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THE PROBLEM OF NON-COMPLIANCE WITH MEDICAL TREATMENT IN GLAUCOMA PATIENTS

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Özet: Erciyes Üniversitesi Tıp Fakültesi Göz Hastalıkları Kliniği Glokom servisinde 1989-1991 yılları arasında düzenli olarak kontrole gelen 44 hastada önerilen ilaçların doğru ve devamlı uygulanma insidansı araştırılmıştır. Hastalara durumları hakkında doğru ve yeterli bilgi sahibi olup olmadıkları, ilaçlarını düzenli uygulayıp uygulamadıkları ve bu esnada başkalarından yardım görüp görmedikleri sorulmuştur. Sonuçların analizinden hastaların çoğunluğunun hastalıklarının niteliği ve muhtemel sonuçları hakkında yeterli bilgiye sahip olmadıkları ve tedavilerini değişen sıklıklarda (% 71.43 - 90.48) aksattıkları ortaya çıkmıştır. Tedaviye uyumsuzluk oranı, ilaç rejiminin günde 2 kezden fazla uygulanmasında %88.46'ya, oral yolla alınması durumunda ise % 80'e yükselmiştir.

Anahtar Kelimeler: Glokom, göziçi basıncı, uyumsuzluk.

Summary: The incidence of correct and continuous application of prescribed drugs was investigated in 44 patients who regularly visited the Glaucoma Clinic of Erciyes University Medical Faculty Department of Ophthalmology, between 1989 - 1990. The patients were asked whether they had correct and sufficient information with regard to their condition, applied the prescriptions regularly and received any help from other persons during instillation. Analysis of the results showed that majority of patients were not aware of the nature and possible outcome of their disease, neglecting their treatment with variable frequency (71.43 - 90.48 %). The rate of non-compliance rose to 88.46 % when the prescribed regimen was to be received more than twice daily, and to 80 % when taken orally.

Key words: glaucoma, intraocular pressure, non-compliance

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Non-compliance with given drug regimens is a major set-back in the treatment of many chronic disorders including glaucoma and this is particularly the case if the patients are to apply the regimens for prolonged periods (1,2). There are specific problems with pilocarpine treatment on patient basis such as the necessity of frequent instillation, the side effects among which miosis, pseudo-myopia or iris cysts are worth noting. Beta-blockers are rather popular recently, however their unwanted systemic side-effects can also be encountered with when they are instilled to the eye. Since the majority of glaucoma patients are in the elderly age group where circulatory and respiratory problems are commonly seen, side effects of these drugs can possibly be avoided with punctum occlusion during instillation to the eye, which also increases the importance of patients' compliance. The incidence rates cited in the literature with regard to the problem of non-compliance are neither uniform nor in agreement with eachother, and this is mainly due to the fact that there is not a standard definition for the term 'compliance'. In this study, the incidence rates of non-compliance in a series of 44 glaucoma patients were investigated and the relevant problems discussed.

Patients and methods

Forty-four patients who regularly attended to the Glaucoma clinic of Erciyes University Faculty of Medicine, Dept. of Ophthalmology between January 1989 and March 1990 were included in this study. Twenty-three were males (52.27%; range of age : 45-79) and 21 females (47.73%; range of age:38-85). Topically applied beta-blockers, miotics and oral acetazolamide were administered to the patients either alone or in various combinations with each other. The patients were asked whether they:

1. Were fully aware of their illness,

2. Took the prescribed drugs by themselves or with the help of some other persons,

3. Followed the instructions about the applicance of the drugs,

4. Carried the drugs with them while going somewhere else,

5. Took their drugs on the same hours of the day or with relation to certain reminder occasions such as 'after getting up' or 'before going to bed' ,

6. Missed some of the doses. If they did, which dose/s was/were most frequently missed ?

The prescriptions received by the patients are listed on the (TABLE).

Beta-blockers and dipivefrine were instructed to be instilled twice a day, pilocarpine 5 times a day and oral acetazolamide was to be taken once or twice a day.

Results

It was found out that 28 patients had good or moderate information about their condition. Twelve had very little information and though they hardly knew the name, they were totally ignorant about the nature and the possible outcome of their illness. Four patients, on the other hand, did not have any sort of information at all. Among patients in the first group, 10 were aware of their condition because they either had an operation for glaucoma, very low vision or one absolute eye because of the disease. One patient believed that the only treatment available was medical, however when he was informed that he could be operated on alternatively, he preferred the opera-

tion.

While 6 of the patients required help to instill the drops or take the drugs, the rest did not. One patients with Parkinson's disease was dependent upon some other person to receive the treatment. One other patient who was helped by his wife remained without any drugs as long as 1 month because of his wife's illness. Majority (71.42%) of the patients preferred receiving their treatment with relation to certain activities of the day, such as 'after geting up' or 'before going to bed', instead of receiving at certain hours of the day.

Among the 26 patients who were on pilocarpine treatment in various forms (alone or in combination with other agents), only 3 were compliant whereas 23 were not (non-compliance rate: 88.46%). The most frequently neglected dose was usually the mid-day's.

Among the 42 patients who were taking timolol maleate in various combinations with other drugs, 12 were compliant with a treatment of 12 hourly intervals (non-compliance rate: 71.43 %).

Among the 30 patients who were instructed to instill the drops on reminder occasions of the day (such as 'after waking up' or 'before going to bed') only 6 was non-compliant (non-compliance rate: 20%).

Among 10 patients who were receiving oral acetazolamide, only 2 were compliant with the treatment (non-compliance rate: 80%).

