

HTA-Report | Summary

Therapy of moderate and severe psoriasis

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Introduction

Psoriasis is a non life-threatening chronic or chronically relapsing inflammatory skin disease. The prevalence rate is 1 to 2 % which means that about 1.5 millions Germans are affected by psoriasis. Psoriasis cannot be healed. Mild psoriasis is usually treated with topical substances. The treatment of moderate and severe psoriasis is primarily performed with photo(chemo)therapy and systemic agents. All systemic drugs may cause side effects. This means that individual benefits and risks have to be considered.

Objective

The health technology assessment (HTA) report focuses on clinical effectiveness and cost-effectiveness of therapy options for the treatment of moderate and severe psoriasis. Thus the HTA report represents an update of the English HTA report by the authors Griffiths et al. in 2000. New literature published between 1999 and June 2004 was systematically evaluated regarding medical effectiveness and the cost effectiveness with relevance for Germany. Important articles which have been published after 2004 were also included into the report.

Medical assessment Methods

The search strategy included randomized, controlled studies (RCT) on moderate to severe forms of psoriasis. This means that the search strategy may have led to the exclusion of some well established therapeutical procedures which are believed to be effective alone or in combination with other procedures when no RCT are available.

RCT published between 1999 and June 2004 were systematically evaluated regarding medical effectiveness. Important articles which have been published after 2004 were also included into the report. Special forms of psoriasis, in particular psoriasis palmoplantaris pustulosa, psoriasis guttata and psoriasis arthritis, were not evaluated in this report.

Each section contains a summary with most important contents the HTA report from the year 2000. We adapted to the inclusion and exclusion criteria of the former report to make the update comparable to the HTA report from Griffiths et al.¹.

Results

The major conclusions from the results of medical RCT on moderate and severe psoriasis vulgaris are:

Oral fumarates are effective in the treatment of moderate to severe psoriasis vulgaris. However, fumarates quite frequently cause moderate side effects which may limit their usefulness. Cyclosporine and methotrexate are both effective in the treatment of severe psoriasis vulgaris as has been shown by one RCT. Both substances have a different spectrum of side effects which may limit the individual applicability.

Acetritin is only moderately effective in the treatment of severe psoriasis of the plaque type even in high concentrations (75 mg or 1 mg/kg). This means

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that a monotherapy is rarely performed with this substance in plaque psoriasis. Of note the substance is more effective in psoriasis pustulosa and when used in combination with UV radiation or with calcipotriol. Systemic PUVA, balneo-PUVA and UVB therapy are all effective for the treatment of severe psoriasis. The combination of UV therapy with vitamin D3 analogues or with topical steroids is more effective than the treatment with UV radiation alone. Saltwater baths increase the effectiveness of UVB therapy. No RCT on the therapeutical effects of topical tar or of dithranol in combination with UV therapy have been published so far. A continuous therapy with PUVA should not be applied due to its proven photocarcinogenicity.

Three substances from the group of biologicals (Efalizumab, Etanercept, Infliximab) are now available in Europe and a further substance (Alefacept) is available in the USA for the treatment of moderate to severe psoriasis. All biologicals have been effective in placebo controlled studies. The substances differ in the times until a clinical effect is observable, in the spectrum of side effects and in their efficiency on psoriasis arthritis.

Discussion

The spectrum of therapeutical options has fortunately increased during the last years. It must be emphasized that a number of therapeutical procedures exist which are not discussed in detail in this HTA report. This is due to the search strategy of literature: Only RCT performed with patients with moderate and / or severe psoriasis vulgaris were included into this evaluation. This led to the exclusion of a number of substances which are traditionally used alone or in combination for the treatment of moderate or severe psoriasis vulgaris (e.g. dithranol, salicyc acid, tar, corticosteroids and topical retinoids). Moreover, other approaches which include neither drugs nor UV light are not discussed in this HTA report although the authors believe in the importance of psychotherapeutical interventions, educational approaches and combined medical and non-medical approaches in rehabilitational medicine in the management of psoriasis vulgaris.

Future studies should address therapeutical approaches which can not easily be studied by RCT, e.g. physical, balneological, climate approaches, educational programs and complex rehabilitation therapy which all may have positive effects on individuals with severe psoriasis.

Economic Assessment

Methods

For identification of all relevant literature, the HTA database of the International Network of Agencies for Health Technology Assessment and the Centre for Reviews and Dissemination, University of York, were accessed and scanned for relevant literature and current projects. Additionally a systematic literature search was conducted in electronic data bases. A manual search in non-MEDLINE German (health economics) journals without time limits and references of literature hints completed the electronic literature research. About 20 German pharmaceuticals companies were asked for information about innovations in therapy of psoriasis und so far unpublished reports.

The presentation of results is carried out separately for each included health economic evaluation as a structured summary. Selected excluded economic analyses are also characterised within the appendix. In a synthesis the results of the health-economic evaluations are combined in an ordinal rank order.

Results

A numerically meaningful scientific discussion about economic questions in therapy of moderate and severe psoriasis in terms of publications started at end of the 90ies. Beside economic analysis also estimations of health care cost or analysis of treatment cost can be found. The literature research identifies 15 full health economic evaluations, of which three should be classified as so called grey literature. Regarding the methodology employed and use of primary and secondary data the included publications represent a wide and mixed spectrum.

The therapy options UVB, UVB plus calcipotriol and PUVA are equivalent and dominate (superiority in an economic sense) balneo-phototherapy, UVB plus tar externals and short-contact dithranol. The relationship of the mono therapy calcipotriol and short therapy dithranol is ambivalent. Methotrexat is equivalent to UVB and PUVA and outperforms UVB plus tar externals as well as ciclosporin. Fumarates exceed ciclosporin and acitretin. Unfortunately the relationship of fumarates and methotrexat is not analysed yet. In health economic evaluations the new biologics are shown less cost effective, so that they should be used as a last resort.

Discussion

The transferability of the health economic evaluation results is strongly limited by the fact that all included health economic evaluations except one were not aligned to a German setting, but the relationships of individual intervention groups in respect to their control groups are less affected. It should be viewed critically that economic outcomes are frequently applied only remission as an economic endpoint. A future research question will be the evaluation of duration of remission and relapse ratios in the context of different therapy options of moderate and severe and psoriasis. Also the consideration of combined outcomes, improvement of psoriatic symptoms and decrease of symptoms in accompanying psoriasis arthritis, represents a future requirement.

Conclusions

From the clinical point of view it is positive that the spectrum of therapeutic procedures for a chronic severe skin disease has increased continuously during the last years. In cases of individual contraindications or individual inefficacies it is now possible to try alternative approaches. Moreover the risk of long-term side effects can be reduced by changing the therapeutical procedure after some time (so-called rotation therapy). The therapeutical algorithm for severe psoriasis vulgaris now includes photo(chemo-)therapy in combination with topical substances, oral fumaric acid esters, retinoids (in combination with phototherapy or topical substances), methotrexate, cyclosporine and the new biologics.

As in medical therapy management of moderate and severe psoriasis the economic evaluation also points out the way of a strategic therapy concept which corresponds to a large extent to the algorithm in medical practice. If a therapeutic change of a primary therapy is necessary, subordinate second-

ary and afterwards tertiary therapy options are available from economic point of view. The rank order of primary, secondary and tertiary therapies correspond largely with medical practice.

References

1. Griffiths CEM, Clark CM, Chalmers RJG, Li Wan, Williams HC. A systematic review of treatments for severe psoriasis. In: Health Technology Assessment 2000; 4(40): 1-125.

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