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The beneficial effect of air cleanliness with ISO 14644-1 class 7 for surgical intervention in a neonatal intensive care unit

A 10-year experience

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Abstract

Whether critically ill neonates needing a surgical intervention should be transferred to an operating room (OR) or receive the intervention in a neonatal intensive care unit (NICU) is controversial. In this study, we report our experience in performing surgical procedures in a NICU including air cleanliness.

This was a retrospective study performed at a metropolitan hospital. The charts of all neonates undergoing surgical procedures in the NICU and OR were retrospectively reviewed from January 2007 to June 2017. Data on baseline characteristics, procedure and duration of surgery, ventilator use, hypothermia, instrument dislocations, surgery-related infections and complications, and outcomes were analyzed.

Ninety-two neonates were enrolled in this study, including 44 in the NICU group and 48 in the OR group. The air cleanliness was International Organization for Standardization (ISO) 14644-1 class 7 in the NICU and class 5-6 in the OR. The NICU group had a younger gestational age and lower birth body weight than the OR group. The OR group had a higher incidence of hypothermia than in the NICU group (56.3% vs 9.1%, $P < .001$). However, there were no significant differences in surgical site related infections or mortality between the 2 groups.

This study suggests that performing surgical procedures in a NICU with air cleanliness class 7 is as safe as in an OR, as least in part, when performing patent ductus arteriosus ligation and exploratory laparotomy.

Abbreviations: CNS = central nervous system, FiO_2 = fraction of inspired oxygen, HEPA = high efficiency particulate air, ISO = International Organization for Standardization, MAP = mean airway pressure, NICU = neonatal intensive care unit, OR = operating room, PDA = patent ductus arteriosus.

Keywords: bedside surgery, neonatal intensive care unit, operating room

1. Introduction

Many critically ill neonates in a neonatal intensive care unit (NICU) require surgical interventions. Traditionally, these neonates are transferred to an operating room (OR) outside of the NICU.[1] However, previous studies have shown that complications can occur when transporting such critical patients.[2,3] Hypothermia has been reported to be the most significant side effect associated with transport, especially in preterm infants.[1,3,4] Other side effects, including hypoglycemia, variations in blood pressure and heart rate, endotracheal dislocation, and changes in blood glucose level, have also been reported.[1,5] Body weight is thought to be the most important risk factor for outcomes associated with the transport of critical patients.[1]

Several studies have discussed ways to avoid these adverse events, one of which is to perform the surgical procedure at the NICU to avoid the risk associated with transport, especially for low birth weight premature infants, clinically unstable neonate, and critically ill patients receiving inotropes or high-frequency oscillatory ventilatory support.[6,7] Other methods include training a transport team or creating guidelines to improve the process to reduce the risk of complications.[1] An increasing

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number of studies have investigated performing surgery in the NICU; however, the risk of infection associated with surgery remains.[8,9] In order to solve this problem, some hospitals have built an OR within the NICU with good outcomes.[6] Despite the number of studies that have investigated performing surgery in a NICU, no study has investigated cleanliness in the NICU. Air cleanliness is based on International Organization for Standardization (ISO)14644-1 with numerical classes.[10] This standard is used to evaluate the environment of an OR.

Because it is impossible to have an OR in all NICUs, we established a standard to perform surgical procedures in our NICU. We controlled the cleanliness of NICU according to ISO14644-1 and evaluated the outcomes of neonates who underwent patent ductus arteriosus (PDA) ligation and laparotomy at our NICU over a 10-year period to develop guidelines to improve medical quality.

2. Materials and methods

There are 15 beds in the NICU of EDA Hospital, Kaohsiung, Taiwan, which is a metropolitan hospital consisting of 1200 beds. Air cleanliness in the NICU is controlled to ISO14644-1 class 7 and is regularly checked every 6 months. Room temperature is controlled to within 23°C to 26°C, and room humidity is controlled between 50% and 60% relative humidity. Comparisons of the environment between our NICU and OR are summarized in Table 1. Before surgery, we moved the neonates to an open incubator in the same NICU room and added extra baby warmers according to their body temperature. The surgical team consisted of surgeons, a neonatologist, an anesthetist, an anesthesia nurse, a scrub nurse, a circulating nurse, and a respiratory therapist. Continued monitoring was provided during the surgery, and the neonatologist and respiratory therapist adjusted ventilation during surgery. After surgery, the primary care nurse and neonatologist looked after the neonate, who was transferred back to the incubator, if needed, after their condition was stable.

