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REPORT   
 CD

COUNTRY USSR DATE OF INFORMATION 1949  
 SUBJECT Medical - Diisopropyl fluorophosphate  
 HOW PUBLISHED Bimonthly periodical DATE DIST. 26 Jan 1950  
 WHERE PUBLISHED Moscow NO. OF PAGES 4  
 DATE PUBLISHED Mar/Apr 1949 SUPPLEMENT TO REPORT NO.  
 LANGUAGE Russian

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SOURCE Vestnik Oftalmologii, Vol XXVIII, No 2, 1949. (Information requested.)

DIISOPROPYL FLUOROPHOSPHATE IN THE TREATMENT OF GLAUCOMA

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Two years ago, Prof A. Ya. Samoylov published a report on a new myotic preparation known as diisopropyl fluorophosphate (DFP). This article presents the results of experiments conducted at the Eye Clinic, Academy of Medical Sciences USSR.

DFP belongs to the class of alkaloids of the choline series, acts on the cholinesterase, and is a mediator of nerve activity. At the same time it causes spasms of the nonstriated muscles, desiccates vessels, and decreases the flow of body fluids. It is very active; data shows that it is five times more active than ecerine, produces prolonged myosis in man and animals, and causes spasm of accommodation and pains in the ciliary tissues. Some of the manifestations are headaches, and prolonged infection of the conjunctiva. A DFP solution with a vegetable-oil base is more stable and less toxic than a solution with an aqueous base.

Experiments were conducted on 24 patients (30 eyes): 14 eyes with chronic glaucoma, seven with decompensation, three with acute paroxysms, and five with absolute glaucoma. Treatment began with two drops of 0.1-percent solution of DFP in a vaseline base, but due to many undesirable effects it was changed to an 0.05-percent solution with simultaneous padding of the eye.

We attempted to determine the quality of the DFP and its place in the general classification of myotic substances by simultaneous complex tests on the dynamics of intraocular pressure, variations in the diameter of the pupil, and size of the blind spot. It was possible to conduct campimetric studies on only 12 of the eyes. It was impossible in the other cases due to the presence of atrophic scotoma, acute or chronic glaucoma.

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Use of the above concentration (0.05 percent) of DFP produced very significant results. After only one hour, in scotoma patients, there was a noticeable vertical adjustment from 52 degrees to 21 degrees. The size of the scotoma remained stable for the first 4 days (24-hour periods), but there was a slight, almost imperceptible change (average 21 to 32 degrees). There was a sudden jump to 38 degrees on the fifth day, while on the sixth day the scotoma decreased to the original size of the edema. In some of the cases this decrease was not observed until the eighth day. All of the data shows that where the average ophthalmotonus was 41 millimeters of mercury it fell after a period of one or 2 hours to 23 millimeters of mercury with a tendency toward still further decrease (down to 20 millimeters of mercury) during the next 2 days. After the third day there was again a gradual rise which ended after the seventh or eighth day.

The intraocular pressure remained unchanged after padding of the eye subsequent to administration of an 0.05-percent solution of DFP (without any other myotics) for a period of 4 days. In isolated cases it was possible to observe considerable variations in the ophthalmotonus (a noticeable decrease) 2 hours after the observations were begun: in one case from 4  $\sqrt{\text{sic}}$  to 14 millimeters of mercury and in the other case from 50 to 10 millimeters of mercury. Myosis was first observed 10 to 20 minutes after padding of the eye, the maximum was attained after 2 or 3 hours, and this condition remained stable on the average for 5 to 6 days. The diameter of the pupil decreased on the average by 1.5 to 2.5 millimeters, where the average original diameter was 3.0 to 3.5 millimeters. A weak photoreaction was observed on the second or third day after the tests with a peep-hole light. This reaction was not observed until after the third or fourth day when utilizing conventional light. Instillation of an 0.05-percent solution of DFP in most cases accompanied a decreased or more clearly defined conjunctival infection, and this condition persisted for a period of 5 to 7 days, while the intensity of the coloring gradually increased toward the end of the first day and during the second day of observation. There was subjective desiccation from the third to fifth day, and in all cases there was some pain in the areas where desiccation was indicated. In some cases ciliary pains, accompanied by acute static contraction of the ciliary muscles, were indicated. Simultaneously there was a disappearance of the iridescent rings and opacity, while in some cases there was a sharpening of the sense of vision.

One patient, a 63-year-old woman, an ambulatory case, was admitted with possible glaucoma of the left eye. The anterior chamber had contracted and the pupil was swollen to 5.5 millimeters. Intraocular pressure was 44 millimeters of mercury. Vision was 0.08, with correction plus 4.0 diopters it was 0.1. After simultaneous padding subsequent to treatment with 0.05-percent solution of DFP, which lowered the intraocular pressure to 20 millimeters of mercury after 30 to 40 minutes, the eyes became glassy while vision after plus 3.0-diopter correction was 0.7. Diameter of the pupil was 2 millimeters. For the first 2 days the intraocular pressure varied between 16 and 20 millimeters of mercury, and the patient did not receive any supplementary myotics in the dispensary. Subsequent to this treatment she was required to use one-percent pilocarpine solution two to four times daily. Ophthalmotonus was 18 to 22 millimeters of mercury. The patient was released 10 days after admittance to the hospital, without an operation.

