ORIGINAL ARTICLE

Efficiency Evaluation of Non-Infectious Uveitis

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SUMMARY

Authors compared clinical and economic effeciency of treatment of the classical corticosteroids therapy and modern immunosuppressive treatment or their combination. Retrospective evaluation carried out in 2012, covering 2006–2011, monitored sample of 27 patients, 16 women and 11 men, 45 eyes with disabilities. The average age in the last year of follow-up monitoring was 30.2, ranging from 14 to 76 years. The mean duration of disease for the whole sample is 16.5 years with a range from 6 to 36 years. Three basic diagnoses were included in investigated group: chronic iridocyclitis in 59 % of eyes, intermediate uveitis in 30 % of eyes and sympathetic ophthalmia in 11 % of eyes. The optimal treatment not be determined, however, combined corticosteroid sparing therapy was the most beneficial to maintain in terms of visual acuity with minimal side effects and cost effectiveness. Successful outcomes of treatment were observed for intermediate uveitis, because the visual acuity improved in nine letetters of ETDRS chart in the study. Satisfactory treatment was proved in chronic iridocyclitis and sympathetic ophthalmia in general, because visual acuity improved in a few letters of ETDRS chart, in the same line as in the beginning of the six-year follow-up. Rounded average annual prize for treatment including pharmacotherapy, outpatient and inpatient care and laboratory follow-up was in chronic iridocyclitis € 990, in intermediate uveitis € 310 and sympathetic ophthalmia € 1550. Pharmacotherapy exceeded the financial appraisal of specialized medical and inpatient care in total cost.

Key words: uveitis, corticosteorids, immunosuppression, costeffectivness

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INTRODUCTION

Uveitis is a serious and potentially blinding disease, but its economic consequences and the social problems caused by temporary or permanent damage to sight are little known. Worldwide, uveitis especially afflicts the population in middle age (20 – 40 years). According to the international literature, the prevalence is 38-714 cases per 100 000 inhabitants and the incidence of 17-52 cases per 100 000 inhabitants annually [28]. In total, uveitides comprise approximately one twentieth of the etiologies of blindness. These numbers are probably higher, since the presented statistical data is primarily from countries with advanced healthcare [6]. From a worldwide perspective, economic and regional-ethnic situation has a fundamental influence on the causes of blindness or a substantial deterioration of vision in adulthood. In European countries the first places amongst the causes of blindness are occupied by diabetic retinopathy, degenerative affliction of the retina, severe myopia and atrophy of the optic nerve [6]. In Japan, uveitis ranks fourth in the causes of blindness, after the aforementioned severe nearsightedness (myopia), degeneration of the retina and atrophy of the optic nerve [11]. In developing countries, in more than one half of cases the cause of blindness is cataract or affliction of the lens, which are treatable in developed countries. Here uveitis ranks in fourth or fifth place amongst the causes of loss of sight, together with untreated ocular trauma [1, 30]. The above facts document the seriousness of this disease, which is not lethal, but the frequency of occurrence of uveitis with potentially serious consequences primarily afflicts a productive group of the population. In comparison with other diseases causing blindness in the field of ophthalmology, patients with uveitis must additionally face several side effects of long-term pharmacological treatment with corticosteroids or immunosuppressants. The potential damage to the sensory organ and overall burden on the organism during the course of treatment has a psychological influence on the patients and has a considerable socio-economic impact on them and their surroundings.

From the above factors, it ensues that in addition to an evaluation of the clinical results of treatment of uveitides, an assessment of the economic perspective of the treatment of this serious immunopathological eye disease is of fundamental importance also in our region, since modern immunosuppressive drugs are financially costly. The aim of the study was to judge this mutual relationship and to attempt to stipulate the possibility of optimum treatment from both perspectives. The model was the ongoing successful AMADEUS project for the treatment of wet age related macular degeneration [9].

