

# Latanoprost drops without added detergent in the treatment of glaucoma



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## HIGHLIGHTS

In the future, more attention should be paid to excipients in eye drops because they appear to have similar deleterious effects on corneal cells as preservatives.

## ABSTRACT

Chronic nature of both the disease and its therapy forces ophthalmologists to choose the treatment with the lowest potential for adverse reactions, which may be caused by the active substance, excipient or preservative. Detergents used in ophthalmic drops include a derivative of macroglycerol hydroxystearate-40 (MGHS-40), which in in vitro tests showed pro-inflammatory and cytotoxic properties towards corneal epithelial cells, and this effect increased with increasing concentration and time. The analyzed observational study showed that latanoprost without MGHS-40 effectively reduces intraocular pressure, and the factors encouraging ophthalmologists to choose this preparation were good local tolerance and a simple composition (without detergents, preservatives and antioxidants), improving compliance. In the observational study, 82.3% received latanoprost without MGHS-40, and almost 60% started antiglaucoma treatment with this preparation.

**Key words:** glaucoma drugs, excipient, glaucoma, cytotoxicity

## INTRODUCTION

According to the World Health Organization (WHO), open-angle glaucoma (OAG) is the second most common cause of vision loss in developed countries, and its incidence is increasing. The disease mainly affects patients over the age of 65, for whom compliance with medical recommendations is largely dependent on a simple prescription. Lowering intraocular pressure (IOP) is the only proven method of treating glaucoma and preventing irreversible damage to the optic nerve and retinal ganglion cells. First-line medications include prostaglandin analogues and prostamides, which are the most effective topical glaucoma medications, reducing IOP by 25–35% [1]. In addition, their widespread use in ophthalmic practice is due to their lack of significant overall side effects and ease of dosing. Their mechanism of action is to increase aqueous humor outflow through the choroidal-arterial pathway. Beta-blockers, which are also considered first-line medications, are slightly less effective in lowering IOP but have more systemic side effects. Ocular surface disease (OSD) is common in patients with glaucoma, increasing with patient age and glaucoma severity, and OSD appears to increase with longer treatment duration [2]. OSD in patients with glaucoma can take various forms, including superficial punctate keratitis, tear film instability, allergy, pseudophthalmos and dry eye. Studies show that in patients with a history of ocular surface disease, exacerbation of OSD leads to decreased mood, increased depression, and thus poor compliance and development of glaucoma [3]. The chronic nature of both the disease and its treatment leads ophthalmologists to choose the treatment with the least risk of inducing side effects, which may be caused by the drug, excipient or preservative [3]. Administering the drug directly into the conjunctival sac allows the therapeutic concentration of the therapeutic agents to reach the target site, but to achieve this, the drugs administered must have the right properties [4]. The most common additives in eye drops are preservatives to ensure sterility, substances to make the drops isotonic, solubility enhancers, buffering agents (e.g. EDTA), stabilizers and antioxidants [4].

The addition of preservatives to eye drops is associated with poorer compliance with medical advice. It is also important to monitor the content and tolerability of other additives, not just preservatives. Excipients used in eye drops include substances that increase the solubility of the active ingredient, namely detergents and antioxidants. Detergents used in eye drops include derivative of macroglycerol hydroxystearate-40 (MGHS-40), which has been shown to have pro-inflammatory and cytotoxic properties against corneal epithelial cells in *in vitro* studies, and this effect increased with increasing concentration and time [5]. MGHS-40 was observed to be responsible for the toxic effect of latanoprost, in which no preservatives were used. According to

some researchers, macrogol should not be used in ophthalmic preparations due to its high hygroscopicity and induction of pain in ocular tissues [6, 7]. Nowadays, physicians' awareness of local tolerability and the choice of simple formulations is increasing, as confirmed by studies [7–11].

According to the guidelines of the Polish Society of Ophthalmology for the diagnosis and treatment of glaucoma, similar considerations lead to the recommendation of the use of combination drugs [1]. This is associated with a lower rate of side effects due to ocular surface damage, better patient compliance and synergistic effects of the active ingredients.

**Discussion of the study** “Clinical and therapeutic profile of patients with glaucoma treated with latanoprost without macroglycerol-40 hydroxystearate (MGHS-40) – observational study” [7].

## METHODS

The study was conducted on a group of 7171 patients with IOP and ocular hypertension and 270 physicians from across Poland. This was a multicenter, observational, and non-interventional study designed to evaluate the clinical and therapeutic profile of patients in whom a physician made an independent decision to change therapy or to include a drug containing latanoprost without MGHS-40.

## RESULTS

In the group of 270 doctors who participated in the study, the main reasons for choosing latanoprost without MGHS-40 were good topical tolerability and simple formulation. Nearly 30% and more than 20%, respectively, chose the drug because of coexisting OSD in a glaucoma patient and because of intolerance to preservatives in eye drops. The most common reason for choosing latanoprost without MGHS-40 was to achieve an IOP reduction of 16–20%. The mean IOP was 22.6 mmHg and the most common comorbidity was hypertension. More than 70% of the patients had risk factors for OAG – positive family history and smoking. In almost ⅓ of the patients, latanoprost without MGHS-40 was the first antiglaucoma medication prescribed by the physician.

## CONCLUSIONS

The study showed that latanoprost without MGHS-40 is effective in lowering IOP, which is the ultimate goal of antiglaucoma treatment. Factors that led physicians to choose this formulation were good topical tolerability and a simple formulation (without detergents, preservatives and antioxidants), which improved compliance. Physicians in the study were eager to start anti-glaucoma treatment with

latanoprost without MGHS-40 as monotherapy in up to 60% of patients. Studies show that 6 months of treatment with latanoprost lowered IOP by 35% when the drug was administered in the evening and by 31% when the drug was administered in the morning, exceeding the expectations of the participating physicians [12].

## SUMMARY

The added preservative, excipient, or active ingredient of the antiglaucoma medication itself may cause or exacerbate OSD. Management of concomitant ocular surface disease includes avoidance of preservatives in antiglaucoma medications, preservative-free lubricating drops, topical cyclosporine, or complete elimination of topical medications by early laser trabeculoplasty or minimally invasive glaucoma surgery. Studies have shown that the good topical tolerability and simple formulation of the eye drops improve patient compliance, thereby increasing treatment efficacy.

Latanoprost, developed in 1996, is a well-studied, safe and, above all, effective antiglaucoma drug. As technology evolves, the goal is to improve the delivery of this drug to the conjunctival sac with fewer local side effects and to rationalize and justify the use of excipients. Developments in biotechnology now make it possible to use modern forms of drug delivery without unnecessary additives. It should be noted that the tolerability of the administered drug is influenced not only by ocular comorbidities but also by added excipients.

In the present study, the main factors influencing the physician's decision to use latanoprost without MGHS-40 were good topical tolerability and simple formulation, as well as sufficient IOP-lowering effect. In the future, more attention should be paid to the excipients in eye drops, as they appear to have similar deleterious effects on corneal cells as preservatives. Today, latanoprost formulations without MGHS-40 are available in single-dose packaging, also without preservatives and EDTA.

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**Ethics:**

The content presented in the article complies with the principles of the Helsinki Declaration, EU directives and harmonized requirements for biomedical journals.