

CLINICAL AND EXPERIMENTAL RESEARCH ON THE ACTION OF CHLORAMPHENICOL, THE TOTAL EYE EXTRACT (ETO) AND VITAMIN B 12

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The research undertaken at the ophthalmological clinics of Bucharest and Iassy during the last 10 years have shown that ETO has numerous biological characteristics which have imposed it as a precious auxiliary therapeutic agent in the treatment of the most varied eye affections (1, 2, 3).

Thus under the action of ETO the experimental ulcerations of the cornea are completely healed in 4-5 days, while the healing of the same ulcerations needs nearly twice that time with the witness animals.

The study of the "in vitro" action of ETO on pathogenic germs (staphilococcus, piocyanic bacillus, bacillus prodigiosus, typhic and carbon bacteride) by different methods (increased quantities of ETO added to cultures, integrated extract in a medium of cultures or disks steeped in extract) have shown that ETO has no action whatever on the development of these bacteria.

The therapeutic effects of ETO being favourable in more than 80% of the cases in which it has been administered (2), we have tried to associate with it other medicamentous agents and in the first place an antimicrobial product. In the choice we have made we resorted to chloramphenicol, an antibiotic with a wide spectrum of action even when administered per os. Indeed it is known that the spectrum of action of this antibiotic bacteriostatic is very wide, comprising:

- Gram-positive cocci (strepto-staphylo-pneumococci)
- Gram-negative cocci (gonococci, meningococci)
- Gram-negative bacilli
- Spirochaetae (syphilis, leptospirosis, recurrent)
- Rickettsiae
- Large size viruses (trachoma), etc.

On the other hand, knowing that vitamin B₁₂ has a regenerative power on the epithelium even in local applications and, apart of the rôle played by it in the general process of growth, that it has an elective action on certain nervous fibres, we have associated this vitamin also to the total eye extract, thus creating a medicamentous catalyzer, of specially favourable action in corneal ulcers.

I. *Experimental research*

The effects of the mixture ETO-vit. B₁₂ chloramphenicol have been studied primarily on traumatic experimental ulcers of the cornea.

The research has been made on rabbits. With a Filatow trephine of 4 mm diameter we provoked ulcerations in the central zone of the cornea interesting the corneal epithelium and the superficial strata of the parenchyma.

The animals of the experiment have been divided into *two groups* each comprising three batches.

The first batch of group 1 comprising 10 rabbits have been treated twice daily with instillations of a collyrium having the following composition: vit B₁₂ 250 gamma, physiological serum 14% q. s. to 5 cc.

To all the animals the medicament was administered to the right eye, the other, the left eye serving as witness. The cicatrization process was followed up by measuring the diameter of the wound with a compass.

In all the cases the cicatrization of the ulcers treated was progressive from the periphery towards the centre and the healing was completed after 3-4 days, while the ulcerations of the witness eyes have healed after 8-10 days.

On the second batch of rabbits, the traumatic ulcerations of the cornea were treated with twice daily instillations of a mixture of vit. B₁₂ (250 gamma), physiological serum 5 cc and ETO 4 cc (corresponding to 0.5 of dry substance).

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The cicatrization of the corneal lesions has taken place in two days, while with the witness eyes the process has been extended to 8-10 days.

With the animals of the third batch the corneal ulcerations have been treated with daily instillations of a collyrium having the following composition: vit. B₁₂ 250 gamma, ETO 4 cc, chloramphenicol 5 mgr, physiological serum 14%, 5 cc.

The lesions were scarred over completely after 3-4 days, while the witness eyes needed a time of 8-10 days.

On the *second group of rabbits* the corneal wounds have been infected with staphylococci of fresh cultures.

After 48 hours the rabbits of the *first batch* were treated like those of the first batch of group I, with instillations of vit. B₁₂.

The results obtained were the following:

- 30% of the cases, the ulcers were healed after 8-10 days
- 20% of the cases, the ulcers were healed after 12-14 days
- 12% of the cases, have shown an evolution to perforation
- 8% of the animals succumbed, while the remaining
- 30% of the animals were healed in 14-30 days

In the *second batch of animals* the corneal ulcers were treated with instillations of ETO and vitamin B₁₂. The proportion of healed was approximately the same. There were no perforations of the cornea and no animal died.

Lastly, *the animals of batch 3* were treated with daily instillations of the collyrium with ETO, vit. B₁₂ and chloramphenicol.

The results obtained have been definitely superior to those of batches 1 and 2. Indeed:

- in 85% of the cases the ulcers were healed in 4-5 days
- in 10% of the cases the healing process has taken 8 days
- in 5% of the cases up to 12 days.

No eye was lost by perforation and no animal died.

From this research it results that the cicatrizing action of ETO is strengthened by vit. B₁₂, while by association with chloramphenicol a therapeutical product of remarkable efficacy in the treatment of suppurating keratitis is obtained.

II. *Clinical research*

The therapeutical effects of the mixture ETO-vit B₁₂ —chloramphenicol— in the clinic have been watched on patients with corneal affections of different etiologies: serpiginous corneal ulcers (25 cases), traumatical erosions (50 cases), herpetic ulcers (17 cases), eczematous ulcers (29 cases).

It is known that the ulcerating keratitis either of infectious or of uninfected origin is characterized primarily by infiltrations, which evolve more or less rapidly toward an ulcerous phase. This evolution represents a reaction of the cornea to a factor which may be toxi-infectious, allergic or dystrophic, a factor which must be known in order to apply an efficient therapy.

