Radiation exposure in extremely low birth weight infants during their neonatal intensive care unit stay

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Background: **Extremely low birth weight (ELBW <1000 g) infants may have increased sensitivity to radiation exposure. Our objective was to estimate the radiation exposure in survivors of ELBW infants during their neonatal intensive care unit (NICU) stay.**

Methods: **In this retrospective cohort study, medical records of all ELBW infants who had been admitted to our NICU between May 1999 and October 2009 were reviewed. The infants' total entrance skin exposure [ESE in micro-Gray (μGy)] was estimated.**

Results: **Among 450 survivors, the mean gestational age (GA) was 26.3±2.1 weeks, and the mean birth weight (BW) was 774.2±144.4 g. Infants received a median of 32 (range: 1-159) X-rays, with an estimated ESE of 1471 μGy (range: 28-9264). Total ESE was inversely proportional to GA (r=-0.34; P<0.01), and BW (r=-0.39; P=0.01) and proportional to the severity of illness [score for neonatal acute physiology-perinatal extension (SNAPPE), r=0.39; P=0.01]. In a linear regression analysis, GA, SNAPPE and necrotizing enterocolitis were associated with radiation exposure (ESE) in ELBW infants (r^2=0.133; P<0.001).**

Conclusions: **During their NICU stay, ELBW infants were subjected to a significant number of diagnostic X-ray procedures. Our data highlight the need to closely monitor the number of X-ray procedures ordered to ELBW infants to avoid unnecessary radiation exposure.**

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Key words: **entrance skin exposure; extremely low birth weight infants; radiation exposure**

Introduction

Extremely low birth weight (ELBW) infants are often subjected to multiple X-ray imaging during their neonatal intensive care unit (NICU) stay. The risk of cancer secondary to radiation induced damage and the negative impact on long-term neurocognitive potential are the most worrying and undesirable consequences of X-ray examinations in neonates.[1] Although the true risks are unknown, the cancer risk is likely higher during the duration of fetal development (akin to a preterm baby) compared with later periods.[2-4]

In this study, we tried to determine the number of diagnostic X-ray procedures received in ELBW infants during their NICU stay.

Methods

In this retrospective cohort study, the medical records of all ELBW infants who had been admitted to our tertiary care NICU between May 1999 and October 2009 were reviewed for patient demographics, and the number of X-ray procedures were obtained during their NICU stay. All ELBW infants were included into this study (defined as a birth weight <1000 g) and those who did not survive their NICU stay were excluded.

All bedside imaging studies performed in the NICU were analyzed including chest X-rays, Kidneys, Ureters and Bladder (KUB) and babygrams (a spontaneously obtained chest X-ray and KUB). The entrance skin exposure (ESE) in micro-Gray (μGy) was calculated using the settings of the portable X-ray machine and the distance from the X-ray machine to the infant's skin, taking into consideration the infant's chest circumference, X-ray technique factor, and the geometry used for each exposure.

All X-ray procedures were performed using a

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portable X-ray unit (G.E. Medical Systems, AMX 4 Plus). The X-ray technique factor was standardized according to the infant's size.

The study was approved by our institution review board at the Metro Health Medical Center.

Statistical analysis

Data analysis was done using IBM SPSS Version 19 software. Data were expressed as mean and standard deviation or as median and range. Student's *t* test was used for comparison of parametric data, and Wilcoxon's rank-sum test was used for comparison of non-parametric data. Since patients with broncho pulmonary dysplasia (BPD) and necrotizing enterocolitis (NEC) required multiple diagnostic imaging studies during their NICU stay, they were divided into groups of presence versus absence of BPD, and presence versus absence of NEC. We decided a priori to use the 75th percentile as a cut-off value, an arbitrary number commonly used to identify, within a population, patients with higher values of exposure and thus higher risks. The 75th percentile of the amount of radiation exposure to our population was calculated to divide the population into high and low exposure and to determine, in a binary analysis, the potential risk factors associated with an increase in radiation exposure (above the 75th percentile). Bivariate correlation analysis was performed to determine the relationship between gestational age (GA) and ESE, birth weight (BW) and ESE, score for neonatal acute physiology-perinatal extension (SNAPPE) and ESE. The Chi-square test and Fisher's exact test were used to compare categorical data. To adjust for confounders, a backward linear regression analysis was conducted with ESE as the dependent variable and potential risk factors as determined by the bivariate analysis as the independent variables.

Results

During the study period, 622 ELBW infants were admitted to our NICU and 450 survived their NICU stay, with a mean length of stay of 93.4±45.1 days, and they constituted the study group. Demographics and characteristics of the survivors are shown in Table 1.

