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CLINICAL CASE

Periorbital pallor and systemic effects post application of mydriatics in infants with hydrocephalus

Palidez peri orbitaria post aplicación de midriaticos en neonatos con hidrocefalia asociado a efectos sistémicos

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Abstract

Adequate pupil dilation is needed to evaluate some neonates at risk of developing illness during this stage. However, this procedure is not free of adverse effects, either local or systemic. One of these complications is the local vasoconstriction of the preterm baby's skin following the application of mydriatic eye drops. **Objective:** To describe secondary local and systemic complications of pharmacological pupil dilation in 2 newborns. **Clinical case 1:** Full term baby with diagnosis of low-birth weight and hydrocephalia. An ophtalmological evaluation was performed at 5 days of age due to the presence of corneal opacities. Peri ocular pallor was observed during the procedure, as well as tachycardia and hypertension 2 hours later, spontaneosly recovered. **Case 2:** Preterm newborn, 27 weeks of gestational age. Neonatal respiratory distress syndrome, patent ductus arteriosus, intraventricular hemorrhage and hydrocephalia were diagnosed at birth. At 28 days of life an ophtalmological evaluation was performed. After 10 minutes of mydriatic drops administration to evaluate preterm retinopathy, peri ocular pallor was observed, with spontaneous resolution; however, 24 hours later, the patient showed abdominal distention and feeding intolerance. Necrotizing enterocolitis was discarded, and symptoms were spontaneosly recovered. **Conclusion:** The establishment of protocols in relation to the number of drops to apply for dilation is needed to reduce deleterious effects on high risk infants, such as premature babies and those with hydrocephalus. Therefore this monitoring practice should be performed during the evaluation.

Keywords:
Phenylephrine,
hydrocephalus,
preterm,
mydriatic drops

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Introduction

The ophthalmologic evaluation is a necessary procedure in neonates because of the risk of retinopathy of prematurity and evaluation of other ophthalmological disorders. The test is mandatory for all newborns at risk, because retinopathy of prematurity is considered the leading cause of blindness in developed and underdeveloped countries, a condition primarily associated with weight and gestational age[1].

However, other pathologies may require ophthalmologic evaluation, such as congenital perinatal infections of the TORCH group. Mydriasis is required to achieve an adequate test, which is achieved with the local application of mydriatics, such as phenylephrine, tropicamide, cyclopentolate, which are not exempt from local and systemic adverse events[2].

Periorbital vasoconstriction, related to skin absorption of phenylephrine, has been reported secondary to skin immaturity, characteristic of prematurity[3]. Phenylephrine is not a selective drug on ocular structures. Although a local effect, such as mydriasis can be observed, this drug can lead to other local effects and coud be absorbed by the conjunctival route, producing systemic effects.

The objective of this report is to present 2 cases of periorbital vasoconstriction and probable systemic effects after mydriatic application in newborns with hydrocephalus.

Clinical Case Nº 1

Neonate product of 32-year-old mother, first-pregnancy, controlled, with prenatal diagnosis of hydrocephalus and restriction of growth. No other anatomical alterations were detected. Neonatal adaptation without complications, weight 2260 g, heigth 42 cm, 38 weeks of gestational age, and cephalic perimeter (CP) 42 cm. Computed axial tomography (CT) of the skull showed supratentorial hydrocephalus with minimal cortical cortex. Complementary studies were performed for TORCH congenital infections, which were negative. Ophthalmology assessment was requested for evidence of corneal opacities. On the fifth day of life, ophthalmologic examination was performed, using mydriatics, based on our protocol, showing at the 15 minutes post-administration of the second cycle, paleness and mild periorbital edema bilaterally (Figure 1). The applied pupil dilation protocol consisted of proparacaine (one drop in each eye), 10 seconds later a drop of 2.5% phenylephrine followed by a drop of tropicamide was waited ten minutes and the cycle of phenylephrine and tropicamide was repeated. It was revalued in 10 minutes if there was dilatation. If a proper mydriasis was not achieved, a third cycle of the medication was performed.

The patient also presented altered vital signs, tachycardia of 190 beats per minute associated with arterial hypertension 121/78/95 mmHg (baseline 80/42/53 mm/hg), in the following 2 hours post-procedure. The pallor resolved a few hours after the application, together with stabilization of the hemodynamic variables.

Clinical Case Nº 2

Preterm neonate, 27 weeks of gestation, with a history of respiratory distress syndrome, referred for closure of the ductus. With weight of 1300 grs, PC 27 cms at the moment of being enrolled. Cerebral ultrasound was performed, which reported grade III of intraventricular hemorrhage. During his hospital stay, an increase in CP was evidenced, and a CT scan of the skull was requested, which demonstrated severe hydrocephalus, and a ventriculoperitoneal shunt was performed. Ophthalmology evaluation was requested to assess the development of retinopathy of prematurity, which was performed at 28 days of age. It was evidenced at 10 minutes post-application of mydriatics, at the time of evaluation before the second cycle, skin pallor and bilateral periorbital edema, without deterioration of vital signs (Figure 2). Paleness and edema were resolved within 2 hours after the procedure. However, 24 hours after the evaluation showed intolerance to oral feeding and abdominal distension, which were interpreted as sepsis and suspicion of enterocolitis. It was studied with abdominal radiography that showed distension of handles without other alterations, hemogram with leukocytes of 7560, platelets of 256,000 and Hb of 11.5. Hemocultures negative on the fifth day of life. Sepsis and/or enterocolitis were ruled out.