We retrospectively reviewed the charts of all neonates who underwent surgical procedures in our NICU from January 2007 to June 2017. Analysis of these data showed that the majority of the neonates underwent PDA ligation, laparotomy, and central nervous system (CNS)-related surgery. CNS-related surgery included surgical treatment for hydrocephalus or repair of meningomyelocele in neonate. Those undergoing surgery in the NICU were classified as the NICU group, and those who received these surgical procedures in the OR were classified as the OR group. Ethical approval was granted for this study by the Institutional Review Board of the E-Da hospital (EMRP-107-016).

The following data were collected from the medical charts: sex, gestational age, birth weight, age and body weight at the time of surgery, surgical procedures and duration, preoperative waiting time from being on call to the commencement of the operation (defined as the time for transfer and preoperative preparation), ventilator information, hypothermia, instrument dislocations, total days of admission, intravenous fluid during surgery, prophylactic antibiotic use and recent antibiotic use before surgical intervention, incidence of surgery-related infections, and outcomes. The mean airway pressure (MAP) and the fraction of inspired oxygen (FiO_2) were used to measure respiratory support. Hypothermia was defined as a temperature < 35.5°C. Surgery-related infections were defined as culture-proven infections at the wound or surgical drainage sites within 1 week of surgery. Mortality was defined as patient who death before discharged due to sepsis after surgery.

SPSS version 17.0 (SPSS Inc., Chicago, IL) was used for all statistical analyses. The mean, standard deviation, median, and range were calculated for continuous variables. The X^2 test and Fisher exact test were used to determine significant differences in categorical variables between groups, and the Wilcoxon rank sum test was used to determine significant differences in continuous variables between groups. Statistical significance was set at $P < .05$.

Table 1

Comparison of environment between neonatal intensive care unit (NICU) and operating room (OR).

	NICU	OR
Temperature, °C	23–26	18–22
Humidity (%)	50–60	55–75
Particle deposition (particles/m^3 of air)	94,500–233,800	0–17,500
Class of ISO 14644-1	Class 7	Class 5–6

Table 2

Procedures and surgical duration performed in the neonatal intensive care unit.

Surgical procedure	Number	Surgical duration, min
PDA ligation	32	78 (35–150)
Exploratory laparotomy	11	96 (40–150)
Repair of meningocele	1	270

PDA = patent ductus arteriosus.

3. Results

There were 44 patients in the NICU group and 48 patients in the OR group. In the NICU group, 32 patients received PDA ligation, 11 patients received laparotomy, and 1 patient received CNS-related surgery. In the OR group, 6 patients received PDA ligation, 36 patients received laparotomy, and 6 patients received CNS-related surgery.

We compared baseline characteristics between the 2 groups, including gestational age, birth weight, age at the time of surgery, and preoperative FiO_2 and MAP in order to understand the baseline status of the neonates before surgery (Tables 2 and 3). The mean gestational age in the NICU group was 30.6 ± 4.4

Table 3

Demographic characteristics among infants who received operation in the neonatal intensive care unit (NICU) group versus the operating room (OR) group.

	NICU (n = 44)	OR (n = 48)	P
Male	20	21	.869
*Gestational age, wk	30.6 ± 4.4	36.4 ± 4.3	<.001
*Birth weight, g	1480 ± 793	2430 ± 874	<.001
*Postnatal age at surgery, d	16.6 ± 20.8	45.9 ± 49.9	<.001
Surgical procedure			
PDA ligation	32	6	
Laparotomy	11	36	
CNS-related surgery	1	6	

Data are presented as numbers of patient or mean ± standard deviation.
CNS = central nervous system, PDA = patent ductus arteriosus.
* $P < .05$.

