Health status and disease burden of patients with rheumatoid arthritis in Hungary

Ph.D. Thesis

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1. Introduction

Rheumatoid arthritis (RA) is a chronic, progressive, inflammatory condition characterized by joint destruction. Patients live with chronic pain and a substantial functional impairment develops with the progression of the disease.

In chronic diseases standardised measures of disease progression, health status and quality of life are of especial importance for the follow-up of the patients. In Hungary, a comprehensive use of such standardised methods did not spread widely in RA. Due to absence of registries there were no sufficient clinical data on RA patients regarding disease severity, therapy use, risk factors and co-morbidities.

Biological agents developed over the recent decade provide a new therapeutic opportunity in RA, especially for patients refractory to previous Disease Modifying Antirheumatic Drugs (DMARD). Therapy history registration, disease activity and risk factor assessments, regular follow-up of standardized clinical parameters are required for the application of biological drugs.

Comorbidities are of especial importance in RA. Cardiovascular risk in RA is comparable to diabetes mellitus but also the rate of infections and lymphomas is high. Osteoporosis is the most common complication in RA,

disease activity and corticosteroid use are determinant factors. Fracture related costs and quality of life loss cause a substantial burden to the society. Analysis of osteoporosis related fractures are of especial interest as these are the target points of antiporotic drug therapies.

Development of biological therapies has sped up the economic analysis in RA due to their high drug costs. In Hungary, health economic analysis is required for the reimbursement of all new drugs. Therefore, country-specific baseline data on clinical characteristics and costs of RA are needed for cost-effectiveness analysis in Hungary.

2. Objectives

2.1. Regarding health status assessment of RA patients in Hungary, our aim was:

2.1.1. To analyse the health status, health related quality of life, disease activity, functional status and health care utilisation rates of the patients.

2.1.1. To compare the health status in RA with the Hungarian general population.

2.1.3. To assess the impact of disease progression on health status and quality of life.

2.2. Fracture risk assessment in RA, focussing on osteoporosis related fractures.

2.3. Our objective was also to estimate the disease related costs in RA and compare with results from European countries.

The research was performed in order to offer baseline data for public health, health-economic analysis and international comparative studies.

3. Methods

3.1. A cross-sectional study was performed in 2004 involving 255 consecutive RA patients in 6 hospital based rheumatology centres. Disease activity (DAS), functional (HAQ) and health status (EQ-5D), disease-specific quality of life (RAQoL) was measured and a questionnaire survey was performed regarding health care utilisation. Results of the EQ-5D questionnaire was compared to published data of the Hungarian general population. Correlation of disease progression, health status and quality of life was analysed.

3.2. The National Health Insurance Fund Administration (NHIFA), covering the whole population, routinely collects data from the health care services. The NHIFA database was searched for records of fractures in age-groups 50-100 years in the period of 1999-2003. Records on RA diagnosis within this group was also collected. Hip, forearm, shoulder fractures and vertebral fractures with hospital admission were analysed separately as these are mainly related to osteoporosis in this age-group. Fracture incidence rates were calculated using mean data of the 5 year period. Results of a previous database analysis was used to assess the prevalence of RA patients aged 50-100 year (38 000 patients) for RA fracture incidence calculations.

3.3. Cost calculation was based on the health care utilisation results of the cross-sectional questionnaire survey and societal perspective was used. RA related direct medical costs (hospital admissions, drugs, diagnostics, GP and specialist visits, bath therapy, physiotherapy, home care, devices), direct non-medical costs (home remodelling, ambulance, transportation, informal care) and indirect costs (sick leave, permanent sick leave, part-time job, disabled) were calculated. Official price and reimbursement lists were used as sources for cost calculations (out-patient: fee-for service point system, acute in-patient: Disease Related Groups, chronic hospitalisation: per diem basis), while non-reimbursed medical services were based upon patients' answers. The average hourly net wage (500 HUF/hour) was used to estimate RA related informal care, and productivity losses were calculated using the human capital approach, based on the average gross income (122 641 HUF/month). (Conversion: HUF250 = Euro1). Mean annual costs per patient was calculated.

Statistical analysis

Microsoft Access 2000 9.0 and SPSS 11.0 were used for the analysis.

4. Results

4.1.1. Clinical characteristics, drugs, health care

255 patients (female/male 6:1) were involved, mean age 55.5 (SD12,3) years, disease duration 9.0 (SD9.3) years, disease activity DAS 5.09 (SD1.42), HAQ 1.38 (SD0.76), EQ-5D 0.46 (SD0.33), RAQoL 16.2 (SD8.1). Non-steroidal anti-inflammatory drugs were used by 60% of the patients and the rate of permanent corticosteroid use was 47.6%. DMARD use occurred in 88%, methotrexate (48.6%; mean dose 12 (SD4.2) mg/week) and leflunomide (27.4%; mean dose 18.6(SD3.5) mg/day) were dominant. Visit to a specialist due to RA occurred in 96.5%, mean number of visits was 5.8 (SD5.5)/year. The rate of hospital admission was 62.6%, mean 1.09 (SD1.3) case/year.

Disease activity of the patients was high, reaching nearly the cut-off score of severe activity (DAS ≥5.1). Methotrexate was the most frequently used DMARD which is in conformity with international findings. However the mean methotrexate dose was rather low taking in consideration that 20 mg/week monotherapy or 15 mg/week combination therapy is required before stepping forward to any biological therapy.