Most X-ray studies were conducted early, during the first weeks of life. Of all X-rays, 40% were obtained during the first 2 weeks of life and 80% were obtained during the first 6 weeks of life. In comparison with infants without BPD and NEC, infants with BPD had a significantly higher number of chest X-ray procedures, and those with NEC had a significantly higher number of KUB respectively (Table 2). Low GA, low BW, high SNAPPE score and presence of NEC were risk factors associated with an increase in radiation exposure to ≥2400 μGray (75th percentile of the amount of radiation in our population) (Table 3).

Our bivariate correlation analysis showed a significant correlation between GA and ESE, BW and ESE (Fig. 1), and SNAPPE score and ESE (Fig. 2).

A backward linear regression model was conducted with exposure to radiation (ESE in μGy) as the dependent variable and BW, GA, SNAPPE score, BPD and NEC as the independent variables. GA, SNAPPE score and NEC were the only independent risk factors that were retained in the model, and were significantly associated with radiation exposure (R^2=0.133, P<0.001).

Table 1. Patients' demographics and characteristics in survivors

Variables	Value
Number of patients	450
Birth weight, g*	774.21±144.39
Gestational age, wks*	26.38±2.19
Male, *n* (%)	206 (46)
Caucasian, *n* (%)	167 (37)
Cesarean section, *n* (%)	306 (68)
Apgar at 1 min†	5 (3-6)
Apgar at 5 min†	7 (6-8)
SNAPPE score*	42.01±14.88
BPD, *n* (%)	338/450 (75)
NEC, *n* (%)	31/450 (7)
Number of X-rays/patient‡	32 (1-159)
ESE‡/patient (in μ Gray)	1467 (28-7790)

*: data expressed as mean±standard deviation; †: data expressed as median with interquartile range; ‡: data expressed as median and range. SNAPPE: score for neonatal acute physiology-perinatal extension; BPD: broncho pulmonary dysplasia; NEC: necrotizing enterocolitis; ESE: estimated skin exposure.

Table 2. The average number of X-rays obtained during neonatal intensive care unit stay

	BPD (*n*=338)	No BPD (*n*=112)	*P* values	NEC (*n*=31)	No NEC (*n*=419)	*P* values
Chest X-rays	24 (12-37)	10 (3-22)	<0.001	16 (11-25)	22 (9-35)	0.170
KUB	2 (0-7)	2 (0-6)	0.801	16 (8-21)	2 (0-6)	<0.001
Baby-grams	5 (3-7)	3 (1-6)	0.002	7 (5-13)	4 (2-7)	0.003
Total X-rays	36 (21-51)	19 (9-43)	<0.001	43 (28-64)	31 (16-48)	0.009
ESE in μGy (range)	1673 (84-7790)	941 (28-6658)	<0.001	2184 (471-5123)	1452 (28-7791)	<0.01

Data expressed as medians with interquartile ranges unless otherwise mentioned. BPD: broncho pulmonary dysplasia; NEC: necrotizing enterocolitis; KUB: kidneys, ureters and bladder; ESE: estimated skin exposure.

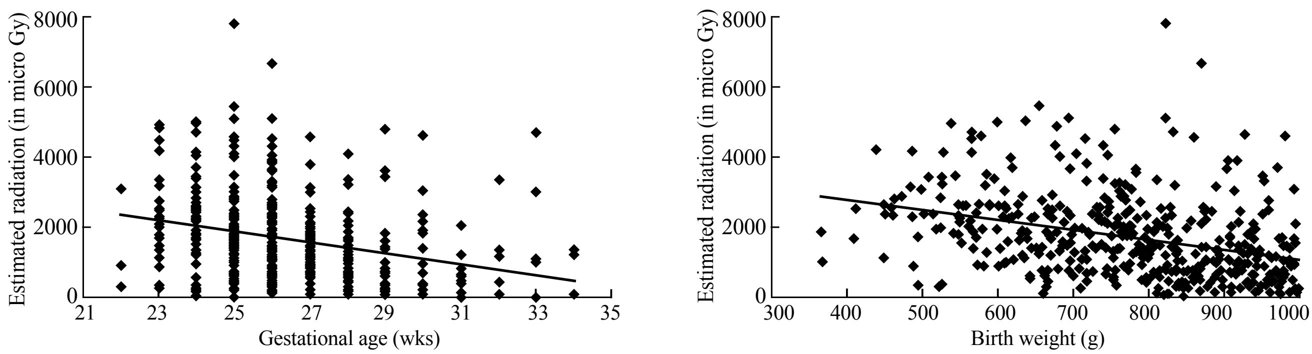

Fig. 1. Estimated radiation exposure among survivors in extremely low birth weight infants according to their gestational age at birth (r=-0.34; P=0.01) and birth weight (r=-0.39; P=0.01).

