We performed a cost-effective evaluation of cyclosporin A versus UVAB phototherapy in the treatment of severe atopic dermatitis. The analysis was based on a one-year open prospective clinical trial conducted in Finland and showed that patients who received intermittent cyclosporin A therapy had on average 191 remission days per year, i.e. where disease activity was reduced by 50% or more. Patients receiving UVAB phototherapy had on average 123 remission days per year. All costs were estimated for the one-year period. Health service utilization of the 2 treatment groups was estimated based on the data gathered during the clinical study. Total costs were USD 5,438 in the cyclosporin A group and USD 5,635 in the UVAB group. Direct health-care costs were USD 4,935 in the cyclosporin A group and USD 3,124 in the UVAB group. The cost of a remission day was USD 28 in the cyclosporin A group and USD 46 in the UVAB group. In terms of direct health-care costs, the cost of a remission day was USD 26 in the cyclosporin A group and USD 25 in the UVAB group. Our results demonstrate that cyclosporin A therapy is similarly cost-effective as UVAB phototherapy in terms of total cost in the treatment of atopic dermatitis unresponsive to topical treatment. In terms of direct health-care costs, i.e. treatment and health services utilization costs; however, UVAB is significantly less costly, but side effects are frequent. Key words: atopic dermatitis; cost-effectiveness; direct costs; indirect costs; patient’s perspective.

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The standard treatment for atopic dermatitis is a combination of topical corticosteroids and emollients. In the Nordic countries, UVAB phototherapy has been the standard treatment for patients who fail to respond to appropriate topical corticosteroids. However, UVAB treatment is time-consuming, requiring regular treatment visits and cannot be given to patients with photosensitivity (1).

For some patients with atopic dermatitis persisting into adolescence, standard treatments are ineffective. Systemic immunosuppression with corticosteroids and azathioprine has been used (2).

Cyclosporin A is an immunosuppressive agent (3); the efficacy of which has been demonstrated in severe psoriasis (4) and atopic dermatitis (5). It is effective and safe for treatment up to one year in patients with severe atopic dermatitis (1, 6–10).

The aim of this study was to evaluate the cost-effectiveness of cyclosporin A versus UVAB therapy in the treatment of atopic dermatitis.

MATERIAL AND METHODS

The clinical study

Granlund et al. (1) have recently published on the clinical outcome of a one-year prospective trial, where cyclosporin A was compared with UVAB phototherapy using an intermittent treatment schedule. Seventy-one patients were enrolled in the study, 36 into the cyclosporin A group and 35 into the UVAB group.

Patients in the cyclosporin A group were given 6 cycles of treatment, each of 8 weeks. Each cycle started with an initial dose of 4 mg kg\(^{-1}\) day\(^{-1}\) of cyclosporin A, which was reduced to a mean dosage of approximately 2.6 mg cyclosporin A kg\(^{-1}\) day\(^{-1}\).

Patients in the UVAB group were also given 6 treatment cycles with 2 to 3 treatment sessions per week. The initial dose depended on the patient’s skin type and previous experience with UVAB therapy. Mean total UVAB dose was 116 Joule for the first treatment cycle increasing to 176 Joule during the study.

The use of emollients and topical corticosteroids was measured, but only for the first cycle. In the first treatment phase (8 weeks) the mean use of emollients decreased by 75 g/2 weeks in the cyclosporin A group, whereas in the UVAB group the mean use of emollients increased by 41 g/2 weeks (p < 0.01). Topical corticosteroids decreased in both groups with on average 45 and 43 g/2 weeks, respectively.

The clinical evaluation demonstrated that cyclosporin A was superior to UVAB regarding time to induction of remission defined as a reduction in SCORAD of > 50%, number of remission days and influence on quality of life (1). In addition, fewer emollients and topical steroids were used in the cyclosporin A group compared with the UVAB group. In
Table I. The prices and average costs used in this study, 1997 price level

<table>
<thead>
<tr>
<th>Cost item</th>
<th>Average costs Total USD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neoral* USD/mg</td>
<td>0.08</td>
</tr>
<tr>
<td>Emollients USD/g</td>
<td>0.04</td>
</tr>
<tr>
<td>Topical steroids USD/g</td>
<td>0.20</td>
</tr>
<tr>
<td>Therapy visit* USD/visit</td>
<td>54.9</td>
</tr>
<tr>
<td>UVAB treatment visit USD/visit</td>
<td>23.5</td>
</tr>
<tr>
<td>Inpatient hospital care USD/day</td>
<td>216.7</td>
</tr>
</tbody>
</table>

*Includes loss of work hours.

terms of number of remission days, treatment with cyclosporin A was 56% more effective than treatment with UVAB. The difference was statistically significant \( (p=0.006) \) (1).

Design of the economic evaluation

In this study only Finnish patients were evaluated, leaving 28 patients in the cyclosporin A group and 27 in the UVAB group. Nine patients from the Finnish cohort of the clinical study population did not return their patient diaries, leaving 46 patients for final evaluation.

