Neuroblastoma in Children: Intraoperative Goal Directed Therapy, Intraoperative And Postoperative Outcomes

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Short Report

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Abstract

Background

Neuroblastoma is the most common tumor in children. Anesthetic management can be challenging due to the localization, catecholamine-secreting characteristic of the tumor. We undertook a secondary analysis in a previously study to describe patients who underwent neuroblastoma resection.

Objective

To describe intraoperative and postoperative outcomes in patients who underwent neuroblastoma resection and to propose optimal intraoperative management for postoperative outcome improvement.

Methods

Secondary analysis of children who had neuroblastoma resection in the initial retrospective study.

Results

There were 16 patients with a mean age of 39.3 ± 22.1 months. Seven (43.8%) patients presented with intraoperative or postoperative complications. One (6.3%) patient had intraoperative broncho-laryngospasm and difficult intubation respectively. Two (12.5%) patients had intraoperative hemorrhagic shock. One patient (6.3%) had postoperative renal failure. Two patients (12.5%) had postoperative respiratory failure and 3 (18.8%) patients had postoperative cardiocirculatory failure. One (6.3%) had postoperative pulmonary sepsis and septicemia respectively. Thirteen (81.3%) patients were intraoperatively transfused. There was no in-hospital mortality.

Conclusion

Neuroblastoma surgery can be a challenging situation where cardiovascular instability, high blood loss and transfusion requirements can be encountered. Consequently, preoperative preparation, intraoperative optimal management with validated means in children are necessary for a better postoperative outcome in this surgical setting.

Introduction

Neuroblastoma is the most common tumor in children with an incidence of 10.2 per million children under 15 years old and is responsible of 13–15% of deaths due to cancer in children (1,2,3,4). Long term prognosis depends on the characteristics of the tumor with five year survival in low risk and high risk

neuroblastoma varying from 90–95% to 40–50% respectively (2,5). Surgical complications after surgery depend on the localization of the tumor and are various including chyloabdomen, chylothorax, Horner syndrome, pneumothorax, injury of the renal blood vessels, injury of the inferior vena cava etc...(6,7).

Neuroblastoma can present different localizations as an abdominal mass from the medulla adrenergic cells in 35% of the cases, as spinal paraspinal ganglia in 35% of the cases, as posterior mediastinal mass in 20% of the cases, as pelvis and neck masses in respectively 5% of the cases (1). Therapeutic management of these tumors is multidisciplinary and can include surgery, chemotherapy, autologous stem cell transplant, radiotherapy, immunotherapy depending on the characteristics of the tumor (1).

Anesthetic management of neuroblastoma surgery can be challenging due the catecholamine secreting characteristics, due to the localization such as a mediastinal presentation which can cause cardiocirculatory collapse at induction of anesthesia and increased blood loss if the tumor is close to great vessels (6,7,8,9,10). This emphasizes the importance of preoperative preparation of these tumors for optimal intraoperative management.

In a previously published retrospective study in 594 patients that reported predictors of intraoperative and postoperative outcomes, there were patients who underwent neuroblastoma surgery (11).

We aimed in this manuscript to describe as a secondary analysis, intraoperative and postoperative outcomes in neuroblastoma surgical patients included in the initial study (11). The secondary objective of this analysis was to propose intraoperative management for optimal postoperative outcome in this surgical setting where intraoperative cardiocirculatory instability, blood loss and fluid therapy requirements can be high.

Methods And Materials

Secondary analysis of patients who underwent neuroblastoma surgery included in the initial study (11).

The study was approved by the Ethics Committee of Necker Enfants Malades University Hospital under registration number 2017-CK-5-R1 on 21 March 2017.

Patients were retrospectively included from 1 January 2014 to 17 May 2017.

Inclusion criteria were patients who underwent neuroblastoma resection aged less than 18 years old and included in the initial study.

Exclusion criteria were patients who did not undergo neuroblastoma surgery and aged more than 18 years old included in the initial study.

Statistics were analyzed with XLSTAT 2020.4.1. software. Continuous variables were expressed as medians with ranges or means with standard deviations. Categorical variables were described in proportions.

In our hospital, patients who are scheduled for catecholamine-secreting neuroblastomas surgery were managed according to a defined protocol described here.

Preoperatively patients had prazosin at 0.015 mg/kg to 0.5 mg/kg/day administered in three times orally.

Labetalol could be administered at 5 to 15 mg/kg/day (as a maximum dose of 5 mg x3/day) in 2–3 times orally or 0.5-1 mg/kg/h as an intravenous (IV) infusion in case of secondary tachycardia with alpha-blocking agents.

