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CONSERVATIVE TREATMENT OF SENILE CATARACT WITH CONJUNCTISAN A EYEDROPS

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Summary

It seems to be a generally held view that there is no way of treating senile cataract successfully. However, this view is contradicted by the results of a long-term study carried out on 192 eyes treated with Conjunctisan A. According to these results, lens opacities in senile cataract can indeed be influenced by therapy. Conjunctisan is a new therapeutic principle which exploits the effect of water-soluble protoplasmic elements, in particular proteins, ribonucleic and deoxyribonucleic acids, phospholipids, polysaccharides, lens-cell specific nucleic acids and amino acid precursors from the lens, vitreous body, retina, optic nerve, cornea, conjunctiva and placenta. Over a period of observation of 5 years (1973 - 1978) Conjunctisan Eyedrops were administered to the conjunctival sac twice or three times a day. Of 192 eyes thus treated, lens opacification was halted in 36%, and vision improved in 45%. These results concur with those of our earlier investigations on 74 eyes (1969 - 1973). It is also worth mentioning that opacification was slowed down much more than previously assumed on the basis of experience: this was demonstrated in a comparison with 75 cases of senile cataract that were not treated or treated only by conventional methods.

Introduction

Over the past 50 years, numerous studies have been performed with the object of developing a method of conservative therapy to prevent the progression of cataract in elderly patients. So far, however, no form of treatment, usually eyedrops, has been proven to be effective.

The use of macromolecular organ lysates from various tissues of the eye (molecular weight $<10^6$), contained in Conjunctisan A Eyedrops, introduces a completely new therapeutic principle into the treatment of cataract. Conjunctisan A Eyedrops contain water-soluble protoplasmic elements, in particular proteins, ribonucleic and deoxyribonucleic acids, phospholipids, polysaccharides, lens-cell specific nucleic acids and amino acid precursors from the lens, vitreous body, retina, optic nerve, cornea, conjunctiva and placenta. The results of molecular biological research and the wide range of positive results obtained with macromolecular cell components in practice preceded the decision to use Conjunctisan A in the eye.

One of the studies which has proved the organotropism of cytoplasmic substances used macromolecular extracts from the cerebral hemispheres, and demonstrated that these extracts specifically stimulate the protein biosynthesis of the brain (Axmann, Chandra). The fact that specific effects were observed in the brain and also confirmed in practice led to the development of eyedrops acting on the same principle. Conjunctisan A Eyedrops contain not only a number of active organ components, but also microgram amounts of lanatoside, and aesculin. Inclusion of vasoactive substances is in accordance with observations made with other eyedrops containing digitalis, since they were found to have an effect on ciliary muscle (Fuchs and Hollwich, 1952; Hollwich, Güth and Dieckhus, 1967). These observations proved that digitalis exerts a pharmacological activity on the ciliary body, and it is known that the ciliary processes are involved in the production of aqueous humour.

Most recent attempts to treat cataract have been based on the assumption that a particular, vital substance is missing in ageing lenses which begin to cloud, and therapy has been aimed at supplementing certain substances in order to prevent the process. A statement made by Sautter in 1960 in the chapter on the lens in the manual "The Ophthalmologist" concluded that there is as yet no proof of the efficacy of any conservative therapy for senile cataract. One thing he emphasises particularly is the fact that senile cataract often does not progress for a number of years, and that during this time there

may even be some improvement in the vision, as a result of stenopaeic gaps in the clouded lens.

This observation is still valid today, but it does not mean that the search for an agent that can successfully prevent cataract cannot continue, since advances in biological and chemical research methods and in molecular biology have meant that our knowledge of the biochemical processes involved in the lens and the development of cataract has increased, and the likelihood of a method of treatment being found has become greater.

Research into the metabolism of the lens was opened up by the work of H. K. Müller and his colleague, O. Kleifeld, in 1960. They attempted to combat cataract development internally, by administration of the sulfonamide Debenal. Initial results in 14 patients were good , but the study was discontinued some time later.

