CRYOTHERAPY VERSUS LASER PHOTOCOAGULATION FOR THRESHOLD RETINOPATHY OF PREMATURITY: IMPACT ON EARLY POSTOPERATIVE CLINICAL RECOVERY

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SUMMARY

In a retrospective study in preterms treated with either cryotherapy (n=16, 2000-2001) or laser photocoagulation (n=19, 2002-2005) for threshold retinopathy, a significant decrease in duration of postoperative ventilation, in postoperative administration of analgesics and in time until regain of full enteral feeding was documented in infants who received laser photocoagulation. We therefore conclude that – compared to cryotherapy – laser treatment for threshold retinopathy is associated with a faster clinical postoperative recovery.

RÉSUMÉ

Une étude rétrospective chez des prématurés traités au laser pour rétinopathie-seuil (n=19, 2002-2005) comparés à ceux traités par cryothérapie (n=16, 2000-2001) a montré que le traitement au laser est associé à une diminution significative de la durée de ventilation, de la durée d'administration des analgésiques ainsi qu'à une reprise entérale plus rapide après l'intervention. Ces données suggèrent que le traitement au laser est associé avec un rétablissement postopératoire plus rapide.

KEY WORDS

Retinopathy of prematurity - postoperative outcome - laser - cryotherapy

MOTS-CLÉS

Rétinopathie du prématuré - rétablissement postopératoire - laser - cryothérapie

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INTRODUCTION

Retinal surgery, either cryotherapy or laser photocoagulation has proven to be effective to prevent posterior pole dragging and retinal detachment when threshold ROP is observed. Ophthalmologic advantages in favour of laser treatment are that the posterior zone of the retina can be reached easier, tissue damage is less pronounced and several authors documented less severe refractive errors following laser treatment although this might at least partially be explained by secular trends in disease severity [5,8,11]. In contrast to the numerous reports on visual outcome, there are no reports on the effect of the surgical technique on clinical recovery after surgery in this population. Since a reduced postoperative inflammatory response after laser photocoagulation compared to cryotherapy was recently described, we evaluated whether the use of laser photocoagulation was associated with a faster clinical recovery [6].

METHODS

Perinatal data of infants admitted in the neonatal intensive care unit of the University Hospital, Gasthuisberg since 1/1/96 are available in a prospectively collected database. This database was used to collect nursing, medical and anaesthetic files of infants who underwent retinal surgery for threshold retinopathy from 2000 to 2005. Laser photocoagulation for threshold ROP was introduced in the unit in 2001 and became the preferred treatment modality based on the above mentioned reports on improved visual outcome [5,8,11].

We therefore were able to compare characteristics of two cohorts of infants who received either cryotherapy (2000-2001) or laser photocoagulation (2001-2005). Clinical characteristics (gestational age at birth, weight at birth, postnatal age and weight at surgery) and data on postoperative management, i.e. duration of postoperative ventilation and time until full enteral feeding were retrospectively collected.

All infants underwent general anaesthesia during retinal surgery as reported earlier [3]. General anaesthesia was provided on the neonatal ward by a certified anaesthesiologist. Anaesthesia was induced using 3 to 5 μgr/kg fentanyl and 3 mg/kg propofol. Muscle relaxation was achieved using pancuroniumbromide (0.2 mg/kg). Following induction of anaesthesia, ventilation was maintained by mask ventilation. If not yet ventilated for medical reasons, endotracheal intubation was performed and ventilation was instituted. Anaesthesia was maintained using intravenous propofol or fentanyl [3].

Following surgery, a pre-emptive analgesia approach was used, based on intermittent administration of propacetamol and continuous administration of tramadol hydrochloride (5 mg/kg/day) or fentanyl (1-3 μgr/kg/hour). Systematic evaluation of pain using a validated pain measurement instrument (Leuven Neonatal Pain Scale, LNPS) and a standard analgesia protocol were used to further adapt or discontinue intravenously administered analgesics [3,9].

Before surgery, atropin 0.5 % and phenylefrine 5 % eye drops were administered twice to attain full pupillary dilatation during surgery. After surgery, atropin eye drops were continued for a few days and in addition, dexamethasone (Maxitrol®, Alcon-Couvreur Puurs, Belgium) eye drops were administered. Local application was further individualised based on repeated examination of the fundus in the first days and weeks after surgery.

Results were reported by median and range. The Mann-Whitney U test was used to compare clinical characteristics in infants who either received cryotherapy or laser photocoagulation.

A p-value level < 0.05 was considered significant.

RESULTS

During the period (2000-2005) studied, retinal surgery was performed in 35 infants. Sixteen infants were treated with cryotherapy (2000-2001) and 19 received laser photocoagulation (2001-2005). Clinical characteristics and data on postoperative management are presented in table 1. There were no significant differences in birth weight, gestational age at birth, weight or postnatal age at surgery. Eleven infants were still on respiratory support for medical indications before initiation of anaes-

Table 1: *Clinical characteristics and data on postoperative management in infants who either received cryotherapy or laser photocoagulation.*
Data are reported by median and range.

