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Clinical manifestations due to pharmacological interactions in pediatric ophthalmic surgery. Topical drugs and general anaesthesia

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SUMMARY: **Clinical manifestations due to pharmacological interactions in pediatric ophthalmic surgery. Topical drugs and general anaesthesia.**

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Introduction. *The authors consider the type and the incidence of the adverse effects due to the interaction between ophthalmic drugs and general anaesthesia in pediatric ophthalmic surgery.*

Patients and Methods. *The experience included 176 general anaesthesia in 100 children aged between 9,2 months and 11,4 years (mean age 4,9 years).*

Results. *In the 100 patients we reported: 4 cases (2.7% general anaesthesias) of sinus tachycardia with heart rhythm varying between 170 and 180 beats per minute (3.6%); 5 cases of sinus bradycardia, varying between 60 and 70 beats per minute (3.3%); 3 cases of bronchospasm (2%); 2 cases of psychomotor agitation/disturbances in preconvulsive state after anaesthesia (1.3%); 3 cases of arterial hypotension (60-70 mmHg) (2%); 7 cases of skin rush around neck and chest (4.6%); 1 case of prolonged apnoea (0.6%).*

Conclusions. The clinical manifestations, principally on the cardio-circulatory and nervous system are subjected to critical revision, to foresee the pharmacological interferences and therefore to prepare the necessary measure of medical treatment.

KEY WORDS: Ophthalmic drugs - General anaesthesia - Adverse effects - Cardio-circulatory and nervous systems.

Introduction

In ophthalmology topical administration of drugs is the main route of administrating of chemical agents due to the absorbing capacity of the drugs applied on the eye external surface/outer sclera.

It is well known that drugs administered topically are absorbed locally, but they always produce effects at a systemic level, more or less evident according to a series of chemical-physical parameters. It has been demonstrated that the quantity of drug remaining at ocular level after administration is below 3%, while 97% is absorbed in a systemic way (1).The administration of drugs and their absorption at conjunctive-corneal level are a complex act susceptible of numerous variables (2). For example the volume retained undergoes a sudden decrease that can reach infinitesimal values after 10 minutes (3), this is due both to blinking and dilution caused by the lachrymal fluid. Moreover some authors affirm that most of the absorption takes place at corneal level where there are various factors that help or hinder the penetration of the agent used. From an anatomical point of view the cornea has three layers: epithelial, stromal, endothelial. The first one, if intact, is the main obstacle to the penetration of drugs.

From a chemical point of view the drug concentration gradient, its liposolubility and ionization are very important in this process. This is why eyewashes are usually tamponed water solutions containing one or more active principles together with preserved, stabilising, antioxidant and tension active ones according to the cases. There is also a subjective reactivity connected to congenital factors, age and related pathologies (4). Indeed, it is well known that children with Down Syndrome have a stronger tachycardic reaction to atropine that can reach dangerous levels; small children have week mydriasis derived fromphenylephrine administration in comparison with elderly; diabetic people haven alterated emato-ocular barrier.

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It is also important to notice that patients of neonatal or pedriatic age with ophthalmo-surgical pathologies are carriers of congenital malformations (Down Syndrome, Marfan Syndrome), conditions that make any procedure more difficult because of the possible side effects deriving from the medical substances used.

Patients and methods

Our experience examines the pharmacological interactions and the connected objective manifestations observed during general anaesthesia in 100 children aged between 9.2 months and 11.4 years (average age 4.9).

The patients were underwent general anaesthesia for surgery of the anterior segment (12 cases), of the posterior segment (9 cases), of extrinsic musculature/muscles (19 cases) and for a diagnostic examination or check-up (60 cases).

A total of 14 of the above mentioned patients underwent two general anaesthesias; 8 patients 3 general anaesthesias, while 6 patients had to be anaesthetized 4 times: a total of 150 general anaesthesias for 100 patients. These patients were carriers of either congenital or acquired pathologies: in the first group we have noticed a Down syndrome in 3 patients, a Marfan syndrome in 9 patients and congenital glaucoma in 18 patients; with regards to acquired pathologies 5 patients were born before time and had an ocular damage (retro-lenticular fibroplasia) caused by oxygen therapy; all the others left over suffered from vascular pathological alterations and traumatic ones.

The anaesthesia scheme/pattern used is the following:

Pre-medication:	*Atropa belladonna* (1drop/2kg) or Atropine Solphate (0.01mg/kg im) + Dehydrobenzperidol (0.16 mg/kg im)
Induction:	Ketamine (4-5 mg/kg im) Halothane through mask at increasing concentrations Thiopentone Sodium (3-4 mg/kg iv) Succinylcholine Chloride (1.0 mg/kg) Orotracheal intubation (OTI)
Maintenance:	N2O + O2 (50:50) Halothane (0.5-2%) Enflurane Fentanyl (0.0005 mg/kg if needed) Pancuronium Bromide

The patients who underwent general anaesthesia for a diagnostic check-up examination were not subjected to OTI, but were aided by manual ventilation with the help of a mask filled with N2O+O2 enriched by an inhaling halogenated agent (halothane or enflurane) at a concentration between 1 and 25%. During induction a surface anaesthetic (novesine) was instilled as analgesic aid.

The pharmacological agents administered before anaesthesia, for time periods varying from a few hours to several weeks, had two main objectives: reducing endo-ocular pressure and obtaining a more or less protracted pupillary mydriasis.