The biochemistry of the lens metabolism

Hockwin continued the research work of Müller, and a decade of intense study threw some light on the previously unrevealed area of the biochemical processes at work in the lens, in particular in the elderly. The most important revelation emerging from his meticulous studies was that the clouding of the proteins in the lens is due to enzymatic changes. No pharmaceutical agent has been found which can cure this metabolic disorder. The most likely approach will be to break down the enzyme block that has built up.

Examination of normal lenses shows a high protein content. It is these proteins which guarantee the transparency of the lens. Enzymes transform amino acids contained in the aqueous humour into protein, but with the process of ageing, these enzymes change their character. The lens must have energy to transform these amino acids and to maintain the membrane potential, physiological equilibrium and growth. As soon as this cellular energy is no longer available, a cataract begins to form. This is the point at which studies with protoplasmic substances in the form of eyedrops begin, on the premise that these substances may be able to provide the lens with energy, and also to transport the energy. Such a method depends on the assumption that the preparation can penetrate the conjunctiva. The fact that the necessary substances can in fact pass this barrier has been demonstrated by Brendel and Seifert at the Surgical Research Institute of the University of Munich. It should be remembered here that mucous membranes do not only form barriers, but also have the facility for absorption. A positive result of an allergen test on the conjunctiva provides convincing proof that this membrane is capable of absorbing substances applied to it.

The principle of action of cytoplasmic organ extracts

The therapeutic efficacy of cytoplasmic organ extracts like the ones used in Conjunctisan A Eyedrops has its history in the use of organ lysates to treat molecular deficiency states (Theurer). Protoplasmic cell components contain induction and growth factors (Spemann) which activate the RNA and DNA synthesis of diploid cells (Paffenholz and Theurer), and improve the repair capacity of enzymes (Altmann and Wottawa).

The broad spectrum of activity of the various protoplasm factors combined with vasoactive and surface active substances is therefore ideal, not only to treat protein changes and their effects (Kramps, Bellows and Bellows), but also to activate the reduced adenosine triphosphatase activity (Gupta, Harley) during the development of senile cataract.

The retina is in fact technically an extrusion from the brain. Alongside considerations on the drug treatment of the defective metabolism of the ageing eye there exist experience gained in practice and clinical investigations into the treatment of the ageing brain with cytoplasm preparations (Jansen, Brückner). We shall now turn our attention to those substances and research results which specifically affect the brain.

The above-named authors consider that the loss of certain brain functions in elderly people is due to impairment of the parenchyma of the brain which is not totally vascular in origin, although defective blood supply may well be a major factor. The following molecular factors are the cause of cerebral impairment:

1. Impaired or restricted transmission of genetic information to the cell organelles responsible for protein synthesis.
2. Increased tendency to error in the synthesis of protein by enzymes.
3. Reduced ability of enzymes to adapt to increased metabolic requirements, together with reduced ability of the brain to maintain metabolic and functional homeostasis.

It would seem logical to apply this concept of the processes at work in the ageing brain to those involved in the eye of ageing people. There is a certain amount of similarity between these processes and the role of enzymatic changes in the formation of cataract.

Our studies in this field

Assessment of a new therapeutic concept requires a large number of test subjects who are selected after critical observation and whose condition has been confirmed by slit-lamp and other ophthalmological examination, and recorded in writing and pictures.

The results of treatment with Conjunctisan A were classified as "unchanged", "improved" or "worse". These clinical assessments almost always coincided with unchanged, improved or worse vision, so that this remained the method of classifying the clinical efficacy of anti-cataract therapy. The forms of clouding of the lens in 192 eyes with incipient or advanced cataract were classified as follows: anterior cortical cataract 12, posterior cortical 40, clefs 26, wedge-shaped spokes 52, coronary 10, punctate 8, nuclear 29, general 15.

