

## Thirty Years Use of 2% Ibopamine Eye Drops, A D-1 Dopaminergic and Alpha Adrenergic Drug

Italo Giuffre\*

Department of Ophthalmology, Catholic University of Roma, Italy

\*Corresponding Author: Italo Giuffre, Department of Ophthalmology, Catholic University of Roma, Italy.

Received: January 30, 2016; Published: April 5, 2016

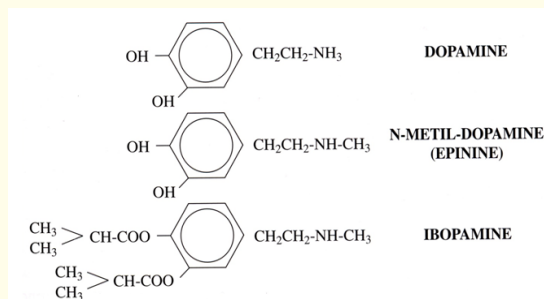
### Abstract

Ibopamine (3,4 di-isobutyryrylester of N-metildopamine) is a D1-dopaminergic and  $\alpha$ -adrenergic agonist. It has a not-cycloplegic mydriatic activity. Its peak of action is at 45 minutes after instillation in the conjunctival sac. Its action lasts after about 360 minutes. Its D1-dopaminergic stimulation increases the aqueous humor production and it is a provocative test for evaluating the function of aqueous humor outflow structures also in relatives of glaucomatous patients. It is also useful to treat ocular hypotension. Its main use is in every ophthalmological assessment, either diagnostic or preoperative, where the cycloplegia is not advised. It is useful for the safe mydriasis of patients treated with  $\alpha$ -1 adrenergic receptor antagonists.

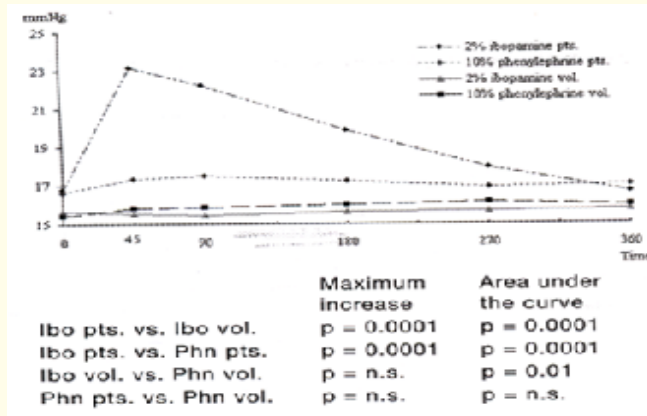
**Keywords:** Cycloplegia; D1- And A-Adrenergic Agonist; Ibopamine Eye Drops; Safe Mydriasis