Discussion

The major reason for poor compliance was forgetting to take the drugs. This was particularly the case when the patients were to instill the drops more than twice a day and the forgotten dose was usually the mid-day's, one reason was forgetting to carry the drugs with themselves. It is understood that the patients were better compliers when drugs were to be received on certain reminder activities of the day.

Bloch et al. (3) found the rate of non-compliance as 28%. This rate was 42% in a series of 168 patients by MacKean and Elkington (2). In our series, various non-compliance rates were obtained according to different forms of therapy. This was 88.46% for pilocarpine treatment and 71.43% for '12 hourly' timolol maleate treatment in various combinations. This rate (71.43 %) for timolol maleate treatment dramatically fell down to 20% when the patients were instructed to instill the drops on reminder ocasions of the day, such as 'after waking up' or ' just before going to bed'. Among 42 patients, only 4 were perfectly compliant with their therapy whereas the rest were not compliant with at least one part of their treatment and this made-up an overall non-compliance rate of 90.48%.

One reason for the neglect may be unawareness of the importance of the disease. One patient, for example, took less than sufficient medication at his will, since he feared that dependence could develop if he took the exact dose. However, when he was assured with regard to this matter and re-informed about his condition, he started to take the drugs regularly with correct dosage. One other reason for non-compliance may be misunderstanding the number and timing of the daily dosage. Although compliance with 'twice-daily' applications seemed to be better, the interval between the two doses was not always the same.

It is stated in the literature that prolonging the treatment caused less effectiveness and more failure (4). Our patients also showed less compliance when they were on oral acetazolamide for long terms, compared to topical forms of treatment. Moreover, when the well-

known side effects of oral acetazolamide treatment were encountered with, patients tended to reduce the dose or completely leave the treatment by themselves which was also a contributing factor to the failure of the therapy and it would not be wrong to expect that the 'good complier 10 % will eventually be poor-compliers because of these adverse side effects. An additional factor for failure was long delays in the treatment of some patients who were not covered by any health insurance and obliged to pay for the high medical costs.

Results obtained from glaucoma patients treated medically, surgically or with laser suggested that the diurnal variation in intraocular pressure (IOP) was maximal in medically treated patients, whereas it was minimal in surgically treated ones (5). The diurnal variation in IOP can not be kept within safety limits even in best compliers in medically treated groups, and it is this irregularity which is suspected to have the potential to cause optic nerve damage (6).

We feel that the topic should be discussed under two main issues:

A. Specific measures to increase the compliance of glaucomatous patients.

B. A new approach to the glaucoma therapy as a whole.

A. Specific measures to increase patients' compliance may be to provide the patients with clear and simple instruction booklets and to make sure that they understand them very well. Use of ocular drug bottles with compliance caps or a well-established color-coding system for the tops of topical eye drops may be considered among those measures (7).

In order to increase the patients' compliance, the mid-day dose may be omitted from the scheme and twice-daily regiments put into practice. Söderstrom et al. (8) combined timoptic with pilocarpine and applied this solution twice daily. This appeared to have an effect similar to the separate usage of the drugs, and the outcome was very favourable in terms of compliance (8,9).

B. On the other hand, as a new approach to glaucoma therapy those points deserve specific consideration:

1. Prostaglandin $F_2\alpha$ ($PGF_2\alpha$) is an agent which does not interfere with aqueous humor dynamics and is known to increase uveoscleral outflow (10,11,12). In a study undertaken at this department, $PGF_2\alpha$ as the tromethamine salt was topically applied to 23 glaucomatous eyes and to appropriate controls. There was a significant decrease in IOP at 2-24 hr (13). Since $PGF_2\alpha$ seems to lower the IOP for longer periods with less dose, for example as long as 24 hours with only one drop, it may help to increase patients' compliance.

2. On the other hand, 6-hydroxydopamine (6-OHDA) is known to increase the adrenergic sensitivity of the anterior segment by making chemical sympathectomy and thus the adrenergic drug concentrations necessary for IOP decrease are kept to a minimum (14-17). Twice-daily subconjunctival injections of 6-OHDA, together with 0.1 % epinephrine resulted in an effective IOP reduction for a period between 3 months and 2 years (18,19).

3. Topically applied acetazolamide (20-22) can be a good alternative since it is most logical to accept that systemic side effects will be kept to a minimum to increase patients' compliance.

4. Surgery seems to be a good alternative to

other forms of treatment even in well developed countries where compliance rates are expected to be higher than elsewhere (5). After surgical intervention, non-compliance rates should dramatically fall down to zero. Many surgeons perform surgery after glaucomatous field defects are detected with perimetry. However, 40 % of patients still may not exhibit such demonstrable changes in spite of important nerve fibre layer (NFL) defects (23). Therefore, optic nerve head and NFL photography, carried out at earlier stages may help to reveal the disease in the remaining 40 %, and this also justifies earlier surgical intervention.

Consequently, we feel that the question as to whether glaucoma should be treated surgically or medically must be re-considered by all glaucoma clinics. Bearing in mind the high non-compliance rates in our series and the reviewed problems with medical treatment, it would be logical to put early surgical intervention or laser application into practice, perhaps by completely abondoning medical treatment in many glaucoma patients.

Table. Prescriptions received by the patients

Prescription	No of patients	%
LB	1	2.27
PC	1	2.27
TM	12	27.27
TM+PC	15	34.09
TM+DPV	3	6.82
PC+DPV	1	2.27
PC+TM+DPV	1	2.27
ACZ+TM+PC	7	15.91
ACZ+PC	1	2.27
ACZ+TM	1	2.27
ACZ+TM+DPV	1	2.27
Total	44	99.98

(LB: Levobunolol; PC: Pilocarpine; TM: Timolol maleate; DPV: Dipivefrine; ACZ: Acetazolamide)

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