SOCIAL – ECONOMIC COSTS OF THE IMMUNOLOGICAL TREATMENT OF SEVERE PSORIASIS COMPARED TO THE CLASSIC THERAPY

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Abstract: *The economic analysis appreciates both the debit (costs and resources), as well as the credit (reducing mortality, morbidity, increasing longevity, improving life quality) of the patients suffering from psoriasis. The clinical trials carried out with biological therapies show significant improvements of the indexes measuring the diseases severity both from the physical point of view (PASI – Psoriasis Area Severity Index) and from the life quality point of view (DLQI – Dermatological Life Quality Index), indexes that are equally important for the patient. A major issue in applying the biological therapies is the high cost, which is ten times higher than the classical systemic therapies.(1,2)*

Cuvinte cheie: *psoriazis, analiza cost-eficacitate, cost-beneficiu, cost-eficienţă, cost-utilitate*

Rezumat: *Analiza economică apreciază atât debitul (costurile şi resursele cheltuite), cât şi creditul (reducerea mortalităţii, morbidităţii, majorarea longevităţii vieţii, creşterea calităţii vieţii) bolnavilor cu psoriazis. Trialurile clinice realizate cu terapiile biologice demonstrează ameliorări semnificative ale indicilor ce măsoară severitatea bolii atât din punct de vedere fizic (scorul PASI – Psoriasis Area Severity Index), cât şi al calităţii vieţii (indicele DLQI – Dermatological Life Quality Index), indici în egală măsură importanţi pentru pacient. O problemă majoră în aplicarea terapiilor biologice este costul ridicat, care este de câteva zeci de ori mai mare faţă de cel al terapiilor sistemice clasice.(1,2).*

INTRODUCTION

The direct cost of severe psoriasis affects the health system as well as the patients dedicating most of their time and money to treat this disease.

In the European Union countries, the costs of the anti-psoriasis medication are borne by the health system and partly by the patient. In the UK, the annual average cost for each psoriasis patient under topic and UV treatment is of 2815 GBP, and for each psoriasis patient under systemic treatment is of 1473 GBP. In Italy, the annual average cost of the intra-hospital treatment of psoriasis is estimated to 905 Euro. The annual cost of the treatment for the psoriasis patients in Germany is of 1426 Euro.(3)

The absence from the workplace is the major component of the social cost of psoriasis, affecting both the output and income earning capacity of the psoriasis patients. Each psoriasis patient annually loses approximately 26 working days because of the disease.(4)

We find that psoriasis generates an economic impact which cannot be neglected by the countries with high economic standards. Moreover, it would be useful to introduce a therapy programme for the psoriasis patients to reduce the social costs determined by the disease (efficient treatment adapted to the clinical form, outpatient treatment by continuing the therapy scheme initiated in the hospital).(5)

Due to the fact that nowadays, the results of the psoriasis standard treatments are highly unsatisfactorily, there is a high demand of new therapies.

The Committee of Experts of the National Fund of Health Insurance was established within the Romanian National Fund of Health Insurance in 2008 to approve the treatment of severe chronic psoriasis using biological agents, according to the therapy protocol approved by *the Order of the minister of health and of the president of the National Fund of Health Insurances no. 1301/500/2008 to approve the therapy protocols on the prescription of the medication afferent to the international common names of medicines the insured persons benefit from, with or without personal contribution, on the grounds of a medical prescription, in the health social security system, approved by the Government's Decision no.720/2008,* with subsequent changes and amendments. The therapy protocol on the treatment with biological products of severe chronic psoriasis represents the grounds for prescribing and monitoring the medicines whose price is 100% compensated from the budget of the Sole National Fund of Health Insurances. The treatment is granted to insured patients on the grounds of a prescription issued by the doctors having a contract relation with the health insurance funds.