ACTUAL CONFIGURATION AND METHOD

In 2012, patients with a chronic form of non-infectious uveitis, requiring general corticosteroid or immunosuppressive therapy or a combination thereof within the period from 2006 to 2011, i.e. from implementation of the new electronic information system at the Eye Clinic at the Royal Vinohrady Teaching Hospital, were retrospectively enrolled in the monitored study

population. The observed group contained 27 patients, of whom 16 were women and 11 men. The average age in the last year of observation was 30.2 years, with a range from 14 to 76 years. In total 45 eyes were monitored and treated, 18 patients had the disease bilaterally, and 9 patients only unilaterally. The average length of the actual duration of the disease for the entire population is 16.5 years, with a range from 6 to 36 years.

The most frequently occurring diagnosis was chronic iridocyclitis in 19 eyes in 16 patients, of which 9 cases were as a part of juvenile idiopathic arthritis (JIA), whilst the remaining patients were classified in the group of hypergic uveitides (positive ANA, increased immunoregulation index etc.). A second disease was intermediate uveitis in 13 eyes in 8 patients. The most prognostically serious disease was panuveitis with late cellular sensitivity, which was represented in three patients by sympathetic ophthalmia, always in one eye.

For the clinical evaluation, the main selected parameter was visual acuity, and the baseline and outcome values were compared over an observation period of 6 years. The results were recorded in the decimal value of ETDRS for each year of observation for each parent separately. Only afterwards the development of vision in the course of the six year observation was evaluated in individual patients, and in conclusion there followed a general assessment according to the particular three diagnoses. "Successful" treatment was considered to constitute an improvement of visual acuity by +0.12 (one letter from the next row of the ETDRS chart) or more, "satisfactory" treatment meant maintenance of visual acuity at the original baseline value, thus within the range of ±0.05, and finally, "unsuccessful" treatment was a value of -0.12 (one letter from the next row of the ETDRS chart) or less.

Other monitored clinical parameters included associated ocular complications (which in their consequences participated or might participate in the main parameter of the clinical monitoring, namely in the deterioration of visual acuity): cystoid macular edema (CME), complicated cataract, secondary glaucoma and keratopathy with the possibility of their potential therapeutic influencing. The general side effects of the overall therapy on the organism were also recorded: acne, Cushingoid facies, gingivitis, hepatic and renal toxicity and increased blood pressure. Cost parameters of the treatment were divided into three groups: outpatient care or hospitalisation including surgeries, and general and local medication were evaluated separately. From the perspective of medical care, the costs for the individual examinations and procedures were calculated according to the list of healthcare procedures with point values, multiplied by the value of the point for the respective medical specialties. Healthcare material (HM) for the procedures was added separately. The healthcare procedures with the evaluation were checked in the List of Healthcare Procedures according to the relevant decree of the Ministry of Health of the Czech Republic (MHCR) for each year. In the observed period this specifically concerns Decrees nos. 493/2005, 331/2007, 409/2008, 27/2009 and 397/2010. The value of the point is stipulated by the MHCR for specialties 705 – ophthalmology, 708 – anaesthesiology, resuscitation and intensive medical care at CZK 1.02. The value of the point for laboratory and immunological specialty 801, 813 and 818 is stipulated at CZK 0.88. In outpatient care, each year the total numbers of examinations were observed, incorporating predominantly targeted eye tests (75022), sporadically also complex eye tests (75021), including noncontact tonometry (75161) and ophthalmoscopy (75121) of one or both eyes in the followed up persons (09532). Further eye tests were not conducted regularly at ophthalmological checks, but in individual cases according to the clinical picture and the need to obtain information for further treatment: fluorescein angiography (75129), A and B-scan ultrasound examination (75147, 75149), photo-documentation for each eye individually (755155) and if applicable also YAG laser treatment (75433). For each eye this was calculated beyond the framework of classic ophthalmological examination.

