Phenylephrine 10% mydriatic effect: comparison between self instillation of eye drop in open eyes and spray in closed eyes

Efeito midriático da fenilefrina a 10% na comparação entre a autoinstilação de gota em olhos abertos e a vaporização em olhos fechados

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ABSTRACT

Objective: To compare the effectiveness of phenylephrine 10% applied by a spray onto the eye closed over drop instillation onto an open eye on patients who will perform ophthalmoscopy and assess the level of difficulty and technical adequacy of the administration methods. Methods: The study was a clinical trial, controlled, randomized and paired, performed in 2014, involving 100 eyes of 50 patients in the Polyclinic Ronaldo Gazolla - RJ, with no ocular or systemic diseases that compromised the pupillary dilation. Patients underwent 10% phenylephrine eye drop instillation onto one open eye and spray application onto the other eye, which was closed. Pupillary diameter was measured before application and 10, 20, 30 minutes after. The process of instillation or vaporization was observed for its technical correctness by one of the authors. A questionnaire was asked to the patient about the difficulty of both methods after topical administration.

Results: The average mydriasis difference between the eye groups assessed at a given time was at most 0.3 mm, which was not clinically or statistically significant (ANOVA: F = 1.97 and p = 0.163609). However, over time, the difference between the average pupil diameter before application and after 30 minutes was 1.15 mm to vaporized eyes and 1.58 mm in eyes instilled with drops (ANOVA: F = 129.22 and p ≤ 0.0001). Sixty per cent of patients touched the tip of the eye drop bottle onto the eye, while 12% touched the tip of the vaporizer with their fingers (p <0.000001). Seventy two percent (72%) considered the drops instillation easy or very easy, while 62% considered vaporization in a closed eye easy or very easy (p = 0.238).

Conclusion: The instillation of drops phenylephrine 10% in open eyes and the vaporization onto closed eyes showed similar clinical efficacy. Vaporization was safer and a little more difficult than instillation, despite the patients being experienced for instilling drops and inexperienced to vaporize the medication in a closed eye.

Keywords: Administration, topical; Ophthalmic solutions/administration & dosage; Phenylephrine; Eye/drug effects
spraying is a therapeutic route often used in medicine for the prevention and treatment of various diseases. Antihistamine medications, steroids, mast cell membrane stabilizers, anticholinergics, among others are released by nasal spray in order to treat allergies or congestion due to rhinitis or sinusitis.(12) Agents for sun photoprotection or temporary skin substitutes that form impermeable dressings may also be applied by spraying on the skin.(14)

In ophthalmology, there are lubricating sprays commercially available in several countries, for application both with eyes open or closed. There are few studies demonstrating the efficacy of medicated solutions when applied by spraying in the eye. The droplets of the ophthalmic solution are placed under pressure between the eyelashes and when the patient opens the eyes, they blend into the tear chamber.(5)

A recent study found that the fluorescein released by ocular vaporization reaches concentrations in the anterior chamber, but in a lower amount than would be reached by the instillation of drops.(5) Portes et al. reported in 2012 that the mydriasis produced by drops of tropicamide 1% was similar to that from spraying the same substance into the eyes. However, the amount of tropicamide released at each spray was twice that found in instilled drops of 1% solution. The diameter of the pupil was measured before the study and was requested to look forward. The lower head backwards, extending the neck and looking up. The lower

**METHODS**

The survey was carried out from September to November 2014 at the Ophthalmology service of Policlínica Ronaldo Gazolla, Universidade Estácio de Sá, Campus Arcos da Lapa – RJ. A controlled, randomized clinical trial was conducted in a series of 50 patients to which phenylephrine 10% was instilled as drops in one eye, while the other was sprayed in the eyelid with the eye closed. Patients were invited to participate in the study at their arrival for the ophthalmoscopy exam in the ophthalmology ambulatory at clinic of Policlínica Ronaldo Gazolla on Thursdays.

The eyes were chosen for the administration of eye drops or spray according to a pseudorandom number Excel table prior to application. The pupillary diameter was measured before the instillation and 190, 20 and 30 minutes after. The eyes with a manual pupillometer “PD-meter”.

A bottle of eye drop of a mydriatic oculcar solution of phenylephrine 10% and a vial coupled to a vaporizer were used. All patients had no ocular or systemic diseases that could affect the pupillary diameter. Exclusion criteria:

- Anisocoria

**RESULTS**

The instillation of drops in the eye produced a mydriatic effect that was similar to that obtained by spraying, the difference between the mydriasis produced by the two procedures was not statistically significant (ANOVA: F = 1.97 and p = 0.163609). However, the amount of tropicamide released at each spray was twice that found in instilled drops of 1% solution. The diameter of the pupil was measured before the study and was requested to look forward. The lower
eyelid was slightly drawn to expose the inferior conjunctival sac fundus. Then 01 drop of eye drops was self-instilled at the inferior sac fundus.