The national programme for the treatment of the patients suffering from chronic psoriasis – average and high severity - is created to introduce the biological therapies in a systematic and planned way, so as to obtain the maximum benefit for the psoriasis patients and to efficiently and surely facilitate the prescriptions. The programme includes all the biological therapies registered in Romania indicated for psoriasis (adalimumab, etanercept, infliximab).(3)

The economic approaches provide arguments to substantiate the decisions of the health policy decisions. The economic analyses allow us to appreciate the relation between the financial dimension and the one of the health condition. The descriptive inquires assess all the disease related costs in a given environment. They represent an X ray of the status at a given time and a starting point for the assessment of certain changes, such as, the introduction of new therapies.(4)

According to the World Health Organization, life quality represents the perception the individuals have on their life taking into consideration the cultural context, the system of values in that person's life, compared to their hopes, standards

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and interests. There are generic and specific instruments to measure the quality of life. The results of a therapy strategy may be described taking into account several points of view: economic, therapy efficiency, impact on life quality.(6)

PURPOSE

This article aimed at highlighting the aspects of the standard and biological therapy of mild/severe psoriasis correlated to the patient's life quality.

METHODS

This research substantiates on a cross over trial highlighting the aspects of the standard and biological therapy of mild / severe psoriasis correlated to the patient's life quality.

For the economic assessment of the study we used the comparative analysis cost – benefit cost – efficiency and cost – utility of the biological therapy of the patients suffering from chronic psoriasis (mild or severe) who received the approval for the initiation of the treatment with biological agents, from the Committee of Experts within the National Fund of Health Insurances to approve the treatment of the chronic psoriasis with biological agents from 01.01.2009 until 31.03.2009.

Of the 425 files, 410 patients met the eligibility criteria for the biological therapy, according to the provisions of the "Therapy protocol on the treatment of chronic psoriasis (mild or severe) with biological medicines)''. Each of the patients included in the study attended treatment with one of the biological therapies used in the mild or sever psoriasis (infliximab, adalimumab, etanercept), that represented the basis of the economic analysis. Depending on the administered treatment, the study population was divided in three batches (infliximab – 88 patients, etanercept – 183 patients, adalimumab – 139 patients).

The research period was 01.01.2009 - 30.06.2010 (18 months). The assessment of the patient's life quality was carried out using the DLQI score – Dermatological Life Quality Index, together with PASI score - Psoriasis Area Severity Index, used to classify the severity of psoriasis. DLQI includes a set of 10 questions with a score between 0 and 3 for each, depending on how much the quality of life was affected by the disease in the last week. PASI is a clinical index estimating the surface of the affected tegument, as well as its degree of affectation. We assessed the DLQI and PASI scores for 4 moments from the initiation of the biological treatment. By using multivariate variance (MANOVA), we assessed the differences between the costs of each biological therapy used (adalimumab, etanercept, infliximab) per DLQI point, namely earned PASI.(7,8)

RESULTS AND DISCUSSIONS

The health services have a cost and a result. To appreciate their efficiency we must measure the costs and the results. This is called **economic assessment.** The economic assessment refers to the diagnosed services and to the therapy and prevention services. The assessment techniques frequently used nowadays are: cost – efficiency analysis, cost – benefit analysis, cost – utility analysis.(9) The **cost-efficiency analysis** reports the costs of the services at their efficiency measured in terms of event (degree of recovery etc.). The comparisons are difficult, especially when we are dealing with different therapy procedures for the same type of disease. Monitoring the severity of psoriasis measured by PASI score for the study batch, we observed its improvement, post-initiation of the biological therapy by 63% at 3 months, by 78 % at 6 months, 83% at 12 months, by 87% la 18 months, from a score of 31.81 – classical treatment to one of 3.88- biological treatment. (table no. 1When the treatment is initiated, the PASI average did not show any significant differences between the three analyzed batches ($F=1.194$, $p=0.304$). The other four times we assessed the effect of the biological treatments on the PASI score there were statistically significant differences between the three batches (3months – $F=13.258$, $p<0.001$, 6 months – $F=26.292$, $p<0.001$, 12 months – $F=5.733$, $p=0.004$, 18 months – $F=3.872$, $p=0.023$), the PASI average of the batch treated with adalimumab being significantly lower than all the other four times. As far as the average of the cost per earned PASI point is concerned, MANOVA showed that there was a significant multivariate effect of the used biological treatment (Pillai criterion $F=3.426$, $p<0.001$, $\acute{\eta}^2$ parial $=0.073$). The average costs per PASI point earned at the times 3, 6, 12, 18 months (table nr. 2) were analyzed using ANOVA to demonstrate if this trend is similar to each of the variables separately considered (3 months – $F=3.808$, $p=0.024$, 6 months – $F=3.439$, $p=0.034$, 12 months – $F=7.37$, $p=0.001$, 18 months – $F=3.101$, $p=0.047$).

