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LETTER TO THE EDITOR

DESIRED PUPILLARY DILATION ACHIEVED WITH A SMALLER DROP VOLUME OF PHENYLEPHRINE IN RABBITS

Sir,

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The tear film of the eye normally contains 7-10 µl of fluid (1, 2). When some eye drop is instilled into the eye, the tear film can momentarily hold as much as 30 µl of the fluid. The remaining part of the instilled solution is drained into the nasolacrimal duct where it is absorbed, leading to systemic side effects (1-4). The systemic toxicity increases with the increase in instilled fluid volume (1, 2).

It has also been reported that as the volume of the drug solution instilled into the eye is decreased, the fraction of the drug absorbed intraocularly is increased (5). Various systemic side effects have been reported when phenylephrine was used to produce pupillary dilation for fundus examination (6-8) and the minimum drop volume used for that was 50 µl. With smaller drop volume the systemic side effects may be decreased and the therapeutic responce enhanced (1, 2, 5). Therefore, the present study was planned to investigate the pupillary dilation by different drop volumes of phenylephrine hydrochloride in albino rabbits.

Ten healthy male albino rabbits (1.5-2.5 kg) were kept in the departmental animal house for 30 days prior to the study for acclimitization. They had free access to food and water. The study was randomized, cross over. A single administration of different drop volumes (10 µl, 20 µl, 40 µl, and 80 µl) of phenylephrine hydrochloride 10% was done in both the eyes of 10 rabbits on different occasions with a wash out period of 10 days between the two instillations. The drop volumes were delivered by the micropipette which had been checked for accuracy by weighing the drops in a balance. The pupil diameter was measured with a Pupil diameter ruler (with 0.5 mm graduations), under standard illumination, before drug administration to see the basal values and at 15 min, 30 min, 45 min, 1.0 hr, 1.5 hr, 2.0 hr, 2.5 hr, 3.0 hr, 4.0 hr, and 6.0 hr after drug instillation. To rule out the effect of circadian variation on pupil diameter a control group was also kept and distilled water instillation was done in that. The observer was masked to the treatment.

The change in the pupil diameter from the baseline was measured for both eyes and mean of these two readings was calculated for each rabbit. The statistical analysis was done by 't' test (paired) and $P<0.05$ was considered statistically significant.

There was no difference in the baseline values of the pupil diameter in all the groups. The pupil diameter was 5.15±0.08 mm in 10 µl, 5.15±0.10 mm in 20 µl, 5.15±0.18 mm in 40 µl, and 5.10±0.16 mm in 80 µl groups. Pupil dilation started after instillation of phenylephrine drop volumes and this continued for 4.0 hr. The maximumdilation was achieved at 1.5 hr (Table I) and it was significantly more in 10 µl and 20 µl groups as compared to 40 µl group ($P<0.05$, $P<0.05$ respectively). 10 µl drop volume produced a significantly more pupillary dilation than 40 µl from 30 min to 6.0 hr, though the dose in the former was 4 times less (Table I). 10 µl drop volume also had a tendency to produce a greater pupillary dilation than 80 µl drop volume though the dose in the latter was 8 times the former (Table I).

It has also been reported that 15 µl drops size

TABLE I : Change in pupil diameter from baseline value for different drop volumes (10 µl 20 µl, 40 µl and 80 µl) of phenylephrine hydrochloride 10% eye drop, at different intervals. Data are mean ±SEM of 10 rabbits. The change in diameter is in mm.

Time	*10 µl*	*20 ul*	*40 µl*	*80 µl*
15 min	1.25±0.14	1.95±0.29^{b***}	0.95±0.31	1.65±0.27
30 min	2.40±0.11**	3.05±0.12****	1.85±0.18	2.75±0.27
45 min	3.40±0.17****	3.30±0.22***	2.35±0.13	3.10±0.24
1.0 hr	3.85±0.21**	3.35±0.20	3.15±0.19	3.50±0.22
1.5 hr	3.95±0.19**	3.80±0.18**	3.15±0.19	3.80±0.23
2.0 hr	3.65±0.26*	3.50±0.14**	2.95±0.19	3.40±0.30
2.5 hr	2.85±0.32*	2.50±0.20*	2.00±0.16	2.75±0.24
3.0 hr	2.50±0.26^{a***}	1.75±0.21	1.55±0.19	1.55±0.22
4.0 hr	2.10±0.20^{b***}	1.35±0.10^{b}	1.25±0.13	0.70±0.28
6.0 hr	1.45±018^{b**}	0.60±0.15^{a}	0.65±0.07^{b}	0.00±0.00

*P< 0.05,**P<0.02, ***P<0.01, ****P< 0.001 vs 40 µl at respective interval.
^{a}P<0.01, ^{b}P<0.001 vs 80 µl at respective interval.

of clonidine hydrochloride reduced intra-ocular pressure similar to that produced by 70 µl without producing any systemic hypotension (9). The greater pupillary dilation with 10 µl drop volume of phenylephrine as compared to 40 µl and 80 µl drop volumes, in our study could be due to better intra-ocular penetration (5) and decreased drainage into the nasolacrimal duct (1, 2).

We conclude that to achieve a desired pupillary dilation the drop volume of the phenylephrine should be 10 µl. However, further studies are required to substantiate our findings.

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