Background & Aim

Ulcers as a result of Diabetes mellitus are a serious problem with an enormous amount in the global disease burden due to the increasing prevalence of the disease. Because of long hospital stays, rehabilitation, often required home care and the use of social services diabetic foot complications are costly. Therapy with growth factors could be an effective and innovative add-on to standard wound care.

The aim of the HTA on behalf of the German Institute of Medical Documentation and Information DIMDI was to assess the safety and efficacy of growth factors alone or in combination with other technologies in the treatment of DFU from medical, economical, social, ethical and juridical aspects.

Methods

We systematically searched relevant data bases limited to English and German language and publications since 1990. Two reviewers independently checked the identified literature regarding preestablished inclusion and exclusion criteria.

Studies about the safety and efficacy of therapies with growth factors for diabetic foot ulcers were included. Using full economic evaluations for answering the economic questions cost values were adjusted for the price level in 2008 and converted into Euro.

Review and assessment of the quality of publications followed methods conforming to widely accepted standards for evidence-based medicine and health economics.

Results

Overall we identified 25 studies; 14 randomized controlled trials (RCT), nine cost-effectiveness analyses, two meta-analyses. The 14 RCT compared an add-on therapy to standard wound care with standard wound care/placebo alone or extracellular wound matrix: six studies use becaplermin, two rHEGF, one bFGF, and five studies the metabolically active skin grafts Dermagraft and Apligraf.

Study duration ranged from 12 to 20 weeks and the study population comprised between 17 to 382 patients, in average 130 patients.

The methodological quality of studies was affected by significant deficiencies.

Figure 1. Complete wound healing in %

Treatment with becaplermin, rhEGF and growth factors secreting skin implants Dermagraft and Apligraf showed in eight out of 13 studies an advantage concerning complete wound closure and the time to complete wound healing with mainly statistically significant differences. With regard to complete wound healing after treatment with becaplermin the differences were in favour of the growth factor Hardikarp < 0,001 and Wiemann p = 0,007 (see Figure 1).

Evidence for a benefit of treatment with bFGF could not be found.

In four out of the fourteen studies the proportion of adverse events was 30 % per study group without differences between treatment groups.

Table 1. Cost-Effectiveness Analyses

<table>
<thead>
<tr>
<th>Study</th>
<th>Overall cost (1 year)</th>
<th>Overall cost (1 year)</th>
<th>bFGF</th>
<th>A Effect</th>
<th>bIEG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ghatnekar et al. 2001</td>
<td>+13,398 Euro</td>
<td>+14,500 Euro</td>
<td>-1,102</td>
<td>0,11</td>
<td>+16,046 Euro</td>
</tr>
<tr>
<td>Ghatnekar et al. 2001</td>
<td>+13,835 Euro</td>
<td>+16,046 Euro</td>
<td>-2,211</td>
<td>0,11</td>
<td>+16,046 Euro</td>
</tr>
<tr>
<td>Kaner et al. 2001**</td>
<td>+17,437 Euro</td>
<td>+17,437 Euro</td>
<td>ns</td>
<td>0,81</td>
<td>+16,046 Euro</td>
</tr>
<tr>
<td>Persson et al. 2000</td>
<td>+13,312 Euro</td>
<td>+13,733 Euro</td>
<td>-401</td>
<td>0,81</td>
<td>+16,046 Euro</td>
</tr>
<tr>
<td>Sibuld et al. 2003</td>
<td>+16,274 Euro</td>
<td>+16,611 Euro</td>
<td>+163</td>
<td>0,81</td>
<td>+16,046 Euro</td>
</tr>
</tbody>
</table>

* To German Euro 2000 PPP; ** calculated for inclusion. 1 calculation with data from 1999


Discussion

The results of the cost-effectiveness analyses of all health economic evaluations showed becaplermin being cost-effective. No obvious statement can be made regarding Dermagraft and Apligraf because of diverging cost bases and diverging incremental cost-effectiveness ratios.

Conclusion

Differences in standard wound care are complicating the comparison of study results. Taking into consideration the small to very small sample sizes and other methodological flaws with high potential of bias the validity of the results with regard to effectiveness and cost-effectiveness has to be considered limited. The duration of treatment and follow-up examinations is not long enough to assess sustainability of intervention and surveillance of ulcer recurrences or potential treatment related adverse events like development of malignancy.

Contact: Dr. Barbara Buchberger, MPH
Institute for Health Care Management and Research, University of Duisburg-Essen
Schützenbahn 70, 45117 Essen, Germany
Tel +49 (201) 183 4075,
Barbara.Buchberger@medman.uni-duis.de

Authors: Barbara Buchberger1, Markus Follmann2, Daniela Freyer1 Grundrik 2005, Wiemann 1998
1 Institute for Health Care Management and Research, University of Duisburg-Essen, Germany
2 German Cancer Society, Berlin, Germany