weeks, compared with 36.4 ± 4.3 weeks in the OR group. The mean birth weight in the NICU group was 1480 ± 793 g, compared with 2430 ± 874 g in the OR group. The postnatal ages at surgery were 16.6 ± 20.8 days in the NICU group and 45.9 ± 49.9 days in the OR group. The mean body weight at surgery was 1566 g in the NICU group, compared with 3237 g in the OR group ($P < .001$). In addition, gestation age, birth weight, body weight at the time of surgery, and postnatal age at surgery were all significantly lower in the NICU group than the OR group ($P < .05$). Before the surgery, significantly more neonates in the NICU group required mechanical ventilation than the OR group (70.5% vs 31.3%, $P = .001$). In addition, significantly more neonates in the NICU group required inotropic agents than the OR group (38.6% vs 8.3%, $P = .001$). The baseline mean FiO_2 (41.2%) and mean MAP (9.1 cmH_2O) were significantly higher in the NICU group than in the OR group (FiO_2 30.8%, $P = .009$; MAP 6.9 cmH_2O, $P = .03$). The mean preoperative body temperature was 36.7°C in the NICU group, and 36.8°C in the OR group ($P = .211$).

The postoperative characteristics and surgery-related events are listed in Table 4. The preoperative waiting time was not significantly different between the NICU group and OR group (32.7 vs 31.6 minutes, $P = .509$); however, the duration of surgery was significantly longer in the OR group (133.5 minutes) than in the NICU group (86.8 minutes, $P < .001$).

The mean postoperative body temperature was significantly different between the 2 groups, although it was similar before surgery (36.4°C in the NICU group, and 35.9°C in the OR group, $P = .002$). The lowest body temperature during surgery was 35.2°C in the OR group, which was significantly lower than that in the NICU group (36.1°C, $P < .001$). Four patients (9.1%) in the NICU group had hypothermia during surgery, compared with 27 patients (56.3%) in the OR group ($P < .001$). The postsurgical FiO_2 was still higher in the NICU group (NICU 46% vs OR 35%, $P = .011$); however, there was no significant difference in postsurgical MAP between the 2 groups (NICU 9.6 cmH_2O vs OR 8.1 cmH_2O, $P = .072$). The mean total days of admission was significantly higher in the NICU group (NICU 81 days vs OR 51 days, $P = .006$).

The OR group received significantly more intravenous fluid supplements during surgery, and significantly more neonates in the NICU group required postsurgical inotropic agents than those in the OR group (NICU 45.4% vs OR 16.7%, $P = .003$).

Although 1 case had endotracheal tube dislocation during the surgical procedure in the NICU group, there was no statistically significant difference in endotracheal tube dislocation rate between the 2 groups. There was also no statistically significant difference in prophylactic antibiotic use and recent antibiotic use before surgical intervention between these 2 groups. Only 1 case in the NICU group had a surgery-related infection, compared with 4 cases in the OR group ($P = .209$). The mortality rate was 9.1% (4 cases) in the NICU group and 6.3% (3 cases) in the OR group; however, the difference was not statistically significant ($P = .608$).

Subgroup analysis is demonstrated in Table 5, which was divided into PDA subgroup and laparotomy subgroup. Most of the results were similar in each group compared with Table 4, except hypothermia in PDA subgroup, which was no statistically significant between OR and NICU group ($P = .385$). The mortality rate and surgery-related infection rate were not statistically significant different between the OR group and NICU group in each subgroup.

Table 4

Preoperative and postoperative characteristics and surgical related events among infants who received operation in the neonatal intensive care unit (NICU) group versus the operating room (OR) group.

	NICU (n = 44)	OR (n = 48)	P
Body weight at the time of OP, g	1566 ± 806	3237 ± 1256	<.001
Pre-OP waiting time, min	32.7 ± 9.0	31.6 ± 7.2	.509
OP duration, min	86.8 ± 41.1	133.5 ± 49.5	<.001
Pre-OP BT, °C	36.7 ± 0.3	36.8 ± 0.3	.211
Post-OP BT, °C	36.4 ± 0.7	35.9 ± 1.0	.002
Lowest BT, °C	36.1 ± 0.4	35.2 ± 0.8	<.001
Hypothermia	4 (9.1)	27 (56.3)	<.001
Pre-OP inotropic agent use	17 (38.6)	4 (8.3)	.001
Post-OP inotropic agent use	20 (45.5)	8 (16.7)	.003
ET dislocation	1 (2.2)	0 (0)	.294
Pre-OP ventilator use	31 (70.5)	15 (31.3)	.001
FiO_2 pre-OP (%)	41.2 ± 18.9	30.8 ± 12.6	.009
FiO_2 post-OP (%)	46.0 ± 20.3	35.0 ± 15.4	.011
MAP pre-OP, cmH_2O	9.1 ± 3.7	6.9 ± 3.8	.030
MAP post-OP, cmH_2O	9.6 ± 3.6	8.1 ± 3.4	.072
Total days of admission, d	81 ± 50	51 ± 51	.006
IVF during surgery, mL/kg/h	17.0 ± 21.6	61.3 ± 54.4	<.001
Antibiotic prophylaxis or recent antibiotic use before surgery	36 (81.8)	32 (66.7)	.098
Surgery-related infection	1 (2.3)	4 (8.3)	.209
Mortality	4 (9.1)	3 (6.3)	.608