These examinations were supplemented as necessary with the required laboratory tests:

a) The basic immunological examination for uveitis comprised examination of sedimentation of erythrocytes (9133), determination of IgG (91129), determination of IgA (91131), determination of IgM (91133), determination of of CRP (91153), determination of C3 element of complement (91159), determination of C4 element of complement (91161), blood count with five population differential number of leukocytes (96167), immunophenotyping of individual cellular subpopulations according to superficial symptoms (91439), analysis of panoptically stained blood smear (96315), determination of CIK by PEG-IKEM method (91355), panoptic staining of smear of peripheral blood or aspirate (96711), preparation of smear (96713) and separation of serum or plasma (97111).

b) The special immunological examination for uveitis involved determination of anti IgA antibodies ENA (91261), determination of anti SS-A/RO AB ELISA (91263), determination of anti SSB/LA AB ELISA (91265), demonstration of antinuclear antibodies (91317), demonstration of ANCA IF (91323), determination of levels of ASLO (91503), determination of HLA--B 27 (86217), determination of rheumatoid factor (91501) and separation of serum or plasma (97111).

c) The control examination of blood for monitoring of undesirable effects in systemic therapy recorded the values of AST (aspartate aminotransferase) or ALT (alanine aminotransferase) (81357), urinary concrement qualitatively (81483), uric acid (81523), analysis of panoptically stained blood smear (96315), panoptic staining of smear of peripheral blood or aspirate (96711) and preparation of smear (96713).

Care by other specialists such as rheumatologists, radiologists etc. in systemic diseases was not observed, since it was not the contents of this study.

Hospitalisation care in its complex incorporated actual hospitalisation in a standard inpatient ward at the Eye Clinic of the Royal Vinohrady Teaching Hospital at the flat rate price for hospitalisation days (Days 1-3 at CZK 1046, days 4-5 at CZK 876 and days 6-8 for CZK 707) and the surgical procedures if applicable under general anaesthesia. Medication and laboratory tests are calculated within the flat rate and as a result were not included. The costs for surgical procedures, including use of separately charged healthcare material (HM), were evaluated separately in different seasons of the year. With regard to the type of eye disease and its manifestations, this concerned the following procedures: extracapsular extraction of cataract by phacoemulsification technology (75345) with implantation of a soft intraocular lens (75347) or without implantation, filtration antiglaucomatous surgery (75339) using different

surgical techniques with the use of implants, enucleation of the bulb (75371) if applicable with use of orbital implant and pars plana vitrectomy (75449). Use of a surgical microscope (71823) was always added according to time demandness. Preoperative examination by an internist (11021) and an anaesthesiologist (78022), intubation (78820) and anaesthesia for the period of the surgical procedure and 20 minutes (78114) were included within the price of general anaesthesia for ophthalmological procedures.

Medication of patients from a financial perspective was monitored in outpatient care according to the ophthalmologist's prescription, with precision to the single whole packages of pharmaceuticals each year. The prices the particular pharmaceuticals were taken from Brevíř (Medical Tribune) for each year separately [17, 18, 19, 20, 21, 22], since their price as reimbursed by the health insurance companies changed continually.

For general anti-inflammatory and immunosuppressive drugs the evaluated prescription was (generic names): azathioprine, bemethasone, cyclosporine A, methotrexate, methylprednisolone, tacrolimus. General medication prescribed by other specialists within the framework of a systemic disease is not incorporated within the study, since it was not possible to monitor it precisely and it did not come within the financial costs of the ophthalmologist. In local treatment this concerned corticosteroids, non-steroid antiflogistics, mydriatics and antiglaucomatous drugs (beta-blockers, carboanhydrase inhibitors and sympathomimetics for treatment of glaucoma, or a combination thereof).

The actual analysis of the data on financial costs was evaluated from the perspective of their composition, inter-year growth with average annual costs per patient overall and for the individual groups of diagnoses. At the same time, the costs for corticosteroid, immunosuppressive and combined therapy were evaluated. For a comparison of the groups, a simple cost-effectiveness analysis is conducted.

RESULTS

Over the six years of monitoring, 10 patients were hospitalised, of whom 6 were hospitalised twice and one patient three times. Cataract surgery was performed on 10 eyes, i.e. 23%. Before 2006 a cataract had already been operated in the study population in 9 eyes, i.e. 20%. An antiglaucomatous surgery was performed by different surgical techniques on 3 eyes, i.e. 7% (in one patient the implant subsequently had to be explanted due to uncontrollable hypotension). Vitrectomy was performed on one female patient due to serious cicatrical vitreous reaction. Enucleation of the bulb was indicated twice due to dolorous blind bulb with secondary uveitic irritation of the immunocomplex mechanism of the seeing eye. The division of surgeries in relation to the three monitored groups of diagnoses is presented in Table 1. The majority were performed for chronic iridocyclitis, whereas in intermediate uveitis no surgical procedure was necessary. The absolute frequency of surgeries was represented by sympathetic ophthalmia, including the previous period.