Our results were obtained in a group of patients with senile cataract. These eyedrops have not been found to have an effect on any other type of cataract. The patients falling into this group are elderly, and they come to us with the request for treatment of their cataract, and not, as is the case with younger patients who are fully engaged in a profession, with the demand for surgical removal of the cataract. Such patients value highly any standstill in progression of clouding and any arrest in the degeneration of visual acuity. Naturally, an improvement in vision, coupled with a reversal of opacities, is even more highly appreciated. My results, which cover a treatment period of 10 years, show what can be achieved in this respect with the aid of drug therapy.

Our "ex juvantibus" study covered 105 patients with 192 eyes to be treated. The effect of Conjunctisan A Eyedrops on the opacification of the lens and on the vision was observed for 10 years, from 1969 to 1978. The data that follow are divided into functional descriptions: "improved", "unchanged" and "worse". On average, the visual acuity and the density of the opacity were factors that went hand in hand (tab. 1).

For the sake of comparison it may be noted that an earlier study which lasted 4 years and covered a total of 76 eyes observed similar effects on vision, taking into account the time and number of cases involved (tab. 2).

During the 5-year treatment period, 9 patients died, at an average

age of 82.4 years. The visual acuity of patients in this age-group had usually remained the same (6 the same, 2 improved, 1 worse), varying between 0.3 and 0.4 dioptres. These patients were satisfied with this degree of visual acuity at this stage in their lives, and did not wish to undergo surgery to have their cataracts extracted.

Table 1: Visual acuity and opacity of the lens following treatment with Conjuctisan A Eyedrops (192 eyes treated, 1969 - 1978).

	improved	unchanged	worse
visual acuity	87	68	37
opacity of the lens (cat. incipiens/proyecta)	87	70	35

Discussion and assessment

Examination of the data presented here immediately raises the question of their validity and conclusiveness. Such a large volume of material has been processed here that its validity is surely unquestionable. It would only be possible to examine this number of patients with senile cataract in a practice serving chiefly elderly patients, many of whom come with visual disturbances. I personally examined and assessed all the cases included here.

A study of this nature has to my knowledge never been published before, and certainly not one covering such a long treatment period in so many cases of cataract. Neither have such statistics for treatment of senile cataract by traditional methods ever been published (Nordmann - quoted by H.K. Müller - spoke of "temporary improvement" in 15%).

The life of a cataract is usually said to be about 3 years from the time of diagnosis of clouding of the lens to the point at which surgery is considered advisable. There are exceptions, but this usual schedule is significantly affected by the use of Conjunctisan A. The cataract matures, i.e. the time for removal of the cataract occurs much later, if at all. Many cataract patients did not require surgery for the rest of their lives, and many others have now been treated for as long as 9 years without the necessity for removal of the cataract becoming

apparent.

The type of senile cataract is actually irrelevant to the success of therapy, although we have found that clefs water and wedge-shaped spokes cataract and diffuse subcapsular clouding of the anterior and posterior cortex react best to this new form of treatment. Surprisingly, nuclear cataract also frequently responds to Conjunctisan A. Two main principles governed studies with eyedrops in cataract:

1. General internal measures, hormones, vitamins or oral administration of lens proteins in some form, or
2. Provision of substances missing from lenses with cataract, or supplementation of substances generally necessary to the metabolism of the lens.

Table 2: The effect of Conjunctisan A on opacities of the lens.

form of treatment	no. of eyes	improved	unchanged	worse
conventional (observed 1964 - 68)	75	8%	24%	68%
Conjunctisan A (1969 - 73)	74	46%	33%	21%
Conjunctisan A (1969 - 78)	192	45%	36%	19%

Following decades of research, Hockwin defined the processes involved in the degeneration of the lens fibres. Enzymes and enzyme blockades are particularly important. It is interesting to note that Hockwin considers it possible to develop a therapeutic method which will lift the enzyme blockade.

Administration of dinitriphenol to laboratory animals induces cataract (Hockwin and Kleifeld), and these cataracts can be reversed by activation of enzymes. Hockwin has already predicted that his work will have therapeutic consequences.