Another patient, a 68-year-old woman, had chronic glaucoma of the right eye. Vision was 0.8, with correction plus 0.75 diopter it was 1.0. Intraocular pressure was 36 millimeters of mercury. Scotoma was 34 degrees, and after instillation of a one-percent solution of pilocarpine it was 27 degrees. Instillation of a one-percent solution of pilocarpine three times daily did not produce any results, and the intraocular pressure remained stable at 45 to 33 millimeters of mercury. A single application of an 0.05-percent solution of DFP and padding of the eye produced a very sharp drop in the

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ophthalmotonus -- 12 to 14 millimeters of mercury after 4 days. The patient was released without surgery. Satisfactory results were also obtained in the case of a 57-year-old man who had absolute glaucoma in the right eye and chronic glaucoma in the left eye. This patient was also released without surgery.

An attempt was made to show the medical world some of the indications as to when to use and when not to use DFP. As a result, simultaneous tests were conducted on the above-mentioned patients, but other myotic agents were used. No extra tests were conducted on those suffering from acute decompensation and absolute glaucoma. Among the other agents used were a 10-percent solution of furamon, a one-percent solution of carbocholine, and a one-percent solution of pilocarpine. Figures 1 and 2 [appended] show the results which were observed after a single application of an 0.05-percent solution of DFP, a 10-percent solution of furamon, one-percent solution of carbocholine, and a one-percent solution of pilocarpine. The graphs show without any doubt that DFP is by far the most effective agent. Tests showed that instillation of one-percent pilocarpine and 0.25-percent prozerine solutions produced only temporary relief, while a single application of an 0.05-percent solution of DFP produced good results which remained stable for a period of 4 to 5 days.

It is safe to say that DFP has an intensive and stable effect on retinitis and ophthalmotonus. All the other agents produced pupillomotor and hypotensive effects, and lowered the intraocular pressure from 36 to 23 millimeters of mercury.

In scotoma cases, furamon appeared to have the least dehydrative effect against retinitis. Scotoma was changed on the average from 53 to 45 degrees with furamon, while it dropped from 52 to 25 degrees after carbocholine treatment and from 58 to 30 degrees after pilocarpine treatment.

Consequently, as a result of experimental tests it is possible to recommend DFP as the best myotic agent in all cases where other myotics appear ineffective (acute glaucoma) particularly in cases of decompensated or subcompensated forms of glaucoma. However, it is advisable that DFP be administered by a competent doctor because in the hands of the uneducated layman more harm than good may result. The doctor is the only one qualified to determine why the first administration of DFP is ineffective, and to recommend some other form of therapy.

[Appended figures follow.]

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Figure 1. Action of Myotic Substances in the Tonus of Glaucomatous Eyes

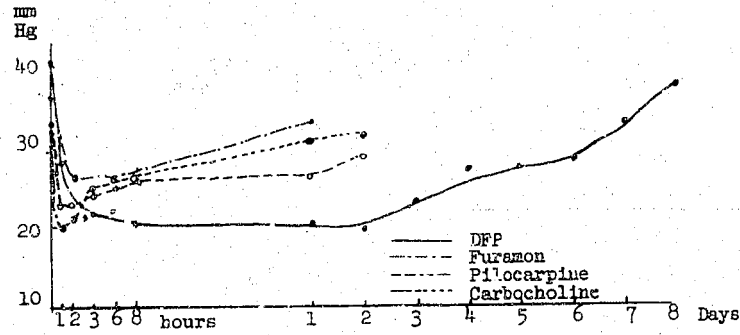
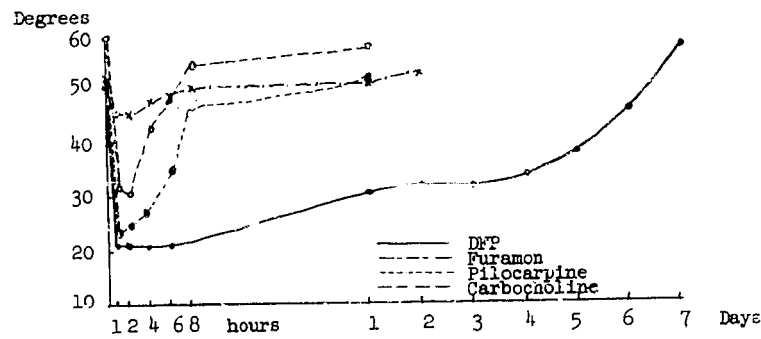


Figure 2. Action of Myotic Substances on Glaucomatous Scotoma



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