During the six year monitoring period, associated ocular complications, which contributed substantially to the reduction of visual acuity, were manifested most under the picture: CME in 17 eyes (38%), complicated cataract accompanied by various degrees of deterioration of vision was diagnosed in 16 eyes (36%) and zonular keratopathy in 5 eyes (11%). Secondary glaucoma was detected in 10 eyes (22%). The connection of ocular complications with the monitored particular types of uveitides was characterised by fundamental differences. Whilst CME influencing negatively visual acuity was present in 7 eyes (69%) in the case of intermediate uveitis, post-inflammatory cataract was present in 14 eyes (48%) in the case of chronic iridocyclitis. Serious zonular keratopathy was diagnosed only in the case of chronic iridocyclitis. Secondary glaucoma was diagnosed in 7 eyes (24%) in the case

Table 1. Overview of eye surgeries in relation to the particular diagnoses

Diagnosis	Chronic iridocyclitis	Intermediate uveitis	Sympathetic ophthalmia	Total
Number of eyes	29	13	3	45
Cataract surgery (2006-2011)	10	0	1	11
Filtration glaucoma surgery	2	0	1	3
Vitrectomy	1	0	0	1
Enucleation (2006 and 2008)	2	0	0	2
Previous cataract surgery	8	0	1	9
Previous enucleation	0	0	3	3

Table 2. Overall evaluation of treatment success, treatment costs and side effects of treatment in relation to the particular diagnoses

Diagnosis	Chronic iridocyclitis	Intermediate uveitis	Sympathetic ophthalmia	Total
Number of eyes	29	13	3	45
Number of patients	16	8	3	27
Successful treatment	22.00%	69.00%	0	41.00%
Satisfactory treatment	30.00%	23.00%	100.00%	43.00%
Unsatisfactory treatment	48.00%	8.00%	0	16.00%
Average increase of vision	0.02	0.27	0.15	0.1
Average annual treatment costs	CZK 24 659	CZK 7 689	CZK 38 495	CZK 20 591
Total side effects of treatment	75%	50%	100%	66.00%

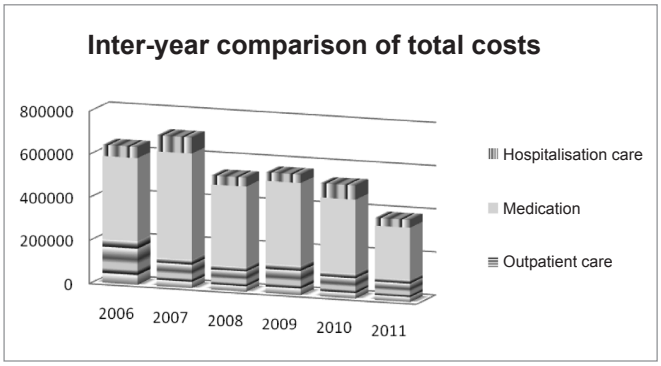
of chronic iridocyclitis and only once (8%) in intermediate uveitis, twice influencing sympathetic ophthalmia.

