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Latanoprost-Induced Skin Depigmentation

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Abstract

Introduction: Prostaglandin analogues (F2α) are often prescribed as first-line medical treatment for ocular hypertension or glaucoma. In this group of pharmacological agents, Latanoprost (0,005%) is the most commonly used and the first being indicated for paediatric patients. The main side effects are iris and periocular skin hyperpigmentation.

Case presentation: We report the third case described in the literature of periocular skin hypopigmentation, in a patient treated with topical 0.005% Latanoprost. A female child developed periocular skin hypopigmentation in the right eye after two months of Latanoprost 0.005% use. In our patient, Latanoprost was preservative free while the other 2 cases described in literature contained Latanoprost with preservatives. Three months after Latanoprost discontinuation, peri-ocular hypopigmentation showed partial reversal, and stayed stable to the most recent follow-up in December 2018 (two years post discontinuation).

Conclusion: Although periocular skin hyperpigmentation is a well-known side effect of Latanoprost, a paradoxical effect can occur with any drug and may be considered in patient's approach and treatment.

Keywords: Latanoprost; Prostaglandin Analogues; Periocular Pigmentation; Periocular Depigmentation,Glaucoma

Introduction

Prostaglandin analogues (F2α) are often prescribed as first-line medical treatment for ocular hypertension or glaucoma. In this group of pharmacological agents, Latanoprost (0,005%) is the most commonly used and the first being indicated for paediatric patients. The main side effects are iris and periocular skin hyperpigmentation. Others side effects such as conjunctival hyperemia, growth of eyelashes, deepening of the upper eyelid sulcus, blepharoptosis, inferior scleral show, and flattening of the lower eyelid bags have been reported and described in the literature [1-8].

We report the third case described in the literature of periocular skin hypopigmentation, in a patient treated with topical 0.005% Latanoprost [9,10].

Case Presentation

A female child, 8 years old, Caucasian, with ocular history of bilateral congenital cataracts, submitted to phaco-emulsification surgery and anterior vitrectomy, developed secondary glaucoma in both eyes and a trabeculectomy was performed in the right eye. Satisfactory intra-ocular pressure (IOP) control was achieved in both eyes with timolol maleate (eye drops, 0.5%, twice a day) until 8 years of age. Thereafter, the right eye showed a sustained IOP rise and Latanoprost 0.005% [(Monoprost®, Théa, France) (unit doses eye drops, once a day)] was added to medical therapy. Two months later, she presented with periocular skin hypopigmentation in this

eye (Figure.1). There was no history of vitiligo, alopecia or skin disorders and Dermatologic evaluation was performed with no other relevant findings. Vogt-Koyanagi-Harada disease was also excluded (there was no history of bilateral iridocyclitis, posterior uveitis including serous retinal detachment or sunset glow fundus, tinnitus, vertigo, dysacusis, meningism, alopecia or poliosis). The Latanoprost treatment was discontinued and a treatment with 2%/0.5% dorzolamide/ timolol was initiated, achieving satisfactory IOP control. Three months after discontinuation, peri-ocular hypopigmentation showed partial reversal, and stayed stable to the most recent follow-up, in December 2018 (two years post discontinuation) (Figure.2).

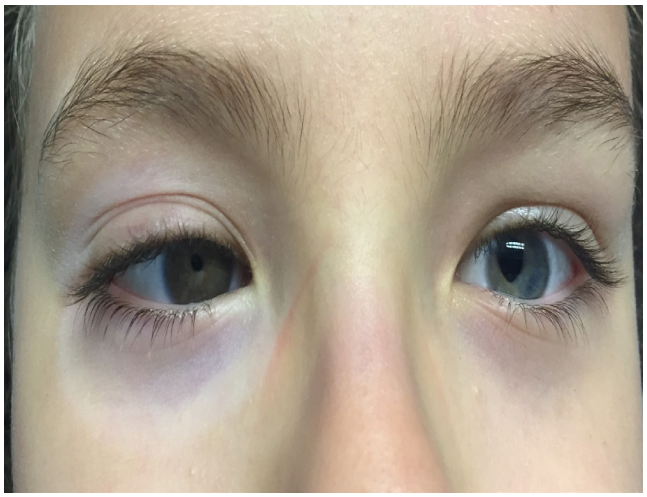

Figure.1. Right eye: periocular skin hypopigmentation 2 months after treatment with topical Latanoprost.

