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Propofol for Procedural Anaesthesia During Laser Treatment of Retinopathy of Prematurity in the Neonatal Intensive Care Unit (NICU)

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Abstract

Background: Anaesthesia in preterm neonates poses certain risks due to such patients' systemic instability and concurrent pathologies, as the procedure itself can accentuate such instability and morbidity in these patients. Anaesthesia for LASER procedures for ROP must be a safe procedure that ensures the patient's stability during and after the procedure. The purpose of this paper is to describe the anaesthesia techniques used in the neonatal intensive care units (NICUs), and evaluate their results.

Methods: Retrospective cross-sectional study carried out from January to December 2012, which included 79 out of 102 patients operated on during such period using laser photocoagulation for ROP under general anaesthesia with intravenous Fentanyl and Propofol administered by a Paediatric Anaesthesiologist.

Results: The anaesthesia had a median duration of 75 minutes, and no periods of hypotension were reported. Seventy-eight patients (98%) were extubated at the end of the surgery and one patient remained intubated due to hemodynamic instability related to sepsis. Additionally, it was necessary to re-intubate 2 patients (3%) and 1 patient (1%) required nasal cannulas for 12 hours due to low O2Sat.

Conclusions: In the NICU, a combination of Fentanyl and Propofol-without administration of muscle relaxants—is a safe, useful technique for treatment of preterm neonates undergoing brief surgical procedures such as laser photocoagulation. The rapid recovery associated to this technique helps to meet the increasing demand for ROP surgeries and reduces the length of hospitalization.

A multivariate regression model considering the complications of intravenous general anesthesia with propofol as the dependent variable was carried out.

We observed that the Durbin-Watson test score presented independence of errors (2,135).

For the regression model with independent variables, we found that none of them explains the variance of the dependent variable as shown in Table 5.

The ANOVA of the regression model with these variables indicates that this does not significantly improve the prediction of complication DV (F = 1.607 and p = 0.129).

For the coefficients of the regression model, T-scores reflect that the variables taken into account do not significantly contribute to the prediction model, and therefore that the values obtained can not be generalized to the greater population.

Keywords: Propofol; Fentanyl; Retinopathy of prematurity; Paediatric anaesthesia; Laser treatment

Introduction

The treatment of choice for type 1 Retinopathy of Prematurity (ROP) is photocoagulation of the avascular retina [1], which has a high success rate despite the systemic stress it can cause in preterm neonates. Anaesthesia in premature patients poses a challenge due to their systemic instability and concurrent pathologies, as the procedure itself can accentuate this instability and morbidity in these patients [2].

Anaesthesia for LASER procedures for ROP treatment must be a safe procedure that ensures the patient's stability during and after the procedure [3]. Ideally, it should also offer rapid recovery, thus allowing several procedures to be undertaken within the same day, reducing the length of hospitalization and increasing the availability of beds in the Neonatal Intensive Care Unit (NICU), which admits a great number of patients on a daily basis from referring hospitals and institutions.

The purpose of this study is to describe the anaesthesia techniques used in the NICU as compared to techniques used in operating rooms, and evaluate the results that have been achieved.

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Materials and Methods

Retrospective cross-sectional study undertaken from January to December 2012, which included 79 out of 102 patients operated on using photocoagulation for ROP at the NICU under general anaesthesia administered intravenously by a Paediatric Anaesthesiologist.

Selection criteria

All preterm neonates with a type 1 ROP diagnosis operated on at the NICU were included. Patients whose medical history was incomplete were excluded.

Programmed surgery: photocoagulation of the avascular retina using a 810 nm Laser Diode, with drug-induced mydriasis, blepharostat placement, indentation and indirect ophthalmoscopy, lubricating the cornea during such procedure with drops of 2% Methyl cellulose.

Anaesthesia procedure

The patients were admitted to the NICU 12 hours prior to surgery for clinical and medical assessment by a neonatologist and preparation, with fasting beginning 4 hours prior to surgery.

The parents' written informed consent was obtained for each patient. Ophthalmic drops of Tropicamide 0.8% with 5% Phenylephrine were applied to each eye 30 minutes prior to surgery. After placing peripheral vein catheter, determining patency and verifying temperature, vital signs were monitored: blood pressure (BP) in mmHg, heart rate (HR) at beats per minute, respiratory rate (RR) and digital O2 saturation (SpO2).