Out of the entire monitored study population of 27 patients, in which 45 eyes were treated, according to the selected evaluation criteria for visual acuity (see above) the treatment was successful in 41% of cases, i.e. in 18 eyes, satisfactory in 43%, i.e. in 19 eyes, and unsatisfactory in 16%, i.e. in 7 eyes. From the given study population, 9 patients (16 eyes) were treated only with corticosteroids and the treatment was successful and satisfactory in 93%. In the remaining patients the actual treatment with corticosteroids before or during the observation period was demonstrated to be insufficient, and 12 patients (18 eyes) were transferred to immunosuppressive therapy, and 6 patients (10 eyes) to a combined form of treatment. The treatment was demonstrated to be at least satisfactory in 67% of eyes treated with immunosuppressive drugs and in all eyes treated with the combined form of treatment. Table 2 presents these relationships for the three single diagnoses of intraocular inflammations. In the case of intermediate uveitis, in the majority of patients the therapy was successful, with an overall average gain of 9 letters of ETDRS chart. In the case of chronic iridocyclitis, treatment was practically successful and satisfactory in a half of the patients, in the general evaluation it remained at the level of the same ETDRS row. An important factor in monitoring the therapeutic effect is always satisfactory vision in three patients with sympathetic uveitis, since the gain of a number of ETDRS letters from the next row in three patients only cannot be evaluated as a successful treatment. Out of the observed 45 eyes (vision 0-0.05) we recorded blindness in 7 eyes (15.5%), fortunately this was not bilaterally in any case and there was always serviceable vision in the other eye, despite the fact that this eye was also afflicted by inflammation. In these patients, the inflammation began on average at the age of 6 years, with an average duration of 19 years, in 71% of cases it was linked to juvenile idiopathic arthritis. To these patients it is necessary to add also three cases of unilateral blindness within the framework of enucleation due to a sympathetic illness in the previous period.

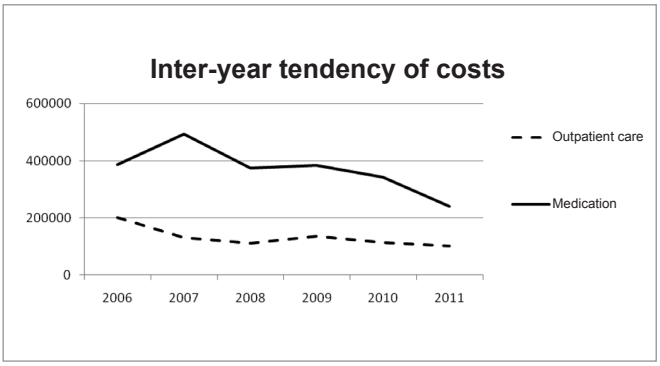
General undesirable effects of treatment occurred to varying extents during the observation period in 18 patients, whilst only 9 treated patients remained without any negative impacts of treatment. Side effects of treatment always accompanied aggressive immunosuppressive therapy for sympathetic ophthalmia (Table 2). It was not necessary to discontinue the indicated treatment due to serious consequences of the undesirable effects of treatment in any case. Increased blood pressure in connection with treatment occurred in all types of treatment, eight times in total. Increased liver test values were recorded in four patients, the largest proportion occurred in immunosuppressive therapy using cyclosporine A. Similarly a toxic effect was manifested in the function of the kidneys, increased creatinine and urea, which occurred in two patients, and gingivitis in three of the patients as a side effect of immunosuppressive therapy. Cushing facies afflicted seven patients due to long-term use of corticosteroids, as well as acne in five female patients.

The average annual costs for the treatment of the 27 observed patients with non-infectious uveitis over the period 2006 – 2011 are CZK 555 960. The largest part of the financial costs comprises outpatient medication, i.e. general and local administration of pharmaceuticals in 67%, and at least it covers hospitalisation care including costs for surgeries in 9%. Outpatient care by an ophthalmologist and with laboratory observation comes to 24% of total costs. In the inter-year comparison of total costs, the maximum was reached in 2007, when the highest costs were for medication and hospitalisation care, and in total comprised CZK 699 632. By contrast, the lowest total costs were CZK 382 129 in the last year of observation, when all items reached the minimum (Graph 1). The inter-year tendency of the individual cost components has a decreasing character (Graph 2). The costs for outpatient care show a slight reduction, whilst no connection to the introduction of the regulation fee for outpatient treatment is demonstrable, since the number of control examinations decreased as a result of the progressive remission of the disease. We understandably succeeded in obtaining the most precise values on the provided outpatient care of patients with diagnosed uveitis in comparison with other diagnoses in the last year of observation. All the examinations of patients with uveitis as the main diagnosis and as an accompanying diagnosis formed almost 4% of all 17 000 outpatient complex and targeted examinations in 2011 at the Eye Clinic of the Royal Vinohrady Teaching Hospital. In our monitored study population, 138 primarily targeted examinations were conducted, i.e. 20% of the provided outpatient care of all the uveitic patients within the given period, which was the lowest number per single year of the study. The largest number of ophthalmological checkups in the six year observation of uveitis, of 179, was recorded in 2006.