The most used drugs among those available on the market are cholinergic ones (pilocarpine), not selective beta-blockers (timolol maleate and befunolol) and selective ones (betaxolol), anticholinesterase drugs (echothiophate), cycloplegic drugs (cyclopentolate), not catecholamine drugs (phenylephrine) and catecholamine ones (ephedrine).

Results

The complications observed during surgery or in the immediate postoperative period were mainly cardiovascular or involved the central nervous System.

In the 100 patients that underwent general anaesthesia we have noticed the following cases:

1. n. 4 cases (2.7% general anaesthesias) of sinusitis tachycardia with frequency varying between 170 and 180 beats per minute (3.6%);
2. n. 5 cases of sinusitis bradycardia, varying between 60 and 70 beats per minute (3.3%);
3. n. 3 cases of bronchospasm (2%);
4. n. 2 cases of psychomotor agitation/disturbance in pre-convulsive state at awakening after anaesthesia (1.3%);
5. n. 3 cases of arterial hypotension (60-70 mmHg) (2%);
6. n. 7 cases of skin rush around neck and chest (4.6%);
7. n. 1 case of protracted apnoea (0.6%).

There were also at least other 20 subjects that presented alterations of the cardiovascular parameters, but of a lower degree, therefore they were not included in the above indicated group.

A more detailed observation of the events above described shows that:

1. The cases of tachycardia in the patients treated with ephedrine administered topically. In fact the combination of the sympathetic-mimetic agent with halogenated vapour and atropine sulphate can contribute to an increase of heart rates especially if the vapour used is enflurane.

2. The bradycardia episodes were related only to the patients treated with not selective beta-blockers for chronic open angle glaucoma.

3. The bronchospasm occurred to 2 patients treated with not selective beta-blockers and to 1 patient to whom the spasm was probably caused by mask inducted high initial concentrated halothane (2-3%). This provoked the bronchial reaction, due to irritative stimulation of the mucous membrane caused by the inhaling agent.

4. The hypotension occurred to the patients treated with beta-blockers, induced and maintained under anaesthesia with halogenated vapours.

5. The cases of psychomotor agitation at awakening occurred to the children administered with cyclopentolate. In 1 case it was necessary to administer 4-5 mg of diapezam i.v.

6. The skin rush is likely due to the patients' subjective sensitivity to the atropine sulphate administered by intramuscular injection in pre-anaesthesia, which disappeared after betamethasone i.v. was administered.

7. The apnoea case occurred to a young patient trea-

ted with echothiophate, an anticholinesterasic agent, and lasted 15-20 minutes.

Discussion

All the data collected show that there can be secondary effects caused by ophthalmologic drugs, especially if they are used together with other agents that increase certain existing negative characteristics.

The tachycardia episodes are certainly more frequent when Atropine-sulphate, Ephedrine and Enflurane are administered together. In these cases it is advisable to substitute Atropine with Glycopyrrolate, a synthetic parasympathicolytic agent that has a lesser tachycardia effect and an optimum anti-secretion activity (5-10).

The use of glycopyrrorato can be decided before anaesthesia after an anamnesis positive to Atropine hyper reactivity or for Down Syndrome subjects, in whom the glycopyrrorate finds it more difficult to pass through the haemato-encephalic barrier.

The drug Ephedrine can be effectively substituted with phenilepherine that has both a mydriatic and a reflex bradychardic effect.

On the other hand beta-blockers-correlate bradycardia presents a problem that cannot often be solved immediately with drugs. This is because the heart rate does not always increase after administering Atropine-sulphate i.v. Therefore a pre- surgery evaluation of the heart conditions of a patient under beta-blockers drugs is necessary and also eventually do a temporary wash-out and a temporary substitution of the anti-glaucoma agent.

The same problem occurs when a bronchospasm, caused by induction during surgery or by an excessive drop of pressure, is feared.

As it is impossible to predict a psychomotor agitation state leading to delirium we can only gather all the information useful to a very accurate anamnesis in order to exclude eventual epileptoid border line manifestations and avoid administering Cyclopentolate (9).

Premature babies are an evident case of contraindication against the use of this Cicloplegic drug (6).

The case of prolonged apnoea presents a complication typical of the association of Echothiophate and Succinylcholine chloride, because this long lasting action anticholinesterasic agent extends the duration of the neuromuscular block caused by the neural plate depolarization.

As a last point it is advisable to remember that an ill-timed association of Acetazolamide with Ketamine, because of the synergetic action of those drugs on endocranial pressure, can create dangerous hypertension states both in normal subjects and with reason in patients with brain/cerebral pressure problems (11-18).

In conclusion we can affirm that a greater part of side effects caused by drugs, whether the drugs are administered alone or in association with others, can be predicted and therefore dealt with some simple but very important measures:

1. patient's accurate anamnesis;
2. evaluation of therapy used in order to choose proper drugs for general anaesthesia;
3. finding a venous route also in cases of examination under anaesthesia in order to counteract the dangerous event that could occur, in the shortest time possible;
4. monitoring the cardiovascular function;
5. patient's careful observation up to two/three hours after surgery in order to be able to evaluate in good time a negative change of vital parameters.

Conflict of interest declaration

All of the Authors do not have conflicts of interest (specific financial interests and relationships and affiliations) relevant to the subject of the present article.

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