I find important to emphasize that the rate of ever taken biological drugs was definitely lower in Hungary than in a

multicentric survey involving 13 European countries (plus USA and Argentina, the QUEST-RA study in 2005-2006 by Sokka et al): 0.8% vs. 23%. Disease activity and functional status of the patients was better in the QUEST-RA (DAS: 4 vs. 5; HAQ: 0.88 vs. 1.38) whilst disease duration was comparable. Results from Poland were the most similar to ours (biological drugs 8%; DAS 5.3; HAQ: 1.38).

Analysis of DMARD consumption rates of the NHIFA database revealed that DMARD therapy use and visits to a specialist were much regular in our sample than the usual practice in RA in Hungary.

4.1.2. Comparison of the health status with the general population

Health status (EQ-5D) in RA was significantly lower than in the age-matched population ($p<0.001$), and 46% of the RA patients were considered to have bad or very bad health from societal perspective.

4.1.3. Disease progression and health status

Correlation between disease progression (HAQ) and health status (EQ-5D) was similar to international findings (EQ-5D=0.850–0.282×HAQ). Quality of life (RAQoL) also worsens when HAQ increase. Disease activity (DAS) has

negative impact on health status. Minimally significant clinical increase of the HAQ (0.25 points) induce 0.0705 decrease of the EQ-5D and 1.884 increase in RAQoL.

RAQoL shows a plateau at HAQ=2.0 confirming that RA patients consider their quality of life damaged when their everyday activities are middle-affected.

4.2. Fractures

404 380 women and 206 009 men had at least one fracture in the 5 years which corresponds to 4% and 2.3% of the age-matched population, respectively. Incidence of fractures were (fracture/10 000 inhabitants/year): hip 36.3; vertebra (inpatient) 4.8; forearm 107.9; shoulder 56.2; other fractures 245.9.

The number of RA patients with fracture was 13 845 in 5 years (women: 11 243, men: 2598) which corresponds to 7.2% of the age-matched RA population. Multiple fractures occurred in 19.7% and 17% in women and men, respectively. Fracture incidence was higher in RA in all types of fractures, rates were between 1.69-2.12.

Fracture incidence of the Hungarian population is in conformity with the north-south decrease trends in Europe. Fracture risk in RA was similar to findings of a general practitioner database analysis in the United Kingdom except

forearm fractures (double rate in our sample). Further comparative studies are needed to specify the results and to assess vertebral fractures on a wider level.

4.3. Costs

Mean total costs was 1 043 163 (SD844 750) HUF/patient/year, rate of direct and indirect costs was 45.2% / 54.8%. Costs of patients with active disease (DAS≥3.2) was mean 1 079 750 (SD856 250) HUF/patient/year whilst lower amount was found at the others (DAS<3.2): mean 881 750 (SD757 750) HUF/patient/year. Disability allowance (514 130 HUF/patient/year), informal care (153 527 HUF/patient/year) and hospital care costs (115 269 HUF/patient/year) were the highest items. Disease progression is the determining factor of the costs.

The amount of RA related costs was significantly lower in Hungary compared to developed countries. Total cost in Hungary was equivalent to direct costs in France and The Netherlands. Differences in wages and health care systems have influence. In Hungary, about half (50.2%) of the patients got informal care regularly from the family or from friends which was the second highest cost item in our results. Institutionalization due to disability did not occur in our sample in contrast to France. Unemployment and households'

rate, differences in social care systems can influence the costs as well.

5. Conclusions

1. Health status of RA patients in Hungary:

a.) Health status is significantly affected by RA. It is considered to be a severe condition from the point of view of the society as well. Health status of RA patients is significantly worse than the age-matched Hungarian population.

b.) Health status, quality of life, disease activity and functional status correlate in RA, disease activity has negative impact on health status at a same functional level. Perception of changes in quality of life is not equal at all disease severity levels. RA patients consider their disease-specific quality of life to be notably affected when their functional status is at a medium-severe level. Our results offer data for cost/QALY calculations in Hungary.

c.) Correlation between disease progression and health status did not differ significantly from international studies involving cohorts without biological drugs. However disease activity and functional status of the RA patients were much better in countries with wider use biological drugs than Hungary in 2004. Reimbursement of biological drugs was

introduced in 2006 in Hungary, thus changes in health status and disease progression are expected also in our country. Follow-ups and registries will confirm the impact of the new drugs.

2. Fracture risk in RA

Incidence of fractures was about double in RA compared to the Hungarian population in age-group 50-100. Occurrence of fractures other than the classical osteoporosis related localisations (hip, forearm, shoulder and inpatient vertebral) were significant. Further studies are needed to assess the total incidence of vertebral fractures. Our study was the first to offer fracture incidence data from Central Europe not only in RA but also in the general population.

3. Costs of RA in Hungary

The amount of RA related costs is lower than in the developed European countries. Cost results of health-economic analysis and cost-effectiveness models cannot be adapted to Hungary without adjustments. Costs increase with disease progression, functional status is determining. Costs are higher in cases with severe disease activity and also quality of life correlates with the costs. Our results offer

baseline data on health status and costs of RA patients in Hungary for cost-effectiveness models.

6. List of publications

6.1. Publications related to the thesis

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6.3. Abstracts

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