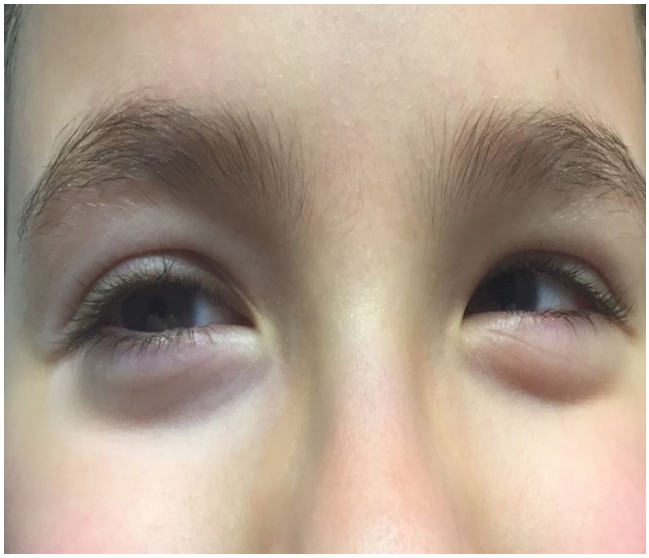

Figure.2. Right eye: periocular skin hypopigmentation, 3 months after treatment with topical Latanoprost has ended.

Discussion

The 12-months incidence of periocular hyperpigmentation with topical latanoprost is 1% and has shown to be reversible after discontinuation of therapy [3,5].

Prostaglandins are important stimulants of melanogenesis. FP prostanoid receptor is localized in ocular tissue and expressed by skin melanocytes and stimulates the activity and expression of tyrosinase, the enzyme responsible for melanin synthesis [11,12]. In the skin, melanin produced in dermal melanocytes is transported to neighbouring keratinocytes in the basal layer of the epidermis. Latanoprost-related pigmentation of periocular skin occurs from increased melanogenesis and increased transfer of melanosomes to basal keratinocytes, with the absence of melanocyte proliferation and melanocyte atypia. As the keratinocytes ascend to the outer surface, the melanin is partly degraded and then lost as the stratum corneum is sloughed off. This mechanism may explain why Latanoprost-induced periocular skin changes are reversible [13,14].

The mechanisms involved in Latanoprost-induced skin hyperpigmentation have some similarities to hyperpigmentation induced by Ultra Violet exposure or inflammation. [13] Furthermore, prostaglandins play a role in ocular inflammation. Lin et al. suggest that postinflammatory hypopigmentation of the skin due to the use of topical prostaglandins is a possible mechanism to explain that paradoxical reaction [9]. However, Latanoprost (alone or in combination with phototherapy) is used with good efficacy, safety, and affordability in Dermatology to induce skin repigmentation in periocular vitiligo [15].

In our 8-year-old patient, Latanoprost was preservative free while the other 2 cases contained Latanoprost with preservatives (Xalatan® and Xalacom®) [9,10]. Both beta blocker and prostaglandin analogue were used in the eye with hypopigmentation (right eye), but the skin changes only appeared after prostaglandin onset. Furthermore, during five years no skin changes occurred with beta blocker in both eyes and the left eye remained unchanged after skin changes occurred in right eye. Besides that, periocular depigmentation seems to be partially reversible after 3 months of therapy discontinuation. In addition, no primary or acquired autoimmune disease was diagnosed. This kind of induced-vitiligo may be particularly important in children undergoing hypotensive therapy with Latanoprost.

In literature, we can find some cases of skin hypopigmentation related to drugs. It was described a case of peri-ocular skin hypopigmentation due to chloramphenicol eye drop allergy following ptosis surgery [16]. Systemic drugs can also induce skin hypopigmentation as Imatinib Mesylate, a tyrosine kinase inhibitor used in chronic myeloid leukaemia. This well-known adverse effect can occur in 1/3 of chronic myeloid leukaemia patients taking imatinib, and seems to be reversible and dose related [17,18]. Platelet derived growth factor receptor and C-kit present in melanocytes have a major role in mel-

anogenesis but are inhibited by this drug. However, even if a rare reaction, hyperpigmentation due to Imatinib can occur and the reason behind that needs to be elucidated. [19,20].

Conclusion

Although periocular skin hyperpigmentation is a well-known side effect of Latanoprost, a paradoxical effect can occur with any drug and may be considered in patient's approach and treatment.

Authors' contributions: COF, SP, JTF and FFR performed the literature research. ABM and SES examined the patient during the treatment. All authors read and approved the manuscript.

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