infection, chronic/recurrent furunculosis, post-operative wound infection, leg ulcer, deep tissue abscess such as pilonodal or breast abscess, pre-existing infected dermatoses such as eczema, diabetes or immunosuppression, a history of liver disease, and known hypersensitivity to the study treatments, were excluded from the study. Also excluded 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 previous 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 United Kingdom (UK).

Dates to which data relate
The effectiveness and costs data were gathered in 1994 and 1995. 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%). 493 patients were included in the study and were randomly allocated to receive either fusidic acid (n=247; mean age 43.2 years; 144 males) or flucloxacillin (n=246; mean age 43.8 years; 140 male). The stratification was carried out according to whether the lesion was "open" or "closed".

**Study design**

This was a multicentre, 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 flucloxacillin. At the end of the treatment, a follow-up assessment was carried out 14 days later.

Assessments were undertaken on day 1, day 6 and on day 11 for those who continued treatment. The final assessment was carried out 14 days after the end of the treatment.

Two patients in the fusidic acid group and 1 in the flucloxacillin group were lost to follow-up. One patient in the fusidic acid group did not receive any study medication.

**Analysis of effectiveness**

The first analysis of the clinical study was conducted on an intention to treat basis. Efficacy data were unavailable for 3 patients in the fusidic acid group and 10 patients in the flucloxacillin group. The intention to treat population comprised 241 fusidic acid treated patients and 235 flucloxacillin treated patients.

A second analysis was conducted on the bacteriological efficacy population. This population comprised patients with an infection due to Staphylococcus aureus, found to be susceptible to the treatment allocated. Bacteriological efficacy data were obtained from 68 patients treated with fusidic acid and 58 patients treated with flucloxacillin.

The primary health outcomes considered in this study were the physicians’ assessment of the clinical efficacy of treatment, the bacteriological efficacy, patient satisfaction with treatment, adverse events, and also the duration of treatment and the 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 with respect to 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 (fusidic acid 76%; flucloxacillin 81%; intention to treat basis). The difference between 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 94% in the fusidic acid group and for 91% in the flucloxacillin group in the intention to treat population. The difference was not statistically significant. In the bacteriological efficacy population, cure was maintained for 92% in the fusidic acid group and for 86% in the flucloxacillin group. No statistics were reported.

Both treatments had good bacteriological efficacy, with no statistically significant difference between treatments (success rate: 94% (64/68) in the fusidic acid group and 97% (55/57) in the flucloxacillin group). Both treatments were similarly effective in "open" (fusidic acid 96%; flucloxacillin 95%) and "closed" lesions (fusidic acid 91%; flucloxacillin 100%).

At the end of the treatment, 82% (n=191) of patients in the fusidic acid group and 89% (n=202) in the flucloxacillin group rated treatment as very satisfactory or satisfactory (p=0.03) in the intention to treat population. Patient satisfaction was similar between groups for the bacteriological efficacy population.
The total number of patients reporting adverse events was similar in the fusidic acid group (32%, n=78/244) and flucloxacillin group (31%, n=75/245). Three patient in the flucloxacillin group experienced severe diarrhoea compared with none in the fusidic acid group. Nausea was experienced by 6% in the fusidic acid group compared with 3% in the flucloxacillin group. Unacceptable adverse events led to premature withdrawal of 7 patients in the fusidic acid group compared to 4 in the flucloxacillin group. No statistics were reported.

In the fusidic acid group, 47% of patients (versus 39% in the flucloxacillin group) received 5 days treatment, and 53% (versus 61%) received 10 days treatment.

Approximately half of the patients recruited in each group took no other medication during the study (fusidic acid 56%; flucloxacillin 50%).

Clinical conclusions
Both fusidic acid and flucloxacillin 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 which was therefore, a cost-consequences analysis.

Direct costs
The perspective was not reported, but it is likely to be that of the health care system. Only drug costs of the two systemic antibiotics at basic National Health Service (NHS) prices in the UK for June 1999 were considered. Unit costs and the quantities of resources used were not presented separately. The resource use data were based on actual data coming from the sample of patients involved in the effectiveness study. Discounting was not relevant, as all costs occurred over less than one year.

Statistical analysis of costs
Statistical analysis of costs was not carried out.

Indirect Costs
Indirect costs were not included.

Currency
UK pounds sterling (€).

Sensitivity analysis
Sensitivity analyses were not performed.

Estimated benefits used in the economic analysis
Please refer to the effectiveness results reported above.

Cost results
The costs of achieving acceptable, good and excellent responses to treatment for the intention to treat population were greater for fusidic acid than for flucloxacillin (13.99, 26.74 and 35.40 for fusidic acid and 10.35, 20.93 and 30.03 for flucloxacillin respectively).

The cost of achieving acceptable response to treatment was greater for fusidic acid (12.94) than for flucloxacillin
(12.07). In contrast, the cost of achieving good and excellent responses to treatment for the bacteriological efficacy population was less for fusidic acid (24.04 and 29.25, respectively) than for flucloxacillin (29.10 and 32.98, respectively).

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

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

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

Validity of estimate of measure of effectiveness
A multicentre prospective randomised double-blind study was performed, which was appropriate for the study question. Power calculations were carried out and this justifies the size of the sample used in the study. Study groups were comparable at baseline and therefore confounding factors are probably low. Investigators were blinded to the allocation of patients to study groups, therefore assessment biases were minimised. 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 groups. Although the compliance of each patient in taking medication was checked, the authors did not report any conclusions on compliance.

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 commentary above.

Validity of estimate of costs
The perspective of the study was not stated and it is thus not possible to assess whether all relevant categories of costs were included in the analysis. Unit costs and 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. Cost estimates were not specific to the authors' setting, and so the generalisability of the results to other settings is facilitated. However, statistical and sensitivity analyses were not performed on 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 reported no limitations of the study.

The main drawback of the study is the lack of a measure of benefits. This would make it difficult to make comparisons with other studies and technologies necessary to help decision makers in the allocation of resources. A second drawback is the limited cost analysis. A third drawback is the absence of sensitivity analyses to take into account uncertainty in the cost or effectiveness data. Consequently, caution should be exercised when extrapolating the study results to
different contexts.

The reader should be aware of the potential conflict of interest with the financial support the study received from Leo Pharmaceuticals (fusidic acid).

**Implications of the study**
The authors did not make any recommendations or suggestions about further research.

**Source of funding**
Sponsored by Leo Pharmaceuticals.

**Bibliographic details**

**Other publications of related interest**

**Indexing Status**
Subject indexing assigned by CRD

**MeSH**
carbuncle /drug therapy; Cost-Benefit Analysis; Floxacillin /therapeutic use; Folliculitis /drug therapy; Furunculosis /drug therapy; Fusidic Acid /therapeutic use; Impetigo /drug therapy; Paronychia /drug therapy; Treatment Outcome; Wounds and Injuries /complications

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