Induction was undertaken after oxygenation with a face mask and "Jackson-Reese" equipment, administering intravenous (IV) Fentanyl at 1.5 to 2 micrograms/kg body weight (µg/kg), followed by Propofol IV 3 milligrams/kg body weight (mg/kg) (increasing such dose to 4 mg/kg bodyweight if the patient showed any movement during intubation). Atropine was administered at 20 µg/kg to those patients whose HR was lower than 120 beats per minute, or who displayed pupil rigidity. 30-60 seconds after apnea set in, a direct laryngoscopy was carried out with a 0-1 Miller blade, introducing a 3 to 4 French endotracheal tube with secured cannula. The procedure continued with manual or mechanical ventilation and Propofol infusion at 150-200 µg/kg/min, maintaining SpO2>90% and HR >120 beats per minute, reporting vital signs every 5 minutes and accepting a 20% change from baseline values as normal. During this period, Paracetamol (acetaminophen) was administered at 15 mg/kg bodyweight as a single dose and Dexamethasone at 0.2 mg/kg, single dose. The ophthalmologist notified the anaesthesiologist 15 minutes before the estimated time of conclusion in order to suspend the Propofol infusion, continuing with ventilation support for 10-15 minutes until spontaneous breathing occurred and extubating the patient after aspiration of any secretion, continuing to phase 1 ventilation with nasal cannula or face mask in order to maintain a SpO2 >90%. Muscle relaxants were not used in any of the patients.

Feeding resumed 4 hours after having suspended Phase III ventilation, except in those patients with complications.

In all cases, the anaesthesia procedures were carried out by a Pediatric Anaesthesiologist with expertise in treating preterm neonates.

Statistical Analysis

The mothers' social-demographic characteristics were evaluated, as were the neonates' demographic characteristics, age and weight at the time of surgery, respiratory disturbances during and after surgery, complications associated to the surgery and anaesthesia, necessary reintervention, transfusions, length of hospitalization, and whether they were discharged to their home or to the referring hospital.

All data was recorded on a standard form, and entered into a database created in Microsoft Office Excel 2010. Data was analysed using SPSS version 21 for Windows. Descriptive analyses were performed. The results are reported using medians and range.

Ethical Considerations

The study complies with the international principles on clinical research set forth in the Helsinki Declaration. The informed consent of each patient's parents was obtained. The study was authorized by the hospital's research and ethics committee.

Results

From January to December 2012, 680 patients were examined using screening criteria in accordance with Mexican technical guidelines by an ophthalmologist trained to use an indirect ophthalmoscope under drug-induced mydriasis, of which 102 premature patients were diagnosed with type 1 ROP and operated on [4]. Twenty-three patients were excluded as their complete medical histories were unavailable. Seventy-nine patients were included; their median weight at birth was 1269 grams (460-1850), median gestational age at birth was 31 weeks (24-36), 40 (50%) were male and 19 patients (24.1%) were born of twin pregnancies (Table 1).

Information regarding the patients' mothers revealed that their median age was 23 years (15-41), 55 (70%) were single mothers and 58 (73%) had no schooling beyond elementary or middle school (Table 2).

At the time of surgery, the patients had a median weight of 2200 (1200-3700) grams and a , corrected gestational age of 39 weeks (29-54). Seventy-one patients (90%) had been referred by other hospitals that did not have the necessary staff or infrastructure for ROP treatment (Table 3).

Anaesthesia had a median duration of 75 minutes (60-105), and no periods of hypotension were reported. Seventy-eight patients (98%) were extubated at the end of the surgery and one patient remained intubated due to hemodynamic instability related to sepsis. Additionally, it was necessary to re-intubate 2 patients (3%) and 1 patient (1%) required nasal cannulas for 12 hours due to low O2Sat. Forty-four (57%) patients received blood transfusions, 39 (49%) prior to surgery, 6 (8%) after the surgery, and none of the patients received a transfusion during surgery. Sixty-five patients (82%) were discharged to their homes, while 14 (18%) were sent to their referring hospital (Table 4).

Gender	N	%
Male	40	50.60%
Birth Weight, g		
Mean ± SD	1269 ± 294	
Median (Range)	1280 (460-1850)	
Gestational Age, weeks		
Mean ± SD	31 ± 2	
Median (Range)	31 (24-36)	
Twin pregnancy	19	24.10%
Type of birth		
Caesarean	50	63.30%
TOTAL	**79**	**100%**

Table 1: Sociodemographic characteristics of premature patients with type 1 ROP.

Mothers age, years		
Mean ± SD	23±6	
Median (Range)	23 (15–41)	
Marital status	**N**	**%**
Married	24	30%
Single	55	70%
Schooling		
Elementary and middle school	58	73%
High School	15	18%
College	7	9%
Drug addiction		
Yes	1	1%
Total	**79**	**100%**

Table 2: Maternal characteristics of premature patients with type 1 ROP.

Weight, g		
Mean ± SD	2226 ± 508	
Median (Range)	2200 (1200-3700)	
Corrected gestational age, weeks		
Mean ± SD	39 ± 3	
Median (Range)	39 (29-54)	
Age in days		
Mean ± SD	58 ± 23	
Median (Range)	58 (22-125)	
Provenance/Referral	**N**	**%**
Same Hospital	8	10%
Other Hospitals	71	90.00%
TOTAL	**79**	**100%**

Table 3: Characteristics at the time of surgery.