Substances contained in Conjunctisan A Eyedrops provide the eye or

lens with proteins which in turn carry energy to stimulate ATP in the cells. It is possible that metabolic enzymes occurring in tears (N. J. van Häringen, E. Glasius, 1974 and 1975) activate the lens-specific nucleic acids and amino acid precursors contained in Conjunctisan A.

The Karl Theurer Research Laboratory for Organ and Immunotherapy has already shown that macromolecular cell components contained in Conjunctisan A Eyedrops are capable of activating the metabolism of human cells (Paffenholz and Theurer).

Hypothesis

The mechanism by which macromolecular cell components are absorbed is not believed to be a simple process of passive permeability, but one of active penetration. All mucous membranes, including the conjunctiva, are able to absorb substances, as has been effectively demonstrated by the absorption of drug preparations by the sublingual route. The bradytrophic lens is more or less suspended in aqueous humour, which provides a situation akin to hydroculture. The lens absorbs nutritive substances through its epithelium and conveys them to the lens fibres (Pau). Clouding or opacity of the lens is reversible in its early stages, as we can now assume on the basis of our observations. It is now known that this reversible stage persists in some forms of opacity for a longer period than previously supposed. This fact is supported by the repeatedly observed cases of spontaneous reversal of senile cataract.

It is still not certain whether Conjunctisan A Eyedrops have an effect on the ciliary body. It is possible that the digitalis component of the preparation does actually have an effect . It is appropriate to mention the studies performed by Hollwich, Güth and Dieckhus (1967), in which the contractility of the ciliary muscle was increased after administration of Stulln eyedrops, which contain digitalis. Irreversible opacity of the lens and degeneration of the cells of the lens mark the condition of advanced cataract and death of the lens itself. Once this stage has been reached, not even Conjunctisan A can be effective in reversing the cataract, but observers repeatedly report a certain degree of clearing of the opacity even in very advanced cataract, following administration of Conjunctisan A Eyedrops. These observations are usually made in relatively old patients who do not request operation of their cataract (usually affecting one eye only), because of their failing general condition . Although observations of this nature are really only of theoretical interest, they do indicate that organotropic macromolecular substances can exert an effect on

advanced cataract. Such cases of course require surgery. The data presented here were obtained in cataract patients without any additional complications in the eye, such as glaucoma, retinopathy or diabetes, which also affect the vision. In the interest of objectivity, 176 eyes examined were omitted from evaluation, as they displayed complicating symptoms. The results are thus unequivocal, but readers will be interested to know that the total number of cases observed is in fact even greater than appears in the statistics for cataract without complications.

The efficacy of this treatment is supported by the following observation: the vision of the patients was tested every three months. In 9% of cases, a particular pattern was observed. Myopia frequently accompanies the initial stages of clouding of the lens, and corrective glasses are prescribed. In patients treated with Conjunctisan A, this myopia can decrease, and weaker lenses are prescribed. This effect, ranging from 0. 5 to 1. 5 dioptres, is observed about 4 - 6 weeks after treatment commences, and is reversed when therapy is discontinued. Many patients purposely stop using the drops when they observe an improvement in vision (cessation of patient compliance), until their vision worsens again. These patients are in fact unconsciously carrying out their own test of the preparation. When they begin taking it again, they once more observe an increase in visual acuity and a lessening of the myopia. This process goes hand in hand with the increase in clouding of the lens.

Observations of this nature are of course only possible if the refraction of the lens and the vision are tested at regular intervals, and diagrams of the clouding are made. This has recently become easier with the introduction of the Scheimpflug camera, which provides a single photograph of all sections of the lens, and computer evaluation of the densogram (Hockwin). It is of interest to state the average age of the patients who had cataract alone and no other concurrent condition of the eye. In our study it was 74. 5 years.

Our study was conducted in a remarkably large group, and thus the results obtained are probably greater in volume than any other study of this nature. Our total observation period is 10 years, and the results derive from cases of senile cataract carefully selected from the 200 or so cataract patients who report each quarter to a practice which deals almost exclusively with elderly people. I consider this fact to be important to the validity of an "ex juvantibus" study of this nature. No side-effects to these biological substances were observed.

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