A randomized trial of amorolfine 5% solution nail lacquer in association with itraconazole pulse therapy compared with itraconazole alone in the treatment of Candida fingernail onychomycosis


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 comparison of combination therapy and monotherapy for the for the treatment of Candida fingernail onychomycosis. Combination therapy consisted of itraconazole (400 mg/day) for one week followed by 3 weeks with no treatment, for 2 months, alongside a weekly application of a 5% solution of amorolfine nail lacquer for 6 months. Monotherapy consisted of itraconazole (400 mg/day) for 1 week followed by 3 weeks with no treatment, for 3 months.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients aged between 18 and 75 years old with clinical evidence of onychomycosis on at least 50% of the whole nail surface. The patients had to have mycological diagnosis by positive potassium hydroxide wet mount, and culture identification of Candida in the absence of dermatophyte. Patients were excluded if they had contraindications to itraconazole, or had received any antymycotic topical treatment within 4 weeks or systemic antifungal therapy in the 6 months preceding screening. They were also excluded it they had liver or renal disease, were pregnant or breast feeding, or had other nail disease.

Setting
The setting was secondary care. The economic study was undertaken in Athens, Greece.

Dates to which data relate
The clinical effectiveness data were collected between 1996 and 1998. The resource use data were estimated for the same period. No price year was reported.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing was carried out prospectively on the same patient sample that provided the clinical effectiveness data.

Study sample
The patients were recruited consecutively from an outpatient department. A total of 90 patients were included in the study and divided equally between each treatment group. Nineteen patients considered for the study were excluded because they did not meet all the inclusion criteria, while an additional five refused to participate. The authors did not report any sample size or power calculations.

**Study design**
The study was a randomised controlled trial that was conducted in a single centre. The authors did not report the method of randomisation. The patients were followed up for 9 months (3 months after the end of treatment). Five patients (5.6%) did not complete the study, two in the combination therapy group and three in the monotherapy group.

**Analysis of effectiveness**
The health outcomes assessed were "cure" at 3 and 9 months after the start of the study. Cure at 3 months was defined as negative microscopy and culture. Cure at 9 months was defined as a negative microscopy and culture, and either a disappearance of all lesions or a reduction of at least 10%. The two treatment groups were comparable in terms of gender, age, number of infected nails, total infected surface and duration of onychomycosis. The data were analysed for treatment completers only.

**Effectiveness results**
At 3 months, the cure rate was 74.4% in the combination therapy group and 59.5% in the monotherapy group, (p>0.1).
At 9 months, the cure rates were 93.2% (combination therapy) and 80.9% (monotherapy), respectively, (p>0.1).

**Clinical conclusions**
The authors concluded that combination therapy appeared to be more effective than monotherapy, although the difference was not statistically significant.

**Measure of benefits used in the economic analysis**
The measure of health benefit used was the cure rate at 9 months.

**Direct costs**
The perspective adopted in the analysis was not reported. However, only the costs of the drugs were included in the economic analysis. The authors appear to have estimated the resource use data. The unit costs of the two drugs used in this study were the prices reimbursed by the Greek National Drug Organisation. Resource use and the unit costs were not reported separately, and no price year was reported. The costs were not discounted, which was appropriate given that they were incurred during less than one year.

**Statistical analysis of costs**
The costs were treated deterministically (i.e. point estimates).

**Indirect Costs**
No indirect costs were included in the study.

**Currency**
Euros (Euro).

**Sensitivity analysis**
No sensitivity analysis was undertaken.

**Estimated benefits used in the economic analysis**
The cure rate at 9 months was 93.2% for patients receiving combination therapy and 80.9% for those on monotherapy.

**Cost results**
The total cost was Euro 151.75 for patients receiving combination therapy and Euro 137.88 for those on monotherapy.

**Synthesis of costs and benefits**
The cost per cure was Euro 1.63 for combination therapy and Euro 1.70 for monotherapy.

**Authors' conclusions**
Combination therapy was at least as effective and as safe as monotherapy, but cost less.

**CRD COMMENTARY - Selection of comparators**
The authors did not provide any justification for their choice of the therapies under consideration in this study. You should consider how the two treatments studied compare with usual practice in your own setting, prior to applying the results of this work.

**Validity of estimate of measure of effectiveness**
The clinical effectiveness data were obtained from a randomised controlled trial. This was an appropriate study design, although the validity of the study results was reduced by the analysis being undertaken for treatment completers only. In addition, the method of randomisation was not reported in the paper, and it is therefore not possible to identify whether it was bias free. The two treatment groups were shown to be comparable at baseline and, given the consecutive enrolment from an outpatient department, should be representative of the study population. No power calculations were reported. The authors implied that the study may not have been powered sufficiently to detect statistically significant differences in the effectiveness of the two regimes.

**Validity of estimate of measure of benefit**
The measure of benefit used in the economic analysis was taken directly from the effectiveness data.

**Validity of estimate of costs**
The authors did not report the economic perspective adopted in the study. The only costs quantified were those of the drugs. The costs used were, in fact, reimbursement rates and it was unclear whether they included any additional overheads. The authors did not consider differences in other resource use, although the impact of excluding them may be minimal. Given the level of costing undertaken, and the lack of reporting around resource use and the unit costs, the generalisability of the study is likely to be poor. No price year was reported, which will prevent any future reflation exercises. In addition, no statistical or sensitivity analyses of the resources used or their costs were performed. This means that the degree of uncertainty around the cost estimates was not assessed.

**Other issues**
The authors compared their findings with other similar studies, although no other studies considered the same comparison. They did not consider directly how the results of this study could be generalised to other settings. The authors presented their data in a transparent manner and their conclusions accurately reflect their analysis. Some form of sensitivity analysis would have given the results a higher level of certainty.
Implications of the study
The authors did not make any recommendations for changes to practice or direct calls for further research. However, they noted that a study with a larger sample might clarify whether the apparent difference in the efficacy of the two treatments is statistically significant.

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None stated.

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