Discussion

Ophthalmologic evaluation in neonates is not free of adverse reactions. These may be related to the manipulation performed during the ophthalmologic examination, or to the medication used to generate mydriasis[5,6]. These side effects can occur immediately, such as altered vital signs, changes in heart rate, blood pressure, apnea events, hypoxemia among others[7]. However, there is a risk of late alterations such as delayed gastric emptying, intolerance of the oral route and increase of ventilatory parameters[8].

Two infants with a history of hydrocephalus are reported, who presented periorbital vasoconstriction after application of mydriatics, in addition to systemic

Figure 1. Bilateral periorbital paleness, post-application of mydriatics. We also observe left corneal opacity.

Figure 2. Great periorbital edema, associated with periorbital skin paleness.

effects, possibly by the sum of association of pharmacological effects of medications used to cause mydriasis and the procedure as such, manipulation during the Ophthalmologic examination. The vasoconstriction periorbital has been reported previously, mainly in relation to the characteristics of the skin of the premature neonate, which are the most susceptible population[3]. However in this report, one of the reported cases is a term neonate, who in theory presents a lower risk, for he possess a less immature skin.

The ocular application of 2.5% phenylephrine can lead to skin vasoconstriction mainly in premature infants secondary to cutaneous immaturity[9]. This condition had not been generated in any of our patients to date, using the institutional dilatation protocol. Hence, there may be other conditions that may increase the risk of periorbital vasoconstriction. Both patients had hydrocephalus, as a variable different from our usual evaluations, but to date there is no data that it behaves as a risk factor for periorbital cutaneous vasoconstriction in neonates exposed to mydriatics.

In addition to local ocular effects, the drug has conjunctival absorption leading to systemic effects, such as altered blood pressure and heart rate[10]. It is clear that the group of infants, especially premature infants due to cutaneous characteristics, are the population at greatest risk for local and systemic complications, but we believe that there must be other associated factors in this population. This is due to the cases of Alpay et al[3], who reported a similar event of vasoconstriction in a term neonate, which was not associated with hydrocephalus, but also did not clarify which factor could trigger it.

On the other hand, the systemic absorption of the medication is related to early alterations such as hypertension or late symptoms as intolerance of the oral route, as presented in case 1 and 2, respectively. Gastrointestinal symptoms can be interpreted as sepsis or enterocolitis, generating non-optimal behaviors in these patients.

We believe that these effects are due to the anticholinergic and alpha adrenergic action of the medication. Our protocol includes the use of 2.5% phenylephrine and tropicamide. Tropicamide has very low affinity for systemic muscarinic receptors and no receptor occupancy, which explains the low incidence of systemic effects secondary to this drug[11]. Therefore, we think that the reported effects are related to 2.5% phenylephrine used in these cases.

It should be noted that other medications not used in our protocol such as cyclopentolate are associated with other complications, such as myoclonic seizures[12].

There are also other factors other than the application of mydriatics that are associated with side effects, similar to the procedure, which generates pain and the oculo-cardiac reflex, which can condition apnea, bradycardia, changes in oxygen saturation, pulse and Blood pressure[6,13].

The medication used to obtain mydriasis requires adequate concentration and dosage. However, the dosage to achieve optimal mydriasis is not based on strong evidence, but it seems that the amount of drops to achieve adequate mydriasis can be conditioned by gender, iris color, postmenstrual age and severity of retinopathy[14]. The protocol used at our Center seems safe from previous reports, but it does not escape ad-

verse reactions[15]. Despite its local application, the risk of local secondary and systemic effects is minimized, but not completely avoided. It is estimated that over 90% of a topical ophthalmic may be a dose potentially available to act systemically[4], however, it is proposed that self palpebral closure age, minimizing flicker and performing a compression of the lacrimal sac for 1 to 2 minutes after application of the drops, thus occluding the lacrimal duct, prevents the passage of the drug by this route and increased systemic absorption. It is clear that these techniques are, apparently, not that frequent to prevent the systemic absorption and there is no generalization of these, for it could imply a risk of injury in preterm infants[3], thus it is rarely applied.

As described, ophthalmologic evaluation should maintain an established protocol, including sequential administration of mydriatics, adequate concentration of the drug, the minimum dose required to achieve adequate mydriasis, in addition to pre and post monitoring during the procedure.

Conclusion

The ophthalmologic examination, which is a safe and necessary, is not free from side effects, which are fortunately infrequent. These adverse reactions are related to the procedure itself and the drugs used to generate mydriasis. On the other hand, it is necessary to optimize the management of the pain that is generated during it and the analgesia should be part of the protocol. For the above, you must have an understanding of any possible complications and keep a record of them. Each service should be aware of the adverse events presented and seek the actions that lead to minimizing them.

In addition, it is recommended that children who are released, who require new controls, should receive those controls under the best safety conditions, providing a strong stability of these patients who are naturally under so much stress associated with the examinations and drugs used to produce mydriasis. The ideal is to associate parasympathetic blockers (1% tropicamide), with sympathomimetics.

Each institution should establish the protocol to be used according to studies that demonstrate efficacy and safety[16].

In addition, parents should be informed of possible alterations, when these assessments are performed in an intrahospital or outpatient setting.

Periorbital vasoconstriction after application of phenylephrine in neonates with hydrocephalus.

Ethical Responsibilities

Human Beings and animals protection: Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

Data confidentiality: The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

Rights to privacy and informed consent: The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the correspondence author.

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Conflicts of Interest

Authors state that any conflict of interest exists regards the present study.

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