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Cyclopentolate in treatment of sarin miosis

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Summary

1. Six young male volunteers were exposed to sarin vapour (isopropyl methyl phosphonofluoridate) at a concentration of 0·5 mg/m³ for 30 min (concentration time (Ct) 15 (mg min)/m³).

2. The resulting clinical syndrome was treated by instilling 0·06 ml of a 1% solution of cyclopentolate into the conjunctival sac.

3. Visual acuity, retinoscopy, objective and subjective refraction and pupil sizes were noted before the trial, after exposure to sarin and after treatment with cyclopentolate.

4. No appreciable difference was demonstrated between the control objective retinoscopy values and those obtained after cyclopentolate treatment of the clinical syndrome induced by sarin. Reduced near visual acuity was observed in some subjects treated with cyclopentolate as compared with acuity after exposure to sarin alone, considered to be due to the partial cycloplegia produced by treatment. Visual acuity after exposure to sarin alone was improved in some instances by the miosis produced.

5. It is suggested that unless full dark adaptation is a consideration, treatment of the ophthalmic condition resulting from exposure to this dosage of sarin should be reserved for those experiencing distressing ocular symptoms.

Introduction

Organophosphorus anticholinesterase compounds are widely used as pesticides and might be used in war. Typical effects of such compounds on the eye are described by Aldridge, Davson, Dunphy & Uhde (1947), using the vapour of di-isopropyl fluorophosphate and by Stewart, Madhill & Dyer (1968) using sarin (isopropyl methyl phosphonofluoridate). These agents produce marked miosis due to the action of accumulated acetylcholine on the sphincter pupillae, which in turn may cause difficulty in adapting to low levels of illumination. Effects upon accommodation also occur, with a moving in towards the subject of the near point of accommodation, which may be accompanied by a referred frontal headache, usually attributed to increased tension in the ciliary muscle, or even ' ciliary spasm '.

Mydriatics have previously been used with the object of countering the effects of miosis on visual function and to obtain symptomatic relief from this ophthalmic syndrome. The problem of such therapy is that the relief of ocular discomfort is achieved at the expense of producing partial cycloplegia.

In view of the lack of information as to the value of 1% cyclopentolate eye

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drops in the therapy of this syndrome, a small group of volunteers were exposed to sarin, then treated with this preparation.

Methods

The subjects were young male volunteers (mean age 20·3 years) who had been shown to be fit by a full medical and ophthalmological examination.

They were exposed to a sarin vapour concentration of 0·5 mg/m^3 for 30 min (i.e. a concentration time (Ct) of 15 (mg min)/m^3) in a 100 m^3 chamber in which vapour concentration was kept even by constant air movement. This Ct is well below the dose which would induce signs of systemic poisoning.

Ninety minutes after exposure to sarin each volunteer had 0·06 ml of 1% cyclopentolate hydrochloride (Mydrilate) instilled into each eye. Ophthalmic examination was made 60 min and 4·5 h after sarin exposure and also 1 h after cyclopentolate instillation.

At each examination, subjective sensations were noted and the following ophthalmic measurements were made:

(a) Visual acuity at 6 m and at 3 cm, with and without spectacle correction.

(b) Objective retinoscopy, where possible.

(c) A subjective test of refractive errors.

(d) Pupil size, measured with a hand-held pupillometer and confirmed soon afterwards by electronic flash photography, after 30 min dark adaptation.

(e) Direct ophthalmoscopy.

(f) Clinical confrontation method of assessment of peripheral visual fields.

Results

Subjective sensations, reported after exposure to sarin alone, included (subject A) a feeling that distance vision was blurred, although in fact his visual acuity was objectively improved. Two men complained of 'peripheral dimness' and one subject had discomfort on looking at close objects. Two volunteers had no complaints.

Control measurements prior to the trial demonstrated that four men (B, D. E and F) had unaided visual acuity in each eye of 6/5 (Snellen). Subject A, who was myopic, could obtain 6/36 unaided and 6/5 in each eye with −2·00 spherical (sph) (right) and −2·25 sph (left). Subject C with an astigmatic correction of $-0{\cdot}50_{180^\circ}$ for each eye achieved 6/5.

After exposure to sarin, subject A unaided had improved visual acuity of 6/12 in the right and 6/24 in the left eye. All other volunteers retained visual acuity of 6/5 in each eye unaided (Table 1).

There was no change of their recorded visual acuity at 6 metres after instillation of cyclopentolate, with the exception of the myopic subject A, who was now worse, with covisual acuity of 6/60 in each eye, while still retaining correctable acuity of 6/5.

The pre-exposure near visual acuity was J1 (Jaeger) in all subjects and was not affected by exposure to this concentration of sarin. Instillation of cyclopentolate

TABLE 1. *Visual acuity before and after exposure to sarin vapour and after treatment with cyclopentolate*

	Control		After sarin		After cyclopentolate	
Subject	Right	Left	Right	Left	Right	Left
A	−2·00	−2·25	−1·75	−1·75	−2·25	−2·25
B	Nil	Nil	Nil	Nil	Nil	Nil
C	−0·50 180°	−0·50 180°	Nil	Nil	Nil	−0·50 180°
D	Nil	Nil	Nil	Nil	−0·50 180°	−0·50 180°
E	Nil	Nil	Nil	Nil	Nil	Nil
F	Nil	Nil	Nil	Nil	Nil	Nil

Value of lenses in dioptres subjectively determined to enable subjects to read 6/5 Snellen.