In the case of medication, the decrease in costs is evidently influenced by the progressive reduction of the prices of certain general immunosuppressive preparations and also a reduction of prescription due to stabilisation of the ocular process. Despite this fact, in 2007 and 2009 costs for medication show a tem-



Graph 1. Inter-year tendency of total costs



Graph 2. Inter-year comparison of costs for medication and outpatient observation

porary increase, conditional upon repeated application of tacrolimus. It was not possible to compare hospitalisation care inter-yearly, since the array covered brief and irregular periods, and only with 10 monitored patients. In a comparison of the groups of patients treated with one type of medicamentous therapy from the groups: immunosuppresants, corticosteroids and combined therapy, the highest costs were reached by the group of immunosuppressive preparations: CZK 30 928 per year for treatment of one patient. The cheapest was the treatment with corticosteroids, at CZK 2 014 per patient per year. Annual treatment with a combination of immunosuppressants with corticosteroid preparations came to an average of CZK 17 935. Upon a comparison between the three individual groups of diagnoses (Table 2), it ensues that understandably the most expensive treatment was for sympathetic ophthalmia with a combination of immunosuppressants, and the cheapest one was for intermediate uveitis, due to the high frequency of general and parabulbar application of corticosteroids.

DISCUSSION

Sight is the most important human sense, the development of which takes place from birth up to the end of the pre-school period. Inflammatory affliction of the uvea represents a serious threat already during this period. An extensive Polish study demonstrates that a role is played in the significant deterioration of vision in children by atrophy of the optic nerves, retinopathy of immaturity, severe short-sightedness, hereditary cataract and degeneration of the retina, and that uveitis also ranks amongst the significant etiological factors [29]. In our study population uveitis occurred in the pre-school period in 8 children, and during school age up to the age of 15 years in a further 12, which had a significant influence on visual acuity and monocular blindness even after the years of observation. In the USA a study was conducted on the economic impacts of reduction of sight to blindness, but it did not take into account the causes of damage to sight. From the epidemiological studies it ensued that 6% of patients with uveitis are blind, with total annual costs for those afflicted in the USA at approx. 240 million US dollars [10]. Another study investigated the character, type and period of duration of loss of sight in patients with uveitis, with the aim of determining the causes of loss of sight and their greatest risk. During the course of three-year observation, 70% of patients had reduced visual acuity after a period of two years of the duration of the disease, and permanent loss of sight afflicted one quarter of the patients [8]. On the basis of experiences in a summary evaluation of 73 studies [25], we also chose visual acuity as the basis of the clinical evaluation of the effectiveness of treatment. In evaluating the change of visual acuity we assessed the gain or loss of individual letters of ETDRS chart separately in individual patients, as in the Czech AMADEUS study, which is based on the foreign studies VISION, MARINA, and on the recommendations of NICE [9]. A significant deterioration or improvement is shown by 15 letters (i.e. three rows), a slight deterioration or improvement is up to 14 letters. The overall evaluation is calculated statistically from the sum of the individual values of all patients, as expressed in the individual rows of the ETDRS chart [9]. The recommendation of the SUN Working Group evaluates improvement or deterioration of visual acuity in uveitides by two rows [12]. In our study we assessed the shift in the change of visual acuity after six years in single letters [9]. We considered entirely "satisfactory" treatment to constitute preservation of vision within the given row. This produced the mathematical value of ± 0.05, which is in total 0.1 = one row of ETDRS chart. With regard to the small number of patients in this pilot study, we refrained from an evaluation of improvement or deterioration expressed in two rows of ETDRS chart [12], since an error of small numbers would prove here.

