Epidemiology and outcomes of inguinal surgery with or without regional anaesthesia in neonates and small infants: a subanalysis of the NECTARINE database

F Veyckemans, Retired Consultant paediatric anaesthesiologist, Brussels, Belgium. veyckemansf@gmail.com

C Sola, Department of Anaesthesia and Critical Care Medicine, Paediatric Anaesthesia Unit, Montpellier University Hospital, France. Institute of Functional Genomics (IGF), University of Montpellier, CNRS, INSERM, France. c-sola@chu-montpellier.fr

J C de Graaff, Department of Anesthesia, Erasmus MC-Sophia Children's Hospital, Rotterdam, The Netherlands. jurgendegraaff@gmail.com

K Becke-Jakob, Department of Anaesthesia and Intensive Care, Cnopf Children´s Hospital – Hospital Hallerwiese, Nürnberg, Germany. Karin.Becke-Jakob@diakonieneuendettelsau.de

M Zielinska, Department of Paediaric Anaesthesiology and Intensive Care, Wroclaw Medical University, Wroclaw, Poland. marzena.zielinska@gmail.com

TG Hansen, Department of Anaesthesia & Intensive Care, Akershus University Hospital and Olso University . tomghansen@dadlnet.dk

SM Walker, Department of Anaesthesia and Pain Management, Great Ormond Street Hospital NHS Foundation Trust, London, UK. suellen.walker@ucl.ac.uk
N Disma, Unit for Research in Anaesthesia, IRCCS, Istituto G Gaslini, Genova, Italy. nicoladisma@gmail.com

W Habre, Department of Anaesthesiology, Pharmacology, Intensive Care and Emergency Medicine, University Hospitals of Geneva, Geneva, Switzerland. Walid.Habre@unige.ch

Keywords: regional anaesthesia, general anaesthesia, complications, neonate, infant

Corresponding author: Francis Veyckemans at veyckemansf@gmail.com

Hugo Verriest Str 19, B 1140 Brussels, Belgium. tel +32 496 785811

Word count: text 1392, refs 208, tables 345

The use of regional anaesthesia (RA) when feasible is often recommended in neonates and small infants undergoing superficial surgery either to avoid general anaesthesia (GA) or to reduce the depth of the associated general anaesthesia (GAR). The aims are to reduce exposure to GA agents (and its potential neurodevelopmental consequences, if any), decrease the risk of postoperative apnoea, or decrease the risks associated with tracheal intubation (difficulties, hypoxaemia, laryngotracheal morbidity) and controlled ventilation. Except for the results of the GAS study (1), there are little data on the associated critical events and outcomes. In the original NECTARINE publication (2) uni- and multivariable analyses showed a trend toward fewer interventions for critical events when RA or GAR was used in comparison with GA. But these were raw data on the whole cohort of infants with different types of surgery and included cases of local anaesthetic infiltration of the wound. To draw more focused conclusions, we decided to reanalyse those data after excluding the local infiltration cases and to compare the results in infants undergoing the same procedures under either GA, GAR, or RA alone.. The main outcome of this subanalysis was thus to evaluate the incidence of interventions in response to predefined perioperative severe critical events in neonates and infants undergoing the same surgery with RA alone, GAR, or GA. The secondary outcomes were morbidity and mortality at 30 days.

Methods

The design of the European multicentre, prospective, observational cohort study NECTARINE (ClinicalTrials.gov NCT02350348) has been described previously (2): 165 participating centres from 31 European countries recruited 5609 patients aged less than 60 weeks postmenstrual age (PMA) undergoing 6542 procedures between March 2016 and

January 2017. Permission to use the NECTARINE electronic database to perform this secondary study was obtained from the ESAIC Research Department.

We extracted from this database the groups of surgeries in which a sufficient number of cases were performed under GA, GAR, or RA alone after excluding the cases in which wound infiltration was used. The 4 most common surgical procedures in which RA, GAR, or GA was used were: 1371 cases of inguinal surgery, 248 cases of congenital pyloric stenosis, 161 cases of anorectal malformation, and 94 cases of club foot repair. We present hereafter the detailed analysis of the data about inguinal surgery.

Statistics

Descriptive statistics. Results are presented as mean ± SD or median. Categorical variables and incidence of events were compared with the Chi^2 test and calculation of Relative Risk (RR) [95% CI] (GraphPad Prism V9).

Results

During the study period, 1371 infants were operated on for uni- or bilateral inguinal hernia repair, orchidopexy or orchidectomy, or an ovarian hernia repair. The anaesthetic technique used according to PMA at the time of inclusion showed a trend toward a more frequent use of RA in the youngest ones (Table 1). The mean ± SD and [median] postnatal age in days at surgery was 73.2 ±36.5 [67.5] in RA, 75.8 ± 42.1 [72] in GA and 80.1 ± 40.9 [76] in GAR. The mean ± SD and [median] weight in kg at surgery was 3.8 ± 1.1 [3.8] in RA, 4.6 ± 1.4 [4.5] in GA and 4.4 ± 1.3 [4.4] in GAR .