### Introduction

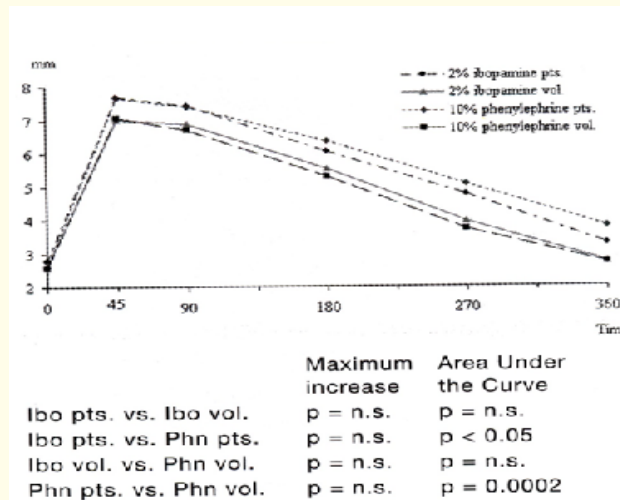
Ibopamine (3,4 di-isobutyryrylester of N-metildopamine) is a D1-dopaminergic and  $\alpha$ -adrenergic agonist [1]. This drug has a not-cycloplegic mydriatic activity. When administered in to conjunctival sac, ibopamine is hydrolyzed to epinine by esterases present in the aqueous humor (Figure 1). Its half-life in the aqueous humor is about 1.9 minutes. The epinine formation causes the mydriatic effect. Its peak of action is at 45 minutes after instillation in the conjunctival sac [2-5]. Its action lasts about 360 minutes (Figures 2-3, Table I) [6-13]. Some Authors stressed that ibopamine-positive subjects have 8 times more risk of developing glaucoma compared to ibopamine-negative subjects [12]. Indeed, ibopamine-positive test subjects with glaucomatous optic disc have 32.4 times higher risk of having glaucoma than those with normal optic disc [12]. Due to its D1-dopaminergic stimulation, it increases aqueous humour production and is a provocative test for evaluating the function of aqueous humor outflow structures in about 40% of relatives of glaucomatous patients [14]. It is very useful to treat ocular hypotension [15-18]. Its main clinical use is in patient's assessment where the cycloplegia is not advised. Compared to all the other mydriatic drugs commercially available (Table I, Figure 3), mydriasis by Ibopamine is safe and reversible by dapiprazole [19]. It is mainly useful in patients who want to continue their far and near activity after the ophthalmological assessment [20]. It is useful in patients with occludable angles and to obtain a maximal mydriasis before any diagnostical and surgical procedures.



**Figure 1:** Chemical formulas of dopamine, epinine and ibopamine [5].



**Figure 2:** The effect of 2% ibopamine and 10% phenylephrine eye drops on the IOP in glaucomatous patients compared to healthy volunteers [6].



**Figure 3:** The mydriatic effect of 2% ibopamine and 10% phenylephrine eye drops in glaucomatous patients compared to healthy volunteers [6].

Drug	Peak	Through
Atropine	1-2 H	10-15 D
Omatropine	1 H	6-48 H
Cyclopentolate	30 M	12 H
Tropicamide	20 M	6 H
Ibopamine	45 M	6 H

**Table 1:** The peak and through features of the most important and widespread used mydriatic drugs in Ophthalmology. D: days; H: hours; M: minutes.

Mainly, before surgery, the use of ibopamine is advised in patients affected by: cardiovascular diseases, diabetes and pseudoexfoliative syndrome with and without glaucoma, hypo- a/or athalamic and hypotonus after vitreo-retinal surgery a/or long-standing uveitis, suspected glaucoma and to evaluate corticosteroid-responders before refractive surgery a/or intravitreal injections of corticosteroids, and patients under oral therapy by  $\alpha$ -blockers. In all these kinds of patients, the ibopamine provocative test may guarantee a safe mydriasis [19] and the possibility to identify the corticosteroid-responders before surgery. From the toxicological point of view, ibopamine is a safe drug and its mydriasis may be easily reversed by dapiprazole eye drops. The ibopamine test is performed by the instillation of the drug in the conjunctival sac twice with an interval of 5 minutes. The IOP is measured after exactly 45 minutes and the test is considered positive if the IOP increases at least 3 mmHg [1] but the IOP remains stable in healthy volunteers (Figure 2). It increases the IOP in 92% of glaucomatous patients and it has no toxic effect on the retinal ganglion cells, from the electrophysiological point of view [21]. It is useful in the pseudoexfoliative glaucoma [22]. It is also useful to detect steroid-responders before any procedures such as phaco emulsification of the cataract a/or refractive surgery. It becomes negative after successful trabeculectomy [23]. Due to A-scan echography, there are no changes of the refraction, anterior chamber depth and lens position [24,25]. About the preoperative mydriasis, 2% ibopamine eye drops is very useful before any surgical procedure, mostly in patients using  $\alpha$ -adrenergic receptor antagonist such as tamsulosin for benign prostatic hyperplasia. In this case, ibopamine may be responsible for a safe mydriasis to avoid the dangerous intraoperative floppy iris syndrome (IRIS) [26-34]. In case of hypotonus, after an excessive filtration post-trabeculectomy, vitreo-retinal surgery a/or long-lasting uveitis, maculopathy, optic disc oedema, choroidal detachment and phtysis bulbi may be observed. In this case, Virno and coworkers used ibopamine, associated to corticosteroids, even every 3 hours. They encountered an increase of about 3-4 mmHg in IOP after 2 months of medical therapy [35].