Table 3. Risk factors associated with an increase in radiation exposure in extremely low birth weight infants

	<2400 µGy (n=345)	≥2400 µGy (n=105)	OR	P values
GA, wks	26.6±2.2	25.6±1.9	-	<0.001
BW, g	795.3±137.3	704.8±145.8	-	<0.001
SNAPPE	39.9±14.4	48.7±14.2	-	<0.001
BPD	253/345 (73%)	85/105 (81%)	1.54 (0.89-2.65)	0.114
NEC	19/345 (5%)	12/105 (11%)	2.21 (1.03-4.72)	0.036

µGy: micro Gray; OR: odds ratio; GA: gestational age; BW: birth weight; SNAPPE: score for neonatal acute physiology-perinatal extension; BPD: broncho pulmonary dysplasia; NEC: necrotizing enterocolitis.

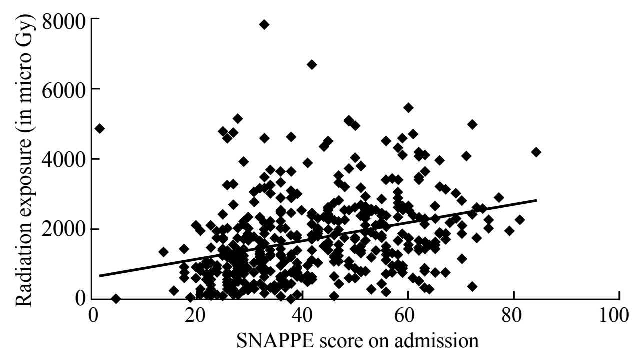

Fig. 2. Estimated radiation exposure among survivors according to score for neonatal acute physiology-perinatal extension (SNAPPE) (r=0.39; P=0.01).

Discussion

In this study, we analysed the iatrogenic radiation exposure in a large cohort of ELBW babies. We found a median of 32 X-ray procedures, somewhat higher than previously described radiation exposures in premature infants.[5-7] We also found that low gestation age, high severity of illness score and presence of NEC are associated with greater amounts of radiation exposure. Studies[6,8,9] found radiation exposure in neonates with a median number of X-ray procedures between 19 and 31. The number of X-ray examinations performed in our study is extremely variable (1-159), but it is higher than that in previously published studies. This is most possible because our patient population, the ELBW infants, represents the sickest group of neonates. Since the smallest, youngest and sickest infants and those with BPD and NEC usually required multiple diagnostic tests, it was not surprising to find an association between radiation exposure and the aforementioned factors. Therefore, a linear regression was conducted to adjust the potential confounding factors.

In our linear regression model, BPD was not found to be a risk factor associated with an increase in radiation exposure. Our findings were similar to the findings of Donadieu et al,[6] where BPD did not significantly affect the cumulative effective dose. The reason of such results could be related to the frequency of BPD in our study. BPD was relatively common, accounting for 75% in all infants.

We have reported exposure as ESE instead of effective dose as it has been suggested to avoid controversy.[10,11] Approaches such as avoiding imaging modalities that involve radiation, minimizing dose of radiations, and introducing diagnostic reference limit (DRL), are measures to minimize radiation. According to the International Commission on Radiation Protection, DRLs are expected not to be exceeded for standard procedures when good and normal practice regarding diagnostic and technical performance is applied.[12,13] The concept of DRL in newborns has been endorsed by the Food and Drug Administration and the Joint Commission.[14,15] At our institution, we diligently monitor patient exposure factors and provide relative dose indications (S-values) on every pediatric radiograph.

The benefit to risk ratio of diagnostic X-ray imaging studies in NICUs is challenging. There are no studies on determination of cancer risk due to radiation exposure in preterm infants, but in-utero radiation exposure has been found to be associated with an increased risk of cancer and behavioral abnormalities.[16] In our study, 40% of all the X-rays were obtained during the first two weeks of life, when ELBW infants would have been in-utero during their late second trimester. Therefore, estimates of cancer risk that are based on radiation exposure during the third trimester may potentially underestimate the risk of cancer in ELBW infants who are born prematurely and exposed to ex-utero radiation.

Our study has several limitations. It is a single center retrospective study. However, with the long study duration we were able to capture the common practice of ordering X-ray procedures by NICU physicians over a decade. Second, our study is a retrospective study, and not all patients were followed up for the same set of time. Some patients were discharged earlier than others, and therefore we could not use a risk ratio or risk difference analysis, instead we used an odds ratio analysis for the different risk factors. Third, we did not include the potential amount of radiation exposure generated from CT scans, and X-rays of the skulls and extremities. Infants are at risk of a higher radiation exposure if CT scans and other X-ray procedures are added to the calculation of their ESE. Our objective was to shed the light on the amount of radiation exposure from routinely and commonly ordered X-ray procedures in ELBW infants.

In conclusion, ELBW infants are subjected to a significant number of X-ray exposures that are correlated with GA, severity of illness, and NEC. There is an urgent need to establish DRLs for this patient population and to determine the impact of low dose radiation (<100 mGy) on the rapidly growing preterm infant.[17]

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