The spray was made in the eye where the eye drop was not applied, as follows: the patient was requested to remain seated, looking forward, and then to position the bottle so that the hole in the sprayer was in front of the eyelashes approximately 2 cm away from the eye of the patient, and the drug was sprayed only once with the lids closed. This whole process was done with dexterity and speed. The patients were requested to keep the sprayed eye closed for up to 10 seconds after instillation of the drop or spray. The bottle used was plastic, 7 cm high and 2 cm wide, with a volume of 7 ml. Each spray released an averaged 0.1 ml of ophthalmic solution, which corresponded to approximately 2 drops of eye drops in a circular dispersion area of 5.5 cm in diameter (measures taken on filter paper). This bottle vial was not available for commercial use with medications, so it was sterilized in ethylene oxide prior to the study, and then phenylephrine 10% was introduced into this bottle in sterile form.

After 30 minutes of the last pupillary diameter measurement, if the patient complained of ocular discomfort he underwent biomicroscopic examination to discard any corneal alteration, and the eyelids were also ectoscopically examined to rule out any sensitivity in the area of dispersion of the sprayer.

The instillation process or spray was followed by one of the authors.

After the process, the patient answered pre-formulated questions about the practicality of both methods. Administration-related aspects were observed and classified by the authors (Annex 1).

The database was created using the program Epi info 7. The test of “Wilcoxon signed rank” was applied to questions 4 and 5 of the questionnaire. Student’s t-test for 2 paired samples was applied to questions 11 and 15, and the binomial test for two proportions of questions 8, 9, 10, 12, 13, 14. The ANOVA test for two factors with replicated measurements compared the results related aspects were observed and classified by the authors.

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with tropicamide 1%. Dilation by tropicamide tends to be greater than that caused by phenylephrine 10%. However, it is greater when the two medications are used together sequentially, resulting in synergistic effect.\(^{(7,8)}\)

Van Rooij in 2015 compared penetration in the anterior chamber of fluorescein instilled by eye drops on the ocular surface in relation to the spray of the same substance with the eye open. The amount of active principle found in the anterior chamber was about half of the observed after instillation of eyedrops. In this study, the values of the mydriasis found were too close between the groups, but the amount of phenylephrine sprayed amounted was equivalent to 2 drops of phenylephrine instilled. The fact that the spray was done about 2 cm from the eyelash also contributed to the good absorption of the mydriatic.\(^{(6)}\)

Most patients instilled drops erroneously, touching the tip of the bottle in eye tissues and around the eyes in order to facilitate the topical administration, stabilizing the product bottle. The touch promotes contamination. The patients did not report difficulties to keep the bottle stable at a distance while spraying. Thus, there was no touch between the sprayer and the eye tissues.

Although the difference perceived between the level of difficulty in spraying in relation to that of drop instillation was small and not statistically significant; there were many more difficulties reported for spray than for droplet instillation. All patients had experience in instilling eye drops and had no experience in spraying their eyes. The training effect in the use of the sprayer could make it easier to use this route of administration in relation to instillation of eyedrops.

### ANNEX 1

**Questionnaire - Perception of ocular self-instillation of drugs:**
Comparison between drops applied with and without face support device

1. Number of medical report: ______________

2. Initial letters of the name: _____________

3. Age: __________

4. Regarding the instillation of eye drops, you consider it:
   1) Very easy ( )
   2) Easy ( )
   3) Neither easy nor difficult ( )
   4) Difficult ( )
   5) Very difficult ( )

5. In relation to spraying in closed eye, you consider it:
   1) Very easy ( )
   2) Easy ( )
   3) Neither easy nor difficult ( )
   4) Difficult ( )
   5) Very difficult ( )

6. In relation to topical administration of eye drops, did you have any difficulties? ( ) Yes ( ) No.
   If so, which ones? ________________________________

7. In relation to spraying in closed eye, did you have any difficulty? ( ) Yes ( ) No.
   If so, which ones? ________________________________
   
   **Note:**
   In relation to the eye drop:

8. Did the drop instilled fall in the eye? ( ) Yes ( ) No.

9. Was it necessary to repeat instillation so that it fell in the eye? ( ) Yes ( ) No.

10. Did the tip of the bottle touch the eyelashes or the eyelid or the eye? ( ) Yes ( ) No.

11. How many drops were applied? _________
    In relation to spraying in closed eye:

12. Did the application reach the palpebral margin? ( ) Yes ( ) No.

13. Was it necessary to repeat? ( ) Yes ( ) No.

14. Did the tip of the sprayer touch your fingers? ( ) Yes ( ) No.

15. How many applications were made? _________
REFERENCES


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