Data are presented as n (%) or mean ± standard deviation.
BT = body temperature, ET = endotracheal tube, IVF = intravenous fluid, MAP = mean airway pressure, OP = operation, PDA = patent ductus arteriosus.

4. Discussion

In this study, we controlled the air cleanliness of the NICU to ISO14644-1 class 7 and compared performing surgical procedures in the NICU to the OR. The results showed that operating in the NICU may be better than operating in an OR outside the NICU. First, there was no significant difference in mortality between the 2 groups, even though the gestational age and body weight were significantly lower in the NICU group. Second, the neonates who underwent surgery in the NICU had a significantly lower rate of hypothermia. Third, there was no significant difference in infection rate between the 2 groups. To the best of our best knowledge, this is the first study to control for air cleanliness in a NICU to perform surgery.

When comparing the outcomes of surgical procedures performed in a NICU or main OR, several factors should be taken into consideration. First, there may be concerns about an increased infection rate when performing surgery in a NICU. An aseptic environment such as in an OR is considered to be crucial when performing surgery. High efficiency particulate air (HEPA) filters are used in modern hospitals to create a cleanroom for surgical procedures. Many industrialized countries use ISO14644 as the standard to classify their cleanrooms, in which operating theaters should be NF S 90-351 zone 4 and ISO14644-1 class 5 with < 3500 particles/m^3 of size $\geqq 0.5\,\mu m$. The cleanliness of our NICU was controlled to NF S 90-351 zone 3 and ISO 14644-1 class 7. To the best of our knowledge, no previous study has investigated the level of cleanliness that is safe for surgery in a NICU. The infection rate may be an index to help us clarify this issue. It has been reported that the surgical site or surgery-associated infections are the major problem in NICU surgery; however, the results of previous studies have been

Table 5

Preoperative and postoperative characteristics and surgical related events among infants who received operation in the neonatal intensive care unit (NICU) group versus the operating room (OR) group, divided into PDA group and laparotomy group.

	PDA group			Laparotomy group		
	NICU (N = 32)	OR (n = 6)	*P*	NICU (n = 11)	OR (n = 36)	*P*
Male	14 (43.8)	2 (33.3)	.635	6 (54.5)	18 (50)	.792
Gestational age, wk	29.4 ± 3.3	34.8 ± 6.3	.003	33.2 ± 5.6	36.9 ± 3.9	.016
Birth weight, g	1263 ± 538	2199 ± 1153	.003	2022 ± 1113	2498 ± 837	.212
Postnatal age at surgery, d	20 ± 22	71 ± 53	<.001	9 ± 14	37 ± 47	.061
Weight at OP, g	1363 ± 616	3253 ± 1095	<.001	2076 ± 1058	3139 ± 1291	.017
Waiting time, min	30.8 ± 7.1	28.7 ± 4.2	.352	37.8 ± 12.2	31.6 ± 7.7	.137
OP duration, min	78.0 ± 26.0	113.3 ± 29.9	.005	95.9 ± 38.6	140.3 ± 53.8	.015
Pre-OP BT, °C	36.8 ± 0.3	36.9 ± 0.6	.511	36.6 ± 0.5	36.8 ± 0.3	.284
Post-OP BT, °C	36.6 ± 0.6	36.8 ± 0.3	.361	36.0 ± 0.8	35.8 ± 1.0	.486
Lowest BT, °C	36.2 ± 0.3	36.0 ± 0.8	.537	35.8 ± 0.6	35.1 ± 0.7	.006
Hypothermia	2 (6.3)	1 (16.7)	.385	2 (18.1)	23 (63.9)	.008
Pre-OP inotropic agent use	13 (40.1)	1 (16.7)	.264	4 (36.4)	3 (8.3)	.022
Post-OP inotropic agent use	14 (43.8)	1 (16.7)	.213	5 (45.5)	7 (19.4)	.083
Pre-OP ventilator use	24 (75)	4 (66.7)	.671	7 (63.6)	10 (27.8)	.086
Total admission day, d	90 ± 44	73 ± 62	.417	58 ± 60	47 ± 51	.566
Surgical related infection	1 (3.1)	0 (0)	.661	0 (0)	4 (11.1)	.270
Mortality	3 (9.4)	0 (0)	.435	1 (9.1)	3 (8.3)	.937

Data are presented as n (%) or mean ± standard deviation.