TABLE 2. *Visual acuity before and after exposure to sarin vapour and after treatment with cyclopentolate*

Subject	Right	Left
A	Nil	Nil
B	+1·00	+0·50
C	Nil	Nil
D	+1·25	+1·25
E	+0·75	+0·75
F	+1·50	+1·00

Value of lenses in dioptres subjectively determined to enable subjects to read J1 Jaeger.

drops reduced near visual acuity in the right and left eyes respectively of subjects B to J5, J6; D to J6, J6; E and F to J8, J8 and J10, J10. A spherical spectacle reading addition (mean value +0·67 dioptres, range +0·50 sph to +1·25 sph) restored visual acuity of J1, J1 (Table 2).

The mean changes in objective retinoscopy values, after exposure to sarin followed by treatment with cyclopentolate, compared with control readings were:

Right (vertically) +0·04 D, range −0·50 to +0·75
(horizontally) +0·04 D, range −0·50 to +0·75
Left (vertically) −0·04 D, range −0·50 to +0·50
(horizontally) −0·33 D, range −0·75 to +0·50

No reliable objective retinoscopy was possible with the marked miosis produced by sarin. Pupil areas measured as areas from the photographs were decreased from a mean control value of 47·1 mm^2 to a mean of 1·8 mm^2 after sarin exposure and increased after treatment with cyclopentolate to a mean of 14 mm^2.

No changes were seen in the appearance of the fundus and no difference in the visual fields was demonstrated clinically.

Discussion

This trial indicates that subjective reports may not be a valid indication of the effect of an organophosphorus compound on visual function. There was no appreciable difference found between the control objective retinoscopy values and those obtained after treatment of the post-sarin exposure syndrome with 1% cyclopentolate.

The physiological tone of the ciliary muscle, which when relaxed with a cycloplegic drug, represents the subject's latent hypermetropia, normally amounts to about 1 dioptre. It might be expected that about +0·05 D of latent hypermetropia would be revealed by the instillation of 1% cyclopentolate drops. At the time of

examination, the relaxation of the ciliary muscle induced by this dose of cyclopentolate was opposed to an almost equal extent by the prior action of sarin. It was found nevertheless that a mean addition of +0·67 D was needed, after exposure to sarin and treatment with cyclopentolate, to allow the subjects to read J1 at 33 cms. The mean value for the accommodative power exerted by the eyes in this group was +2·30 D, while the mean age of the subjects was 20·3 years, at which age the availability of accommodation should be 7–10 D (Duke-Elder, 1969). It appears that when 0·06 ml of 1% cyclopentolate is instilled into the conjunctival sac of an eye previously exposed to this dosage of sarin, there is a relaxation of the pupil (to a mean diameter of 14 mm^2) and a degree of cycloplegia produced sufficient to require a subject aged about 20 years to wear a reading addition in order to be able to see small print. In contrast, with extreme miosis caused by sarin, the moderate myope had improved visual acuity at distance, and the acuity of 3 other subjects for distant vision was a little improved; an effect no doubt due to the small pupil acting as a 'pin-hole' in reducing aberration. Despite some discomfort in focussing on near objects after exposure to sarin, none of the men were prevented from reading J1 type at 33 cm.

Although it is recognized that the distressing ocular symptoms produced by sarin were relieved by 1% cyclopentolate eye drops, the relaxation of the iris was not complete after this treatment. There may be several notable consequences of the effects of sarin on eyes which are not treated.

Severe miosis is considered by Stewart *et al.* (1968) to affect the performance of tasks in dim light. Rubin & Goldberg (1957) and Rubin, Krop & Goldberg (1957) found a rise of the scotopic threshold after dosages (Ct's) of sarin smaller than those used in this trial, which was allegedly due to a systemic effect on the central nervous system. Confirmation of this view was suggested (Rubin & Goldberg, 1958) by the observation that the effect on the scotopic threshold was reduced by the injection of atropine sulphate but not by the injection of atropine methyl nitrate. The peripheral action of a mydriatic such as cyclopentolate clearly cannot affect any central action of sarin, but those local effects consequent on miosis and 'ciliary irritation' or 'ciliary spasm' may be improved though at the expense of interference with visual acuity due to relative cycloplegia.

It would appear from this small trial that, unless ocular symptoms are disabling or there is a requirement for an individual to work under conditions of low illumination, where the dilatation of the pupil may increase the degree of dark adaptation, treatment of the ophthalmic syndrome resulting from exposure to an organophosphorus anticholinesterase vapour in doses comparable to that used in this trial should not include the use of a local mydriatic drug such as cyclopentolate eye drops.

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