Acetabutolol could be administered at 5–15 mg/kg/day in two times in case of secondary tachycardia with alpha-blocking agents or refractory hypertension.

Nicardipine could be administered preoperatively as an intravenous (IV) infusion at 0.5-2µg/kg/minute for refractory hypertension.

Surgery was scheduled at least 14 days after anti-hypertensive therapy was started and controlled. All patients had a preoperative echocardiography, a complete blood cell count, coagulation tests depending on the patient's status, blood urea nitrogen, creatinin plasmatic levels, complete plasmatic electrolyte levels, available cross-match and packed red blood cells in case of intraoperative transfusion.

Before induction of anesthesia, an intravenous peripheral line was available.

Induction of anesthesia was performed in a smooth manner with sevoflurane in a mixture of air and oxygen, intravenous sufentanil at 0.2 µg/kg bolus. Airway was secured with endotracheal intubation. Maintenance of anesthesia was performed with sevoflurane in air-oxygen, sufentanil at 0.05/kg bolus, Muscle relaxation for surgical reasons could be performed with cisatracurium at 0.15 mg/kg or rocuronium at 0.6 mg/kg bolus.

Antibiotic therapy was performed with cefazolin 50 mg/kg intravenously.

Two large bore peripheral intravenous lines were inserted, an indwelling catheter, a naso-gastric tubing, a central core temperature probe, muscle relaxation monitoring device were inserted. All patients had a rapid fluid infusion pump and a fluid warming device available.

After induction of anesthesia an arterial catheter and a central venous line were inserted. According to the surgical technical approach (laparotomy versus laparoscopy), an epidural catheter or paravertebral catheter was inserted for intraoperative and postoperative analgesia. Analgesia with epidural catheter or paravertebral catheter was performed with levobupivacaine 0.125% or 0.0625% at 0.2-0.3ml/kg/h according to the age of the patient.

Intraoperatively, intravenous urapidil was administered at 2 mg/kg/h as a starting infusion dose and at 0.8 mg/kg/h as a maintenance infusion dose to manage hypertension.

Intravenous esmolol in case of tachycardia or refractory hypertension could be started as an infusion at 25–200 µg/kg/h.

Intravenous labetalol as an infusion at 0.25-2mg/kg/h could be administered as an alternative to urapidil or esmolol.

Intraoperative fluid therapy with crystalloids (Ringer Lactate® or chloride sodium 0.9%) or with colloids (plasmion® or voluven ®) was managed with the aims to avoid catecholamine induced hypovolemia, vasodilation due to anti-hypertensive medications and hypotension after tumor resection.

Glycemia was monitored and 5% glucose containing crystalloids were administered to avoid hypoglycemia after tumor resection.

Postoperative analgesia was performed with IV acetaminophen 15 mg/kg/6h, epidural or paravertebral catheter with levobupivacaine 0.125% or 0.0625% at 0.1–0.2 ml/kg/h, IV nalbuphine at 0.2 mg/kg/6h or IV morphine as patient controlled analgesia bolus if necessary.

Patients were extubated in the operating room and transferred in the postinterventional care unit and afterwards in the pediatric intensive care unit for surveillance.

Results

Table 1 illustrates general characteristics

There were 16 patients with a mean age of 39.3 ± 22.1 months and a median weight of 13[5.2-22] kilograms. There were one (6.3%), three (18.8%), and twelve (75%) American Society of Anesthesiologists (ASA) grade 1, 2 and 3 patients, respectively. All patients had elective surgery. There were no reoperations. Seven (43.8%) patients presented with intraoperative or postoperative complications. One (6.3%) patient had intraoperative broncholaryngospasm and difficult intubation. Two (12.5%) patients had intraoperative hemorrhagic shock. One patient (6.3%) had postoperative renal failure. Two patients (12.5%) had postoperative respiratory failure, and 3 (18.8%) patients had postoperative cardiocirculatory failure. One (6.3%) had postoperative pulmonary sepsis and septicemia. Thirteen (81.3%) patients were intraoperatively transfused with packed red blood cells (PRBCs) and/or fresh frozen plasma (FFP) and/or concentrated platelet units (CUPs). There was no in-hospital mortality.

The mean preoperative and postoperative hemoglobin levels were 10.1 ± 0.9 g/dL and 11.1 ± 2.2 g/dL, respectively. The median crystalloid and colloid volumes were 1300 [100-2900] ml and 305 [60-1000] ml, respectively. The median length of intensive care unit stay (LOSICU) was 7[0-16] days. The median length of hospital stay in the conventional ward (LOS) was 8.5[1-17] days. The median total length of hospital stay (TLOS=LOSICU+LOS) was 15[3-33] days. The median length of mechanical ventilation (LMV) was 0.5[0-5] days.