The cost efficiency analysis compares the benefit obtained by a new treatment through the difference between the additional costs incurred by its introduction and the reduction of other resources. These analyses substantiate the implementation of new therapy strategies. There is no curing treatment for psoriasis. All the presently used medicines achieve a suppressive treatment, inducing the remission of the lesions or reducing their clinical signs to the tolerance threshold of the patient. The treatment of the patient is a long term one. The occurrence of flares is not predictable and it cannot be prevented by the administration of topic therapy. If, for example, for a month of treatment with metothrexat (currently the standard therapy in psoriasis) the costs are of maximum 350 lei/month, comparing the average monthly costs of the treatment with biological medicines for the patients of the study, we found that the treatment with Infliximab is the most expensive (4823.34 lei/month) of the available alternatives through the Romanian therapy protocol, followed by the one with Adalimumab (4463.8 lei/month) and the one with Etanercept (4200.72 lei/month). At the same time, the pressures for the prescriptions of new therapies are increasing, this is why it is necessary to identify the cost – efficiency criteria arguing for their use.

The cost – benefit analysis better compares the interventions from various fields of the medical services, because both the costs and the results are expressed in money. The feasibility of the method is reduced because of the small number of products of the medical services which can be transformed into money. The cost – benefit analysis takes into account the ratio between the effects (results, benefits) and efforts (expenses)

Table no. 1. The evolution of the average of the DLQI and PASI scores for the patients with biological treatment for mild and severe psoriasis

Biological treatment	Time of the assessment									
	Time 0		3 months		6 months		12 months		18 months	
	DLQI	PASI	DLQI	PASI	DLQI	PASI	DLQI	PASI	DLQI	PASI
Adalimumab	22,91	31,01	8,55	9,96	3,91	4,78	2,23	3,35	1,51	2,30
Etanercept	24,40	31,69	13,85	14,98	7,36	8,40	4,94	6,60	3,43	4,1
Infliximab	23,82	33,33	9,18	10,78	4,97	5,50	3,70	4,16	5,11	4,85
Total average	23,77	31,81	11,2	12,05	5,81	6,70	3,98	5,24	3,39	3,88

Table no. 2. The evolution of the mild costs per earned DLQI and PASI points for the patients with biological treatment for mild and severe psoriasis

Biological treatment	Assessment time							
	3 months		6 months		12 months		18 months	
	DLQI*	PASI*	DLQI*	PASI*	DLQI*	PASI*	DLQI*	PASI*
Adalimumab	1421,08	1126,6	1820,71	1513,13	2746,31	2549,69	4332,88	3686,45
Etanercept	1431,40	877,16	1724,07	1216,41	2736,62	1708,61	3817,82	3063,20
Infliximab	1645,13	1263,7	1791,16	1256,32	3116,47	3211,26	4107,73	3217,81

*Mild cost/earned point

The direct benefits include:

- reduction of the morbidity and mortality; 39% of the patients with standard therapy had 3 hospitalizations per year.
- the means saved in the provided nursing (hospitalization expenses, medical services and medicines). Our study highlighted an average number of 6.89 hospitalization days for the biological therapies versus an average number of 12.46 hospitalization days of classical therapy.

The indirect benefits include:

- reduction of the patient's absence from the work place. We ascertained an important reduction of the number of sick leave days after the introduction of the biological treatment; from approximately 26 days/year for the classical treatment (3) to 7.81 days / immunology treatment.
- the means saved by the patient's family related to the visitation of the patient (transport expenses).