No significant differences were noted at baseline between the cyclosporin A group and the UVAB group regarding sex, age, body weight, duration of disease, SCORAD, use of potent topical steroids and use of previous phototherapy. The average distance from home to the hospital was 34.5 km in the cyclosporin A group and 23.6 km in UVAB group.

The primary endpoint of the clinical study was the number of days in remission, defined as days when the clinical severity score, SCORAD (12), is at or below 50% of the baseline. Relapse was defined as an increase in SCORAD to >50% of the patient’s baseline value. For example, if baseline SCORAD value is 50, and because of treatment decreases to 10, a relapse is considered to have occurred, if the SCORAD increases to 25 or more (>50% of the baseline value).

Each patient was asked to note the use of health services, other concomitant medication, duration and number of pharmacy visits, and time off work using a diary. The treatment costs consisted of cyclosporin A and UVAB therapy costs plus the costs of emollients and topical steroids. Other health-care costs included visits to the physician’s office not related to the study, hospital inpatient care because of atopic dermatitis, and laboratory examinations during cyclosporin A therapy. The treatment costs added to other health-care costs formed the direct health-care costs. The indirect costs included non-medical costs and work and leisure time lost (visits to the physician’s, pharmacy, UVAB treatment and travel expenses). The direct health-care costs and indirect costs together constitute the total costs.

If one of the two treatments is both more effective and more costly, an incremental cost-effectiveness ratio of the more effective treatment should be calculated. Incremental cost-effectiveness ratio shows the additional costs for the additional health outcome (11).

Prices used in the economic evaluation

Time used for therapy and pharmacy visits, UVAB treatment and time off work were valued as the weighed mean of the average gross wage rates of Finnish men and women aged between 30 and 34 years (Statistics Finland 1997). This age

group was used because the mean age was 33 years in both treatment groups (1).

Visits to the physician’s office, UVAB treatment visits, hospital inpatient care and laboratory examinations were valued at the prices of Helsinki University Central Hospital. The prices included all the production costs of the services. The costs of medication used (cyclosporin A, emollients and topical steroids) were the retail prices of Helsinki University Pharmacy 1997.

All costs were first estimated in Finnish marks (FIM), but converted to US dollars (USD 1 = FIM 5.1).

Statistics

Confidence intervals (95%) were estimated for all costs. The cost difference between the treatment groups was tested using Student’s t-test.

RESULTS

Health-care utilization

There were no statistically significant differences in the number of additional visits to the physician’s office, i.e. visits not required in the study. Patients in the UVAB group had 73 UVAB phototherapy visits per year on average. One patient in the cyclosporin A group and two patients in the UVAB group were treated as inpatients during the study.

Time spent on pharmacy visits was almost twice as long in the UVAB group than in the cyclosporin A group. This difference was significant \( (p=0.02) \).

Costs

Direct health-care costs were USD 1,811 higher in the cyclosporin A group than in the UVAB group \( (p<0.001; \text{Table II}) \).

Direct health-care costs were divided into treatment costs and other health-care costs. The treatment costs were USD 1,660 higher in the cyclosporin A group than in the UVAB group \( (p<0.001; \text{Table II}) \). In the cyclosporin A group, however, the annual costs for topical therapy including emollients and topical steroids were USD 324 lower than in the UVAB group \( (p=0.005) \).

The other health-care costs (physician visits, laboratory tests and hospital inpatient care) were USD 151 higher in the cyclosporin A group than in the UVAB group mainly because of the costs of laboratory examinations required by cyclosporin A therapy \( (p=0.019; \text{Table II}) \).

The indirect costs were USD 2,008 lower in the cyclosporin A group than in the UVAB group \( (p<0.001; \text{Table II}) \). This difference was due to the time required for UVAB treatment.

The total costs per patient per year were USD 197 lower in the cyclosporin A group than in the UVAB group \( (p=0.913; \text{Table II}) \).
Table II. Itemized breakdown of the costs per patient during the one-year study period (USD), 1997 price level