The fundamental and initial treatment of non-infectious uveitides at present remains general administration of corticosteroids, which are also taken periocularly [5, 23, 27], and we chose this application for unilateral intermediate uveitides. In determining the clinical effectiveness of treatment of uveitis with immunosuppressive preparations between 1980 and 2007 [25], the results of a total of 73 studies were compared. Of these 12 were randomised, 20 prospective and 40 retrospective studies, and 1 was an non-controlled blind study. Immunosuppressive treatment evaluated the effectiveness of pharmaceuticals in 4 groups of T-lymphocyte inhibitors, antimetabolites, alkylating substances and biological treatment. The greatest effect was seen in biological treatment [25]. Our study compared immunosuppressive therapy using cyclosporine A (T-lymphocyte inhibitor), and antimetabolites were represented by azathioprine and methotrexate. This method of treatment was applied also to child patients with non-infectious form of uveitis [14, 16]. The assessment of biological treatment was not classified due to the small number of patients, since to date this treatment in the Czech Republic is only within the competence of rheumatologists.

In accordance with the above-stated study [25], a positive effect of all three drugs was confirmed in our patients with non-infectious uveitides, and so was a positive impact on the treatment of CME using cyclosporine A for intermediate uveitis. In a longer study with 376 patients, a higher effectiveness of treatment with cyclosporine A was demonstrated, since after one year of treatment complete control of the inflammation was achieved in 52% of patients, as against 36% in the case of therapy using corticosteroids [13]. This experience was also confirmed, since in the case of insufficient effectiveness of general therapy by corticosteroids alone we were necessitated to switch to immunosuppressive therapy or a combined therapy. In the combined therapy we added antimetabolites to the generally administered corticosteroids, which increases effectiveness of treatment [2]. It is just the combined treatment, which is used also in the Czech Republic [27, 28], in the schemes which save on corticosteroids has a good effect and also a lower occurrence of general side effects of therapy [2, 16, 24, 31]. In the case of insufficient effect of cyclosporine A it is possible to choose treatment with tacrolimus [15, 31]; in our observation this concerned 3 patients who already had corticoresistant iridocyclitis accompanied with secondary glaucoma, provoked precisely by corticosteroids.

Our study also involved monitoring of undesirable effects of treatment on the human organism, which was concentrated on two main pharmaceuticals, namely generally administered corticosteroids and cyclosporine A. In the case of corticosteroids these were acne and Cushing facies, predominantly in young girls. We did not confirm pronounced systemic hypertension, hyperglycaemia or adrenal insufficiency [23] also with regard to the low age composition of the monitored patients in the study. In the case of cyclosporine A, the most frequent complication was systemic hypertension in 25% of cases, also recorded were manifestations of mild hepatoxicity, increase in levels of creatinine and uric acid in the evaluation of renal functions and gingivitis, as described