## Conclusions

This review article stresses the main pharmacological, toxicological and clinical features of ibopamine. This drug has its main use in ophthalmology in different fields: safe mydriasis of every patient without cycloplegia, provocative test in glaucoma suspects and offspring of glaucomatous patients, treatment of hypotony after vitreo-retinal surgery and long-lasting uveitis. During 30 years of its use, ibopamine proved to be an important tool in Ophthalmology without any clinical significant side-effects. The author advises future studies of the effect of this drug in occludable angles by the use of Pentacam Scheimpflug camera and OCT Visante. Indeed, in the future, it will be important to compare the predictive effect of ibopamine eye drops on the onset of glaucoma versus the molecular genetic testing of glaucomatous patients and their relatives as for sensibility and specificity.

## Bibliography

1. Virno M., *et al.* "Ibopamine: a new non-cycloplegic mydriatic". *Boll Ocul journal* 65 (1986): 833-845.
2. Virno M., *et al.* "Intraocular hypertensive effects of topically administered ibopamine in eyes with hydrodynamic disorders: provocative test for glaucoma". *Glaucoma* 12 (1990): 88-92.
3. Virno M., *et al.* "Dopamine, dopaminergic drugs and ocular hypertension". *International Council of Ophthalmology* 16.4-5 (1992): 349-353.
4. Boles Carenini B., *et al.* "Ibopamine: a new drug and its use as provocative test for the diagnosis of glaucoma". *New Trends in Ophthalmology* 7 (1992): 03-08.
5. Virno M., *et al.* "Ibopamine: D1-dopaminergic agonist in the diagnosis of glaucoma". *Journal of Glaucoma* 22.1 (2003): 5-9.
6. Giuffre' I., *et al.* "The effect of 2% ibopamine eye drops on the intraocular pressure and pupil motility of patients with open-angle glaucoma". *European Journal of Ophthalmology* 14.6 (2004): 508-513.
7. Giuffre' I. "Ibopamine stimulates  $\alpha$ -adrenergic receptors and D1-dopaminergic receptors in the eye". *Current Drug Therapy* 11.2 (2007): 127-132.

**Citation:** Italo Giuffre. "Thirty Years Use of 2% Ibopamine Eye Drops, a D-1 Dopaminergic and Alpha-Adrenergic Drug". *EC Ophthalmology* 3.3 (2016): 309-313.