In the treatment of corneal ulcers, it is necessary to ensure the defence of the cornea and more generally of the anterior segment of the eye. This is necessary for establishing a potentiating therapy and for applying on the pathogenic factors an action both precocious and as energetic as possible, especially when it is a matter of bacteria and viruses (therapeutics of attack).

Potentiating therapy. The potentiating therapy comprises the application of heat by means of moist or dry dressings, lightly alcoholized, generalized proteino-therapy, autohaemotherapy, reconstituents, vitaminotherapy, calcium, helio-marine cure, etc.).

The *attacking therapeutics* purpose the destruction of the germs which produced the corneal ulcer. By classical means this is obtained by galvanic cauterization, by curetting the ulcer followed by chemical cauterization by diathermy, ultraviolet rays, beta-therapy, radiumtherapy, etc.

There are also applied *local medicamentous means of potentializing and of attacking* among which we mention: caustics or antiseptics, sulfonamides, antibiotics, and as is well understood, mydriatics.

In general our patients have been treated according to this scheme.

With one of them, patient B. C., 54 years of age, having an ulcer with hypopyon and iritis on the R. E., this treatment stopped the evolution of the ulcer, but the process of cicatrization being lingering, the instillations of ETO, vit. B₁₂ and chloramphenicol have healed the ulcer in 2 days.

Another patient, P. B., 44 years of age, having a serpiginous ulcer with hypopyon of a height of approximately 4 mm, treated exclusively with atropine, ETO, vitamin B₁₂ and chloramphenicol in instillations from 2 to 2 hours only after three days began to reduce it gradually, so that it was completely healed

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after 10 days. The inflammation phenomena, the watering of the eyes, the photophobia and the pain began to diminish after 48 hours. The hypopyon was evacuated during the 5th day from the beginning of the treatment by a paracentesis and it has not formed again.

The third patient treated under the same conditions was healed in three days.

Traumatic erosions of the cornea were brought to cicatrize in 2-5 days without leaving any traces.

Herpetic keratitis. It is known that at present no therapeutic may be counted specific in the affections with herpetic virus. The gravity and the frequency of the herpetic corneal lesions has led to the use of a number of remedies in corneal herpes.

The results obtained are extremely contradictory so that it is very difficult to form an idea on their efficacy as long as we have no personal experience in this problem.

From a clinical point of view, the herpetic keratitis are divided into *superficial* and *profound* ones, each of them requiring local and general treatment, besides the treatment of the complications and of the sequelae.

The local treatment in the incipient or *limited* forms will be a treatment of attack by which the ulcer is cleaned with a view to removing the tissue in which the virus is hidden. This is followed by the disinfection of the virus by chemical substances of the type of iodine tincture, methylene blue, phenol.

Recently antibiotics have been resorted to. At the same time the eye which is touched is dressed and mydriatics are administered against the iridic reaction.

The *profound* forms have benefitted less of antiinfectious treatments, the local treatment tending to reduce the infiltration phenomena and the necrosis while tending to increase the power of defence of the cornea by activating the lymphatic circulation and the limbic sanguine circulation.

In these forms the tissue-therapy finds the most suitable indications and the results which we have obtained with ETO are conclusive from this point of view.

With all the patients subjected to treatment with ETO, vit. B₁₂ and chloramphenicol, there has been a clear improvement both from a subjective point of view and objectively. The pain, the photophobia, the watering have diminished progressively and the daily colouring of the ulcer with fluorescein showed a progressive reduction of its surface.

These results however are not lasting. In five cases a new outburst of keratitis took place after 7 days;

— in two cases after 12 days

— in one case after 20 days, and

— in three cases the duration of the improvement has exceeded 30 days.

The *eczematous ulcers* have all reacted favourably to the treatment with ETO, vit. B₁₂ and chloramphenicol, some of them healing up in 4-5 days, although previously they had been treated for weeks on end with atropine, dionin, aureomycin, vitamin A, etc.

From the study of the cases observed we can affirm that the corneal erosions and the serpiginous ulcers are best influenced by ETO, vitamin B₁₂ and chloramphenicol.

Another affection which is favourably affected by this medication is the eczematous ulcer. The herpetic keratitis, although it is much improved both as regards the subjective symptomatology as also the objective one, shows no lasting results.

CONCLUSION

1. ETO, vit. B₁₂ and chloramphenicol represent a medication with favourable effects on traumatic ulcers of an infectious character of the cornea, shortening the evolution and speeding up the cicatrization.

The medication influences first the subjective symptoms: the pains, the photophobia, which diminish progressively; later the cicatrization of the lesions takes place.

2. Eczematous kerato-conjunctivites are also benefiting by the treatment with ETO, B₁₂ and chloramphenicol, especially if the classical treatment has yielded no results.

3. The herpetic keratitis show results which are not constant, because after a period of improvement which is variable, new outbreaks of lesions take place at the level of the cornea.

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ABSTRACT

Associating the total eye extract (ETO) with chloramphenicol and vitam B₁₂, there is obtained a catalyzing medicament which is specially favourable in corneal ulcers, either experimental or clinical. Constant action in the case of serpiginous or eczematous ulcer. Important improvement in herpetic keratitis, but of temporary (non-durable) results.

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