The beginnings of the **cost – usefulness** analysis techniques represented an evolution in the economic approach of the health services. It generated various controversies, especially in the ethic field, as it mainly allows the society to choose between the medical services it provides that turn out to have a higher impact on the average lifespan adjusted according to the life quality of its members. The essence of the method resides in measuring the results of the medical services as usefulness, namely expressing the life years earned and rating them with an indicator representing the subjective value of these years from the social point of view. The usefulness is expressed by the quantitative perspective (increasing the life expectancy) and the qualitative perspective (life quality).(10)

It was assessed using the life quality index DLQI – Dermatological Life Quality Index. The higher the score, the more the patient's life was affected by the disease. The DQLI score between 21- 30 means an extremely important effect on the patient's life quality. In the studied batch, the average DLQI index – classical therapy was of 23.7756 (standard deviation – SD=±4.54), with a minimum value of 2 and a maximum value of 30, module of 30, median of 24. In the biological therapy, the average of the DQLI score showed an 53% improvement at 3 months, 75.5% at 6 months, 83% at 12 months and one of 86% at the end of the monitoring period, 18 months (from 23.77 – classic therapy at 3.39 – immunology treatment). (table no. 1)

The average of the DLQI score when the treatment was initiated showed significant differences between the three analyzed batches ($F=4.334$, $p=0.014$), the batch treated with Etanercept showing more significant differences. At the other times, when assessing the effects of the biological treatment on the DLQI score, there were significant statistical differences between the three batches (3months – $F=33.19$, $p<0.001$, 6 months – $F=25.694$, $p<0.001$, 12 months – $F=10.432$, $p<0.001$, 18 months – $F=7.358$, $p=0.001$), the average of the DLQI Score being considerably lower for the batch treated with adalimumab compared to all the other four batches.

Using the MANOVA analysis, we were able to demonstrate that there are significant statistic differences, as far as the average cost per earned DLQI point depending on the used biological treatment (Pillai criterion $F=1.954$, $p=0052$, $\acute{\eta}^2$ partial $=0.044$) is concerned. The average costs per earned DLQI point at the times 3, 6, 12, 18 months (table no. 2) underwent an ANOVA analyses to demonstrate if this trend is similar to each separate variable (3 months – $F=1.747$, $p=0.177$, 6 months – $F=2.303$, $p=0.103$, 12 months – $F=0.37$, $p=0.964$, 18 months – $F=0.127$, $p=0.881$).(11)

The direct non medical costs refer to the price for the access to the medical services, their invalidity, the time of the family visits during the hospitalization of the patient, the costs of the necessary materials, others than the medicines (the price of the detergents, the patients with psoriasis use a higher quantity of detergents as a consequence of dirtying the clothes and the underwear by the ointments and of the new clothes, cosmetics, used for the special care of the skin, hair and nails).(12)

The intangible costs and benefits refer to the loss of the patients' wellbeing and of the ones around because of the disease, meaning that these are human, psychological, difficult to quantify costs.

CONCLUSIONS

The biological therapies show significant improvements of the disease severity indicators from the physical point of view, PASI score, life quality and the DLQI index.

The economic analysis reflects a significant difference between the different types of biologic therapies applied to the patients with mild and severe psoriasis in terms of the costs per earned PASI point, but it does not emphasize a significant difference in terms of the mild cost per DLQI point, according to the used biological therapy.

A major issue in applying the biologic therapies remains the high cost of the medicines, medical tests and examination, which is tens of times higher than the one of the classic systemic therapies, recommended in the psoriasis management. Furthermore, the financial impact of the psoriasis increases proportionally to the severity of the disease, together with the appreciable decrease of the patients' life quality. Economically, the comorbidities increase the cost of the psoriasis treatment.

As such, we must take into account the fact that the biological therapies maintain an adequate control of the disease, diminishing the frequency and the severity of the potential relapses.

Passing from the level of health policies to the one of doctor – patient relation, the doctor has the responsibility of correctly selecting the patients who apply a biological therapy, as this, beyond the evolution of the efficiency, efficacy and of the usefulness, is encumbered by significant secondary effects.

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