Duration of anaesthesia, minutes	**N**	**%**
Mean ± SD	71 ± 11	
Median (Range)	75 (60-105)	
Extubation after surgery	78	99%
Minutes after end of photocoagulation procedure		
Median (Range)	11 (1-26)	
Hemoglobine, mg/dl		
Mean ± SD	11.4 ± 2	
Median (Range)	11.1 (8-22)	
Transfusion		
Prior to surgery	39	49%
After surgery	6	
Reintervention		
Yes	6	8%
Complications	4	
Discharge		
Home	65	82%
Other hospitals	14	18%
TOTAL	**79**	**100%**

Table 4: Characteristics during and after anaesthesia.

To this date, all patients have continued with medical follow-up through appointments with pediatricians and ophthalmologists at our hospital.

Discussion

In Mexico, no studies have been conducted on the types of anaesthesia employed at hospitals treating ROP; studies conducted in the United Kingdom have not yet reached an agreement on the ideal method of anaesthesia-analgesia [5].

Several studies have been conducted to evaluate the options regarding anaesthesia during laser photocoagulation, among these Morphine analgesia, Ketamine sedation, local anesthesia, paralysis sedation and analgesia, local anaesthesia sedation (associated to severe respiratory complications), general anaesthesia, or combinations of such methods without having reached a definite conclusion regarding the best method of anaesthesia with the least complications during and after surgery [2,6-10].

In our experience, in general or ophthalmology operating rooms, in many cases, the materials necessary for anaesthesia procedures in premature patients are not available. The support of a specially-trained nursing staff or a neonatologist is generally also unavailable. The staff assigned to these areas usually has not been trained in the skills necessary for intubation, or to calculate and dilute medications for preterm neonates, thus exposing them to multiple vein punctures, dosage errors, and other unnecessary risks. Productivity with respect to programmed surgeries is also affected as such risks may result in emergencies that can take up the time allotted to 4-6 out-patient or same-day surgeries, as is the case in phacoemulsification cataract surgery in adult patients. When such procedures are undertaken in general operating rooms, treatment is delayed as there is competition with life-threatening emergencies for operating-room time. Moreover, a premature patient may require 2-3 days in the NICU to recover from anaesthesia procedures carried out in such areas.

Performing the surgical procedure in the NICU allows for constant evaluation of the patient by a qualified neonatologist, and for systemic evaluation, as proven by the fact that more than half of the patients were found to require a blood transfusion before the surgical process.

The anesthetic technique used in the NICU, where intravenous anesthesia is of short duration and carried out in a radiant heat warmer, is a technique that does not contaminate surrounding areas, when compared to inhaled general anaesthesia. It allows for patient treatment with immediately-available specialized material and human resources. It avoids having to transfer the patient from the operating room to the NICU after the surgery, and reduces the length of hospitalization. A rapid respiratory recovery makes it possible to perform several surgical procedures within a single day, as well as to return patients referred

Model	Constant	B	Error tip	Beta	t	Sign
1	Sex	0.008	0.115	0.009	0.068	0.946
	Pregnancy type	0.037	0.100	0.049	0.369	0.713
	Delivery type	0.126	0.120	0.204	1.042	0.302
	Pathology at birth	0.192	0.088	0.296	2.178	0.034
2	Drug use	0.102	0.165	0.093	0.620	0.538
	ROP Diagnosis	0.091	0.160	0.087	0.568	0.573
	Transfusions	0.053	0.047	0.175	1.137	0.262
	Marital Status	0.072	0.047	0.140	1.52	0.131
	School	0.056	0.028	0.177	2.026	0.045
3	Gestational Age	0.002	0.022	0.011	0.085	0.932
	Birth Weight	0.000	0.000	0.115	0.656	0.514
	Mother´s Age	0.014	0.010	0.171	1.304	0.197
	Weight at surgery	0.005	0.000	0.036	0.270	0.788
	Adjusted age	0.014	0.018	0.108	0.761	0.450
	Age in days	0.003	0.004	0.133	0.633	0.529
	Hemoglobine	0.001	0.036	0.003	0.020	0.984

Table 5: Regression model with independent variables.

from other hospitals back to their hospital of origin soon after surgical treatment, thus complying with the post-anaesthesia monitoring period established in official practice guidelines within the NICU itself or at the referring hospital [11].

Although in the majority of cases, patients do not require ventilator support in the minutes following surgery, a ventilator must be available at all times.

As demonstrated by multivariate analysis, the existence of aggregate pathologies at birth presupposes the need for post-anesthesia ventilator support.