Awake spinal blockade was the most frequently used technique in the RA group (n = 153, 78.9%) while caudal blockade was most frequently used in the GAR group (n = 640, 75.1%; Table 2). However, 41 awake caudal blocks and 39 spinal blocks were recorded as associated with a GA. Due to the design of the electronic case report forms (eCRF), we were unable to determine whether GA was used in the latter cases to help perform the block or to supplement a failed or insufficient awake spinal or caudal block.

The incidence of any critical event requiring intervention varied across groups (Chi^2 $P<0.001$). The proportion requiring interventions did not differ between GA and GAR groups (28.3 vs 27.1%) , but was greater in the GA vs RA group (28.3 vs 9.3%, RR 1.27 [95%CI 1.17 – 1.38]) (Table 3a). This does not control for the type of surgery or additional co-morbidities that may have influenced the choice of anaesthetic technique. There were however more interventions for an airway event in the GA than in the GAR group: 7.7 vs 3.9% (RR 1.04 [95%CI 1.01 – 1.08). Due to the small numbers and limited granularity of the data recorded, we were unable to determine whether there was any association between the type of airway interface used, or the presence of preoperative congenital, respiratory, or cardiac problems.

Interventions concerning oxygenation occurred more frequently in the GA and GAR groups and were equally distributed between induction, maintenance, and awakening (Table 3a). Surprisingly, 8/9 oxygenation events in the RA group occurred during maintenance; whether this is related to excessive cephalad spread of the block, pain or sedation could not be determined.

The incidence of haemodynamic events varied across groups (Chi^2 $P<0.001$). There were more haemodynamic events in the GAR (15.4%) than in the GA (6.8%) and RA (5.2%) groups (RR 1.10 [95%CI 1.06 - 1.15] and RR 1.12 [1.07-1.17], respectively). Moreover, most occurred during the maintenance of anaesthesia. In the GAR group, due to a lack of precise intraoperative data, we were unable to determine whether neuraxial blockade (n = 684) was more often associated with cardiovascular instability than an abdominal wall block (n=159). The 30-days outcomes were similar among the three anaesthetic strategies (table 3b).

Discussion

This sub-analysis of the NECTARINE database is consistent with observations across the whole cohort: i.e. that there is a small reduced risk of critical events requiring intervention in the RA group, especially for respiratory and airway management events. While, the overall incidence of critical events requiring intervention and 30-day outcome did not differ when a regional technique was added to GA (i.e. GAR versus GA), more interventions for haemodynamic events were required in the GAR group.

Regarding safety, although the complication rate of regional anaesthesia is reported to be 4 times greater in children less than 6 months old (3), no complications were observed in the NECTARINE study. We acknowledge that the NECTARINE eCRF was not designed to record events such as total spinal or local anaesthetic systemic toxicity, but we assume that these complications would have resulted in a report of an intervention for associated haemodynamic or respiratory critical events. For comparison, the incidence of local anaesthetic systemic toxicity in neonates and infants less than 6 months of age was 1/220 spinal blocks (0.45%) and 3/6182 caudal or epidural blocks (0.05%) in the 2018 PRAN series (3). In the same way, the incidence of bloody taps was 30% in the spinal cases of the GAS study (4).

It is generally assumed that combining a regional block with general anaesthesia does not increase the anaesthetic risk. Based on our findings, we would claim that in neonates and small infants, GAR reduces the procedural risks associated with RA (immobile target), as also demonstrated by the PRAN data (3) but could increase the risk of haemodynamic instability when compared with GA or RA: whether this is due to the additional effects of vasodilation produced by general anaesthesia and a neuraxial block or to relative overdose in general anaesthetics cannot be determined from the current data. Theoretically, a wall block should not have any haemodynamic effect but this needs to be confirmed given that a caudal block can generally be combined with a lighter general anaesthetic than a wall block.

The results of this secondary analysis should be interpreted with caution because NECTARINE was not a randomised trial but an observational study with large variability of practice among the participating centres. Moreover, the eCRF was not designed to report the success rate nor the complications (e.g., bloody taps, total spinal) of the regional blocks used. Last, some data were missing.

The limitations of the current subanalysis suggest additional data for inclusion in future prospective studies of regional anaesthesia in children: 1) the initial anaesthetic strategy chosen (RA, GA, GAR) and why (e.g. anatomical cause, level of expertise, parental refusal, comorbidity, etc), 2) the technique performed, including airway management, 3) the problems encountered (bloody or dural tap, systemic toxicity), 4) whether the strategy had to be modified in the OR and why (technical failure, insufficient block, too long surgery, airway problem), as well as 5) the intraoperative ventilation and haemodynamic parameters, and 6) the outcome.