8. Giuffre I. "A new alpha-adrenergic and D1-dopaminergic drug. Chapter 19 in: Ophthalmology – current clinical and research updates". Ed. Pinakin-Gunvant Intech (2014): 471-478.
9. McLaren JW, et al. "Effect of ibopamine on aqueous humor production in normotensive humans". *Investigative Ophthalmology & Visual Science* 44.11 (2003): 4853-4858.
10. Ullrich K, et al. "Ibopamine challenge test can be used to differentiate glaucoma suspects from glaucoma patients". *Clinical & Experimental Ophthalmology* 42.4 (2014): 342-346.
11. Landers J, et al. "Ibopamine challenge testing differentiates glaucoma suspect, stable glaucoma and progressive glaucoma cases". *Clinical & Experimental Ophthalmology* 43.9 (2015): 808-814.
12. Dominguez-Duenas F, et al. "Early glaucoma screening using the ibopamine provocative test". *Journal of Glaucoma* (2015).
13. Brogliatti B, et al. "Ibopamine test in healthy and glaucomatous eyes: tonometric and pupillographic study". *Acta Ophthalmologica* 78.232 (2000): 13-14.
14. Virno M, et al. "Ibopamine: D1-dopaminergic agonist in the diagnosis of glaucoma". *Journal of Glaucoma* 22.1 (2013): 5-9.
15. Ciappetta R, et al. "Use of ibopamine eyedrops in the treatment of ocular hypotony after glaucoma filtration surgery". *Ophthalmology* 76 (1996): 161-162.
16. Virno M, et al. "Topical ibopamine and corticosteroids in the treatment of post-surgical ocular hypotony". *International Ophthalmology* 20.1-2 (1997): 147-150.
17. Pivetti Pezzi P, et al. "Ibopamine treatment in chronic hypotony secondary to long-lasting uveitis. A case report". *European Journal of Ophthalmology* 10.4 (2000): 332-334.
18. Ugahary LC, et al. "Topical ibopamine in the treatment of chronic hypotony attributable to vitreoretinal surgery, uveitis, or penetrating trauma". *American Journal of Ophthalmology* 141.3 (2006): 571-573.
19. Mapstone R. "Safe mydriasis". *British Journal of Ophthalmology* 54 (1970): 690-692.
20. Giuffre' I, et al. "Evaluation of near- refraction after administration of ibopamine 2%". *Acta Ophthalmologica* 78.232 (2000): 11-12.
21. Giuffre' I, et al. "Pattern electroretinogram assessment during ibopamine test in ocular hypertension". *European Journal of Ophthalmology* 23.6 (2013): 819-822.
22. Taverniti L, et al. "The ibopamine test in patients affected by monolateral pseudoexfoliative glaucoma". *Acta Ophthalmologica* 232 (2000): 9-11.
23. Landers J, et al. "Ibopamine challenge testing becomes negative following successful trabeculectomy surgery". *Clinical & Experimental Ophthalmology* (2015).
24. Marchini G, et al. "Effects of 2% ibopamine on pupil, refraction, anterior segment anatomy and intraocular pressure". *Journal of Ocular Pharmacology and Therapeutics* 17.3 (2001): 215-223.
25. Marchini G, et al. "Comparative study of the effects of 2% ibopamine, 10% phenylephrine, and 1% tropicamide on the anterior segment". *Investigative Ophthalmology & Visual Science* 44.1 (2003): 281-289.

26. Chang DF and Campbell JR. "Intraoperative floppy iris syndrome associated with tamsulosin". *Journal of Cataract & Refractive Surgery* 53.7 (2005): 664-673.
27. Chang DF, et al. "Prospective multicenter evaluation of cataract surgery in patients taking tamsulosin (Flomax)". *Ophthalmology* 114.5 (2007): 957-964.
28. Chang DF, et al. "ASCRS Clinical Committee. Clinical experience with intraoperative floppy iris syndrome. Results of the 2008 ASCRS member survey". *Journal of Cataract & Refractive Surgery* 34.7 (2008): 1201-1209.
29. Chang DF. "Use of malyugin pupil expansion device for intraoperative floppy-iris syndrome: results in 30 consecutive cases". *Journal of Cataract & Refractive Surgery* 34.5 (2008): 835-841.
30. Chang DF, et al. "Prospective masked comparison of intraoperative floppy-iris syndrome severity with tamsulosin versus alfuzosin". *Ophthalmology* 121.4 (2014): 829-834.
31. Yuksel N, et al. "Anterior segment morphologic changes related to  $\alpha$ -1 adrenergic receptor antagonists use". *European Journal of Ophthalmology* 25.6 (2015): 512-515.
32. Rosen P. "Practices across the European Union to manage mydriasis and their related risks/benefits". *Eurotimes* (2016): 2-3.
33. Labetoulle M. "Efficacy and safety of the new intracameral combo-solution for mydriasis". *Eurotimes* (2016): 4-5.
34. Behndig A. "How intracameral administration of mydriatics may improve our cataract surgery". *Eurotimes* (2016): 6.
35. Virno M, et al. "Topical ibopamine and corticosteroids in the treatment of post-surgery ocular hypotony". *International Ophthalmology* 20.1-3 (1997): 147-150.

**Volume 3 Issue 3 April 2016**

**© All rights are reserved by Italo Giuffre.**