As is the case with nearly all medication used in neonatology, information on propofol pharmacokinetics and pharmacodynamics in neonates is still scarce [12]. There are studies that report a hypotensive effect of Propofol in preterm neonates at a rate that diminishes with every additional day of life; we did not observe such an effect in the patients in our study [12,13].

Experimental animal model results have shown that intraperitoneal administration of propofol induces neuroapoptosis in mouse brains without evidence of such an effect in humans.

Limitations

Although the retrospective nature of this study is a limitation to the research, preliminary conclusions suggest that this is a safe procedure for newborn patients. Yet, further long-term prospective randomized studies are clearly warranted in order to confirm this [14,15].

Although it is highly recommended to perform an echocardiogram on all premature patients to detect possible complications and pathologies, we did not perform echocardiograms in our patients. Nonetheless, none of our patients suffered any complications related to cardiac dysfunction [16].

Conclusion

In the NICU, a combination of Fentanyl and Propofol-without administration of muscle relaxants-is a safe, useful technique for treatment of premature patients undergoing brief surgical procedures such as laser photocoagulation in the NICU. The rapid recovery associated to this technique and performing it in the NICU instead of in general operating rooms helps to meet the increasing demand for ROP surgeries and reduces the risk of complications related to the surgical process, as well as cost and length of hospitalization.

References

1. Good WV, Hardy RJ (2001) The multicenter study of Early Treatment for Retinopathy of Prematurity (ETROP). Ophthalmology 108: 1013-1014.
2. Kirwan C, O'Keefe M, Prendergast M, Twomey A, Murphy J (2007) Morphine analgesia as an alternative to general anaesthesia during laser treatment of retinopathy of prematurity. Acta Ophthalmol Scand 85: 644-647.
3. Zepeda-Romero LC, Aguirre-Jáuregui OM, Angulo-Castellanos E, Gómez-Ruiz LM, Meza-Anguiano A, et al. (2013) Prevalencia de prematuros en riesgo visual y de Retinopatía del Prematuro tipo uno en el Hospital Civil de Guadalajara. (Prevalence of preterm neonates at risk for visual loss and type one RoP at the Civil Hospital of Guadalajara). Rev Med MD 4: 62-67.
4. Manejo de la (2010) Retinopatía del Recién Nacido Prematuro. Lineamiento Técnico, México.
5. Chen SD, Sundaram V, Wilkinson A, Patel CK (2007) Variation in anaesthesia for the laser treatment of retinopathy of prematurity--a survey of ophthalmologists in the UK. Eye (Lond) 21: 1033-1036.
6. Lyon F, Dabbs T, O'Meara M (2008) Ketamine sedation during the treatment of retinopathy of prematurity. Eye (Lond) 22: 684-686.
7. Jalali S, Azad R, Trehan HS, Dogra MR, Gopal L, et al. (2010) Technical aspects of laser treatment for acute retinopathy of prematurity under topical anesthesia. Indian J Ophthalmol 58: 509-515.
8. Haigh PM, Chiswick ML, O'Donoghue EP (1997) Retinopathy of prematurity: systemic complications associated with different anaesthetic techniques at treatment. Br J Ophthalmol 81:283-7.
9. Anand D, Etuwewe B, Clark D, Yoxall CW (2007) Anaesthesia for treatment of retinopathy of prematurity. Arch Dis Child Fetal Neonatal Ed 92: F154-155.
10. González-del Pino RI, Dávila-Ramírez R, Rodríguez-Fundora M, Castellón-Guerrero LN, Alemán-Díaz LE, et al. (2012) Anestesia para el tratamiento con láser de la retinopatía de la prematuridad. (Anaesthesia for laser treatment of RoP) Revista Médica Electrónica 34: 68-80
11. Para la práctica de la anestesiología (2011) (Mexican Official Standard for the Practice of Anaesthesiology) NORMA Oficial Mexicana NOM-006-SSA3-2011.
12. Bell SG (2010) Off-label medication use in the NICU. Neonatal Netw 29: 253-255.
13. Welzing L, Kribs A, Eifinger F, Huenseler C, Oberthuer A, et al. (2010) Propofol as an induction agent for endotracheal intubation can cause significant arterial hypotension in preterm neonates. Paediatr Anaesth 20: 605-611.
14. Cattano D, Young C, Straiko MM, Olney JW (2008) Subanesthetic doses of propofol induce neuroapoptosis in the infant mouse brain. Anesth Analg 106: 1712-1714.
15. Shah PS, Shah VS (2011) Propofol for procedural sedation/anaesthesia in neonates. Cochrane Database Syst Rev: CD007248.
16. Ciccone MM, Scicchitano P, Zito A (2011) Different functional cardiac characteristics observed in term/preterm neonates by echocardiography and tissue doppler imaging. Early Hum Dev 87: 555-558.