in the literature [29]. With regard to the continuous laboratory monitoring, doses of the drug were reduced according to situation without a perceptible clinical impact. The toxic effects were never so pronounced as to necessitate discontinuation of immunosuppressive or combined therapy [13, 25].
Corticosteroids administered generally, locally and periocularly were the main cause of secondary glaucoma (22%); the condition was resolved by discontinuing corticosteroids if the condition so permitted, or by a change of therapy. Above all local antiglaucomatous drugs were used: beta-blockers and carboanhydrase inhibitors [27], which were if applicable supplemented with sympatomimetics for glaucoma. Three patients had to undergo antiglaucomatous surgery with a favourable result. The formation of a cataract was above all induced by the inflammation itself as its most frequent complication [27], the secondary influence of corticosteroids was only an accompanying effect. The relatively low number of complicating cataracts (36%) in our study is conditional upon their 9 operations (Table 1) in the preceding period. The surgical technique was governed by the form of complicated cataract with or without implantation of an intraocular lens, the condition was remission of the inflammation for at least three months and peroperative intravenous application of methylpredinsolone [27].
Pharmacoeconomics is a relatively new scientific discipline, which has been developed since the 1960s, as an interdisciplinary connection of pharmacological, clinical, economic and epidemiological methods. This scientific discipline assesses the overall value of pharmacotherapeutic interventions, services and programmes. Pharmacoeconomics seeks an answer to the question of the benefit that it is possible to gain per price unit of the pharmaceutical. It also has significant social and political aspects [7]. Cost-effectiveness analysis (CEA) ranks amongst the methods of pharmacoeconomic studies dealing with a comparison of costs for treatment and the effect of treatment. CEA is an analytical method used for the evaluation of overall costs and attained results. Its main function is to make visible the relative cost of various interventions with regard to the patient's improvement in health. This type of analysis is suitable for use where procedures are compared with a similar type of outcome. The result of the analysis is costs for the specific clinical unit. It cannot be used in the case of studies of illnesses with varying outcomes. From the perspective of costs, direct costs are evaluated: namely in connection with treatment, as well as indirect costs: those influencing the patient and society. The benefits of treatment, or clinical effectiveness, are expressed in specific clinical units. Upon a comparison of two different therapeutic interventions on one patient, which have different costs and generate a different level of effectiveness, it is necessary to determine the "incremental" cost and benefit analysis. The aforementioned analysis states what the costlier treatment brings and what its effectiveness is. The result is the Incremental-cost-effectiveness ratio (ICER). This is the ratio of the differences of costs and effectiveness, which demonstrates how many more resources need to be expended in order to attain the additional therapeutic benefit. A disadvantage of CEA is that it differentiates only between various therapeutic interventions within the framework of a single diagnosis, but it is not capable of comparing the cost-effectiveness of therapeutic procedures across various illnesses. It does not enable a conversion of the results of the treatment to a common denominator, as is the case e.g. in the cost-utility (CUA) type of analysis and also does not take into account the patient's quality of life and point of view. A problem is the disparity of the units in which the costs and results are contained. The advantage of the CEA is the high clinical comprehensibility of results, since they are expressed in real practical parameters [7, 26].
The average annual costs for treatment of one patient from the observed group in the Czech Republic are CZK 20 591. The largest number of these is composed of costs for medicamentous treatment, on average CZK 13 746, which is as much as 67% of total costs. Outpatient care by ophthalmologists, immunological or laboratory observation and hospitalisation care in our study came to CZK 6 845 in total, thus 33%. An analogous study over only one year, conducted in France in 2008, observed treatment and the associated costs in four professional centres [3], whilst our observation was conducted at one clinic, but over the course of six years. The most frequent diagnosis of the French study was chronic anterior and intermediate uveitis, panuveitis and also posterior uveitis. The average annual costs for treatment of one patient were approximately CZK 85 100 (€ 3403). The largest proportion of these was professional care by doctors and hospitalisation, in total as much as CZK 72 250 (€ 2889), which is 85% of the total costs. Hospitalisation episodes were very frequent across all the observed clinics. Costs for actual medication comprise only a small amount of total costs, in total approximately CZK 12 850 (€ 514), thus a mere 15% of total costs [3]. There is a clear difference between the amount and the composition of costs for treatment of patients with uveitis in the Czech Republic and in France. In total the costs for treatment of uveitis are considerably lower in the Czech Republic. The price of indicated medication is similar in comparison with an advanced EU country, which testifies to the comparable level of diagnostic and therapeutic professionalism. The costs for financial remuneration of professional care of doctors and other healthcare employees in outpatient care and the hospitalisation sphere in the Czech Republic cannot be compared.

CONCLUSION

It is not possible to recommend a precise optimum variant of treatment, since the actual diagnosis of the form of uveitis is decisive. Despite this fact, a cost-effective treatment was combined, incorporating an optimum dose of immunosuppressive preparations (azathioprine, cyclosporine A, methotrexate) and a low dose of corticosteroids from the perspective of the clinical impact on maintaining the most beneficial visual acuity, at the same time as minimising the undesirable effects of treatment. The least financially demanding, together with a beneficial clinical effect, appeared to be the treatment of intermediate uveitis. In chronic iridocyclitis the connection with juvenile idiopathic arthritis was of decisive significance, in which the current presence of this general systemic disease had a fundamental influence on not very optimal clinical result and effectiveness of treatment, which was not always sufficient. The financial costs for professional medical care of patients in the Czech Republic are substantially lower than the costs of the actual medicamentous procedure.

LITERATURE

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