References

1.Davidson AJ, Morton NS, Arnup SJ, de Graaff JC, Disma N, Withington DE et al. Apnea after awake regional and general anesthesia in infants . The general anesthesia compared to spinal anesthesia study. Anesthesiology 2015; **123**: 38-54.
DOI 10.1097/ALN.0000000000000709

2. Disma N, Veyckemans F, Virag K, Hansen TG, Becke K, Harlet P et al. Morbidity and mortality after anaesthesia in early life: results of the European prospective multicenter observational study, neonate and children audit of anaesthesia practice in Europe (NECTARINE). Br J Anaesth 2021; **126**: 1157-1172. DOI 10.10116/j.bja.2021.02.016

3. Walker BJ, Long JB, Sathyamoorthy M, Birstler J, Wolf C, Bosenberg AT et al. Complications in pediatric regional anesthesia. An analysis of more than 100,000 blocks from the Pediatric Regional Anesthesia Network. Anesthesiology 2018; **129**: 721-732. DOI 10.1097/ALN.0000000000002372

4. Frawley G, Bell G, Disma N, Withington DE, de Graaff JC, Morton NS et al. Predictors of failure of awake regional anesthesia for neonatal hernia repair. Anesthesiology 2015 ; **123** :55-65. DOI 10.1097/ALN.0000000000000708

Assistance with the study: the authors thank Mrs Katalin Virag, M Stat, the statistician of the NECTARINE study, for helping to retrieve the data and starting the statistical analysis.

Financial support and sponsorship: none to declare

Conflicts of interest: TGH is a Deputy-Editor-in-Chief of the EJA

Table 1 : Distribution of anaesthetic techniques according to PMA at inclusion (n (%))

PMA weeks	GA	RA	GAR
28-31	2 (0.6)	0	0
32-36	10 (3.1)	11 (5.7)	18 (2.1)
37-40	41 (12.6)	43 (22.2)	108 (12.7)
41-44	78 (24.0)	65 (33.5)	216 (25.4)
45-60	194 (59.7)	75 (38.7)	510 (59.9)
total	325	194	852

Table 2 : Distribution of the regional blocks used

	RA	GAR
n cases (%)	325	852
spinal	153 (78.9)	39 (4.6)
caudal	41 (21.1)	640 (75.1)
epidural	0	5 (0.6)
TAP	0	25 (2.9)
ilioinguinal	0	128 (15)
periumbil	0	6 (0.8)
other	0	7 (0.8)

Table 3a. Incidence and distribution of interventions for critical events. The major differences are printed in bold

Variable N (%) [ ] = missing data	**GA 325**	**RA 194**	**GAR 852**
At least 1 intervention	**92 (28.3)**	**18 (9.3)**	**231 (27.1)**
Airway event Unplanned intubation Laryngospasm Bronchospasm	**25 (7.7)** 5 2 1	**0**	**33 (3.9)** 15 2 2
Difficult airway	**25 (7.7)**	**0**	**33 (3.9)**
Hypoxaemia Induction Maintenance Awakening Induction and awakening	**46 (14.2)** 11 (3.4) 11(3.4) 17 (5.2) 4 (1.2)	**9 (4.6)** 0 8 (4.1) 1 (0.5) 0	**85 (10.0)** 26 (3.1) 24 (2.8) 24 (2.8) 4 (0.5)
Hypoxaemia	**46 (14.2)**	**9 (4.6)**	**85 (10.0)**
Hypo- or hypercapnia	**22 (6.8)**	**0**	**38 (4.5)**
Metabolic	7 (2.2)	1 (0.5)	6 (0.7)
Haemodynamic instability	**22 (6.8)**	**10 (5.2)**	**131 (15.3)**
Hypo-hyperthermia	6 (1.8)	2 (1)	18 (1.3)
Brain oxygenation	2 (0.7) [54]	0 [14]	6 (0.8) [126]
Transfusion for anaemia	0	0	3 (0.4)
Postop NICU/PICU/HDU	116 (35.7)	48 (24.7)	209 (24.6)
Postop ward	207 (63.7)	139 (71.6)	631 (74.1)
Postop other	2 (0.6)	7 (3.6)	12 (1.4)

Table 3b. Outcome at 30 days. The major differences are printed in bold.

Variable N (%) [ ] = missing data	**GA 320**	**RA 192**	**GAR 837**
home	281 (93.7) [20]	162 (93.6) [19]	750 (96.5) [60]
hospital	17 (5.7)	10 (2.9)	23 (3.0)
death	0	0	1 (0.1)
PICU	1(0.7)	1 (0.6)	3 (0.4)
Morbidity 30d	14 (4.8) [26]	6 (3.5) [19]	23 (3) [82]