BT = body temperature, ET = endotracheal tube, IVF = intravenous fluid, MAP = mean airway pressure, OP = operation, PDA = patent ductus arteriosus.

inconsistent.[11,12] Our results showed no significant difference in the infection rate between the NICU and OR groups, including nosocomial and wound infections. Although 1 previous study suggested that surgical procedures performed in a NICU may increase the infection rate,[9] this study did not take the cleanliness of the NICU environment into consideration. In addition, there are currently no cleanliness guidelines for a NICU in Taiwan. Therefore, this study may provide a possible cleanliness standard for surgery in a NICU.

Neonates or premature infants who need surgery are transported outside the NICU in most hospitals, and only a few hospitals in Taiwan have dedicated operating theaters in their NICU. The transport of neonates has been reported to be associated with more complications than children of other ages, especially as most of these neonate are critically ill.[1] Shirley and Bion[13] and Wallen et al[5] reported an incidence rate of side effects that occurred during intrahospital transport of 6% to 70%, and the most common of these complications has been reported to be hypothermia.[1] Our results are consistent with previous studies in that the rate of hypothermia was significantly higher in the OR group than in the NICU group. Even though the baseline body weight and gestational age were lower in the NICU group, the rate of hypothermia was also lower. This result suggests the benefit of operating in a NICU. Several studies have reported strategies for transferring neonates with critical illnesses, including good transport team training, thorough pre-transport scheduling, specialized pediatric staff, and using a checklist to prevent hypothermia and other complications.[14–18] However, these strategies may be difficult to implement in every hospital due to the requirements of time, money, and skilled staff.[19] Furthermore, temperature control in the main OR may be another problem. In our NICU, the room air temperature was kept between 23°C and 26°C with a humidity between 50% and 60% so as to avoid heat loss when the infant underwent surgery. In the main OR, we try to achieve the same room air temperature; however, it is difficult to heat the room temperature above 18°C and 22°C and maintain a suitable temperature for neonates in our hospital. In a resource-limited hospital, performing surgery in the NICU may decrease the risk of hypothermia and other complications associated with transporting neonates.

Some studies have reported that performing PDA ligation in a NICU does not increase the mortality rate compared with performing the procedure in a main OR.[20,21] However, another study reported that laparotomy for necrotizing enterocolitis in a NICU can increase the mortality and mobility of critically ill neonates.[7] The poor outcomes in their study may have been due to a younger gestational age, smaller body weight, and more unstable/critically ill neonates undergoing the procedure in the NICU. In this study, the NICU group had a lower body weight, lower gestational age, higher rate of ventilator use, higher ventilator settings, and higher use of inotropic agents than the OR group, which is consistent with previous studies. In addition, all the mortality cases were not associated with surgical related infection. This might indicate the safety of operating in this air condition in neonates. Furthermore, the mortality rate was not significantly different between the 2 groups under this strategy, which may be because surgery in the NICU reduced the incidence of hypothermia compared with the OR group.

There are several limitations to this study. First, the major limitation is the limited case number that may contribute to the nonsignificant difference and heterogeneous characteristics between NICU and OR groups. Second, our resources are limited, and we do not have an OR in our NICU. Further studies should compare performing surgery in an OR within a NICU, NICU bedside, and main OR. Third, we did not analyze different operating sites or different operating procedures, which may also have affected the outcomes.

In conclusion, the safest place to perform a surgical procedure is in the OR. However, our study provides possible guidelines to control the cleanliness of the environment and make operating in a NICU safer. Using this strategy, there was no increase in complications or mortality, and the risk of hypothermia and

transport-associated problems was reduced. Due to the promising results of this study, further study will be investigated in the long-term outcome about surgery in our NICU in the future.

Author contributions

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