Table 2 illustrates co-morbidities

The most common comorbidity was cancer in eight (50%) patients, followed by chronic renal failure in one (6.3%) patient.

Discussion

Intraoperative neuroblastoma surgery can be a challenging situation because of the possible hemodynamic instability that can be observed in catecholamine secreting tumors, due to the anatomic position of the tumor which can be near great vessels with possible increased blood loss and transfusion requirement during surgery. Intraoperative fluid and hemodynamic therapy guided with validated tools in children is mandatory in this surgical setting. Esophageal Doppler probe and transthoracic echocardiography to assess for fluid responsiveness with aortic peak flow velocity are validated tools in children and they should be integrated in intraoperative patient management (12,13,14,15,16,17) in this setting. Non optimal regional renal, cerebral oxygen saturation (as assessed with near infrared spectroscopy NIRS), lactate levels and mixed central venous oxygen saturation values have been correlated to adverse postoperative outcomes in terms morbidity and mortality in children, thus these parameters should be part of the monitoring in neuroblastoma surgery (18).

Neuroblastoma resection is a potential hemorrhagic surgery as illustrated by the results of this study where the transfusion rate is high. Transfusion goal-directed therapy with point of care viscoelastic assays need to be part of patient blood management in this surgery in order to optimize blood product administration and postoperative outcome in terms morbidity and LOS (19,20,21,22). As described previously in other potential hemorrhagic surgeries, point of care viscoelastic methods serve as a guide to transfuse the right product at that right time with results available with ten minutes which is faster than conventional coagulation tests.

Intraoperative goal directed therapies with validated tools need to be part of patient management in major surgery in children for intraoperative and postoperative optimization (27,28,29,30,31,32).

Conclusion

Neuroblastoma surgery can be a challenging situation where cardiovascular instability, high blood loss and transfusion requirements can be encountered. Consequently, preoperative preparation, intraoperative optimal management with validated means in children are necessary for a better postoperative outcome.

Declarations

Conflicts of Interest: The author declared no conflicts of interest.

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Author contributions: Claudine Kumba conceptualized and designed the study and drafted the initial manuscript. She designed the data collection instruments, collected data, carried out initial and final analyses.

Ethics Approval: This study received approval from the Ethics Committee of Necker on 21 March 2017 under registration number 2017-CK-5-R1 and waived patient consent.

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Tables

Table 1 General Characteristics

Characteristic	N=16
Mean age $\pm$ standard deviation in months	39.3 $\pm$ 22.1
Median weight [range] in kilograms	13[5.2-22]
ASA I n (%)	1(6.3)
ASA II n (%)	3(18.8)
ASA III n (%)	12(75)
Emergency surgery n (%)	0(0)
Elective surgery n (%)	16(100)
Re-operation n (%)	0(0)
Patients with intra-operative and or postoperative complications (organ failure or sepsis) n (%)	7(43.8)
Intraoperative broncho-laryngospasm n (%)	1(6.3)
Intraoperative difficult intubation n (%)	1(6.3)
Intraoperative hemorrhagic shock n (%)	2(12.5)
Postoperative renal failure n (%)	1(6.3)
Postoperative cardio-circulatory failure n (%)	3(18.8)
Postoperative respiratory failure n (%)	2(12.5)
Postoperative pulmonary sepsis n (%)	1(6.3)
Postoperative septicemia n (%)	1(6.3)
In-hospital mortality n (%)	0(0)
Transfusion n (%)	13(81.3)
Median packed red blood cells volume in ml [range]	1[0-2]
Median fresh frozen plasma volume in ml [range]	0[0-5]
Median concentrated platelet units [range]	0[0-1]
Mean preoperative hemoglobin levels $\pm$ standard deviation in g/dL	10.1 $\pm$ 0.9
Mean postoperative hemoglobin levels $\pm$ standard deviation in g/dL	11.1 $\pm$ 2.2
Median crystalloid volume in ml [range]	1300[100-2900]
Median colloid volume in ml [range]	305[60-1000]
Median length of intensive care unit stay in days [range]	7[0-16]
Median length of hospital stay in days [range]	8.5[1-17]
Median total length of hospital stay in days [range]	15[3-33]
Median total length of mechanical ventilation in days [range]	0.5[0-5]

Table 2 Co-morbidities

orbidity	number of patients (%)
er	8(50)
nic renal failure	1(6.3)