	Cryotherapy	Laser photocoagulation	p-value
Number of infants	16	19	
Gestational age at birth (weeks)	25.8 (24-28)	26 (23-29)	NS
Weight at birth (gram)	729 (400-1065)	689 (485-1330)	NS
Postnatal age at surgery (days)	60 (48-79)	63 (47-90)	NS
Weight at surgery (gram)	1595 (1020-2700)	1488 (995-2500)	NS
on respiratory support	6/16	5/19	NS
of whom on ventilatory support	1/16	1/19	NS
Duration postoperative ventilation (hours)	45 (24-72)	20 (6-108)	$p < 0.05$
Postoperative ventilation $\leqslant$ 24 hours	3/16	12/19	$p < 0.05$
Duration administration continuous opioids (hours)	71 (28-112)	43 (15-120)	$p < 0.05$
Duration regain full enteral nutrition (hours)	144 (68-580)	75 (42-140)	$p < 0.05$

thesia of whom 9 were on nasal CPAP and 2 were ventilated. Duration of postoperative ventilation was therefore calculated in 33 infants. A significant decrease in duration of postoperative ventilation (hours, $p<0.05$), in postoperative administration of intravenous analgesics (hours, $p<0.05$) and in time until regain of full enteral feeding (hours, $p<0.05$) were documented in infants who received laser photocoagulation compared to cryo-treated infants (table 1).

DISCUSSION

There are several reports on ophthalmologic advantages of laser treatment compared to cryotherapy for threshold ROP, but reports on anaesthetic and analgesic management during and following retinal surgery are limited [5,8,11].
There is still debate on the optimal anaesthetic strategy during retinal surgery for threshold ROP [9]. In contrast to adults in whom a locoregional approach is feasible, the perceived need for sedation and specific anatomic findings in neonates limit such an approach [10].
Retinal surgery is associated with a relevant pain response. This was illustrated in adults who underwent laser photocoagulation to treat diabetic retinopathy while we already reported on the increase in duration of administration of analgesics following cryotherapy when systematic evaluation and treatment of pain were introduced as standard of care [2,4].
Using the same structured approach, a decrease in duration of administration of analgesics with an associated reduction in duration of postoperative ventilation and a faster regain of full enteral feeding were observed in infants who received laser photocoagulation compared to cryo-treated infants. Although based on retrospective analysis, we believe that the reduced need for intravenous analgesics reflects a reduced postoperative pain response due to a less prominent tissue damage after laser photocoagulation.
We are aware that this study lacks the strength of a prospective design. More precise data on duration of anaesthesia and duration of surgery were not available and therefore, we can not discriminate between a potential shorter surgical time with an associated reduced duration of anaesthesia or a reduced postoperative inflammatory response. Finally, postoperative decisions on ventilation and on nutrition were made by the attending neonatologist not blinded for the type of surgical intervention.
Taking the above mentioned restrictions into account, a strong argument in favour of reduced tissue damage is the recent observation on the lack of increase in C reactive protein following laser photocoagulation [1,6].
In conclusion, besides long term visual outcome data following retinal surgery, there is also a clinical need to document the optimal surgical and anaesthetic approach. The potential increase in the number of interventions in line with the early treatment study makes a critical evaluation of this approach only more urgent [7]. The present findings do suggest that if short term non-ophthalmologic outcome crite-

ria are considered, laser photocoagulation is superior to cryo-treatment.

REFERENCES

(1) ALLEGAERT K., DEVLIEGER H., CASTEELS I. – Reduced inflammatory response after laser photocoagulation compared with cryoablation for threshold retinopathy of prematurity. J Pediatr Ophthalmol Strabismus 42; 264-266

(2) ALLEGAERT K., TIBBOEL D., NAULAERS G., TISON D., DE JONGE A., M. VAN DIJK, C. VANHOLE, H. DEVLIEGER – Systematic evaluation of pain in neonates: effect on the number of intravenous analgesics prescribed. Eur J Clin Pharmacol 2003; 59:87-90

(3) ALLEGAERT K., VANDEVELDE M., CASTEELS I., NAULAERS G., VANHOLE C., DEVLIEGER H. – Cryotherapy for threshold retinopathy: perioperative management in a single center. Am J Perinatol 2003;20:219-226

(4) COOK H.L., NEWSOM R.S., MENSAH E., SAEED M., JAMES D., FFTYTCHE T.J. – Entonox as an analgesic agent during panretinal photocoagulation. Br J Ophthalmol 2002; 86:1107-1108

(5) CRYOTHERAPY FOR RETINOPATHY OF PREMATURITY (CRYO-ROP) COOPERATIVE GROUP – Multicenter trial of cryotherapy for retinopathy of prematurity. Ophthalmological outcomes at 10 years. Arch Ophthalmol 2001; 119:1110-1118

(6) DANIELS J.G, ADAMS G.G. – Effect of laser photocoagulation for retinopathy of prematurity on C reactive protein. Arch Dis Childh Fetal Neonatal Ed 2004; 89:F470

(7) EARLY TREATMENT FOR RETINOPATHY OF PREMATURITY COOPERATIVE GROUP – Revised indications for the treatment of retinopathy of prematurity: results of the early treatment for retinopathy of prematurity randomized trial. Arch Ophthalmol 2003; 121:1684-1694

(8) FOROOZAN R., CONNOLLY B.P., TASMAN W.S. – Outcomes after laser therapy for threshold retinopathy. Ophthalmology 2001; 108:1644-1646

(9) HAIGH P.M., CHISWICK M.L., O'DONOGHUE E.P. – Retinopathy of prematurity: systemic complications associated with different anesthetic techniques at treatment. Br J Ophthalmol 1997; 81:283-287

(10) KALLIO H., PUSKA P., SUMMANEN P., PALOHEIMO M., MAUNUKSELA E.L. – Retrobulbar or peribulbar block with 0.2% ropivacaine or 1% lidocaine for transscleral cyclophotocoagulation or retinal panphotocoagulation. Reg Anesth Pain Med 1999; 24:341-346

(11) LAWS F., LAWS D., CLARK D. – Cryotherapy and laser treatment for acute retinopathy of prematurity: refractive outcomes, longitudinal study. Br J Ophthalmol 1997; 81:12-15

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