<table>
<thead>
<tr>
<th></th>
<th>Cyclosporin A therapy (n=28)</th>
<th>UVAB phototherapy (n=27)</th>
<th>Cost difference USD</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct health-care costs</td>
<td>4,935 (4,244, 5,626)</td>
<td>3,124 (2,554, 3,695)</td>
<td>1,811</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Treatment costs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Cyclosporin A therapy</td>
<td>3,710 (3,078, 4,343)</td>
<td>2,319 (1,857, 2,782)</td>
<td>3710</td>
<td></td>
</tr>
<tr>
<td>- UVAB treatment</td>
<td></td>
<td>1,726 (1,410, 2,041)</td>
<td>-1,726</td>
<td></td>
</tr>
<tr>
<td>- Emollients</td>
<td>125 (90, 159)</td>
<td>306 (183, 429)</td>
<td>-181</td>
<td>0.006</td>
</tr>
<tr>
<td>- Topical steroids</td>
<td>145 (108, 181)</td>
<td>288 (141, 435)</td>
<td>-143</td>
<td>0.074</td>
</tr>
<tr>
<td>Other health-care costs</td>
<td>956 (775, 1,136)</td>
<td>805 (617, 993)</td>
<td>151</td>
<td>0.194</td>
</tr>
<tr>
<td>- Therapy visits*</td>
<td>668 (574, 763)</td>
<td>730 (572, 889)</td>
<td>-62</td>
<td>0.511</td>
</tr>
<tr>
<td>- Laboratory examinations</td>
<td>203 (181, 224)</td>
<td>0</td>
<td>203</td>
<td></td>
</tr>
<tr>
<td>- Hospital inpatient care</td>
<td>85 ( -82, 252)</td>
<td>75 ( -29, 179)</td>
<td>10</td>
<td>0.918</td>
</tr>
<tr>
<td>Indirect costs</td>
<td>503 (405, 602)</td>
<td>2,511 (2,017, 3,005)</td>
<td>-2,008</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>- Time (therapy visits)</td>
<td>342 (287, 396)</td>
<td>336 (245, 427)</td>
<td>6</td>
<td>0.972</td>
</tr>
<tr>
<td>- Time (UVAB treatment)</td>
<td></td>
<td>1,618 (1,264, 1,972)</td>
<td>-1,618</td>
<td></td>
</tr>
<tr>
<td>- Time off work</td>
<td>46 ( -11, 103)</td>
<td>113 (20, 205)</td>
<td>-66</td>
<td>0.200</td>
</tr>
<tr>
<td>- Time (pharmacy visits)</td>
<td>73 (48, 97)</td>
<td>137 (91, 184)</td>
<td>-65</td>
<td>0.022</td>
</tr>
<tr>
<td>- Travel (therapy visits)</td>
<td>43 (37, 49)</td>
<td>49 (39, 59)</td>
<td>-6</td>
<td>0.340</td>
</tr>
<tr>
<td>- Travel (UVAB treatment)</td>
<td>259 (212, 305)</td>
<td>259 (212, 305)</td>
<td>-197</td>
<td>0.913</td>
</tr>
<tr>
<td>Total costs</td>
<td>5,438 (4,716, 6,160)</td>
<td>5,635 (4,630, 6,641)</td>
<td>-197</td>
<td></td>
</tr>
</tbody>
</table>

Cl 95% = 95% confidence interval.
*Visits to the physician’s office not related to the study.

Cost-effectiveness

Two different therapies can be compared in terms of cost-effectiveness as defined by the cost per remission day (11). Table III indicates that in terms of direct health-care costs the cost of a remission day was USD 26 in the cyclosporin A group and USD 25 in the UVAB group. In terms of total costs, the cost of a remission day was USD 28 in the cyclosporin A and USD 46 in the UVAB group. Thus, in terms of total costs, cyclosporin A therapy is equally cost-effective as UVAB phototherapy.

Incremental cost-effectiveness

Because cyclosporin A is more effective and more costly in terms of direct health-care costs than UVAB therapy, it is necessary to examine the incremental cost-effectiveness ratio of cyclosporin A (11). The difference in remission days was 68 days (ΔE) and the cost in terms of direct health-care costs difference was USD 1,811 (ΔC). The incremental cost-effectiveness ratio was USD 27 (ΔC/ΔE) in terms of additional direct health-care costs per additional remission days achieved. As cyclosporin A in terms of total costs is more effective and less costly than UVAB therapy, there is no need to calculate the incremental cost-effectiveness ratio.

DISCUSSION

Cyclosporin A is both effective and safe in treating severe atopic dermatitis (1, 5–10). The clinical study, which this economic evaluation is based on, has demonstrated that intermittent treatment lasting up to one-year can adequately manage patients with atopic dermatitis unresponsive to topical treatment (1).

Cyclosporin A has been shown to improve the quality of life in patients with atopic dermatitis (13). Cases of atopic dermatitis often achieve the highest morbidity scores on disability scales in clinical studies (14). The high impact of atopic dermatitis on quality of life justifies the use of powerful and expensive treatment modalities such as cyclosporin A or UVAB phototherapy.

Atopic dermatitis is an important economic burden in industrialized countries. In the United States it has been estimated that treatment costs for childhood atopic dermatitis were USD 364 million in 1992 (15). In Great Britain, atopic dermatitis accounted for at least 10%–20% of all referrals to dermatologists (16).

This study examined the cost-effectiveness of cyclosporin A compared with UVAB phototherapy in the treatment of severe atopic dermatitis. The analysis was based on a one-year open, randomized, prospective clinical trial which showed cyclosporin A to be more
effective than UVAB phototherapy in terms of remission days (1).

In terms of direct health-care costs, cyclosporin A is more costly than UVAB phototherapy. In severe atopic dermatitis, however, the total costs of cyclosporin A therapy are lower than those of UVAB phototherapy. This is because of the time-consuming nature of UVAB phototherapy.

Intermittent cyclosporin A therapy offers a therapeutic approach to adult dermatitis unresponsive to topical therapy. Up to one year of treatment is effective and safe and compares favourably with UVAB in terms of cost-effectiveness and thus improves social efficiency.

ACKNOWLEDGEMENTS
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REFERENCES