IMPROVED OUTCOMES OF OUTBORN PRETERM INFANTS IF ADMITTED TO PERINATAL CENTERS VERSUS FREESTANDING PEDIATRIC HOSPITALS

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Objectives **To examine whether admission hospital type (13 perinatal centers vs 4 freestanding pediatric hospitals) was associated with differences in risk and illness severity adjusted mortality and morbidity among outborn preterm infants.**

Study design **Records of singleton outborn infants ≤32 weeks' gestational age (n = 605) admitted to 17 tertiary level neonatal intensive care units participating in the Canadian Neonatal Network for the period 1996 to 1997 were examined.**

Results **Outborn infants admitted to freestanding pediatric hospitals were at higher risk of death (adjusted odds ratio [AOR], 2.25; 95% confidence interval [CI], 1.20, 4.20), nosocomial infection (AOR, 2.48; 95% CI, 1.64, 3.73), and oxygen dependency at 28 days of age (AOR, 1.77; 95% CI, 1.14, 2.75) when compared with outborn infants admitted to perinatal centers.**

Conclusions **After adjustment for perinatal risks and admission illness severity, outborn infants had better outcomes if they were admitted to perinatal centers compared with freestanding pediatric hospitals.** ***(J Pediatr 2005;146:626-31)***

Outcomes for preterm infants born in tertiary care centers (inborn) are better when compared with preterm infants born in a level II or level I hospital and then transferred to a tertiary care center for further treatment (outborn).[1-4] Kitchen et al[5] reported serious functional impairment in 72% of outborn infants compared with 23% of inborn infants who weighed 500 to 999 g at birth. Factors accounting for these differences may include a lack of adequate facilities at the outborn centers, ineffective or inappropriate resuscitation and postnatal stabilization, and delay in therapies such as surfactant or artificial ventilation.[1,5] Outborn infants tend to be sicker than infants born at the tertiary care centers.[1-4]

In most countries with regionalized perinatal care systems, outborn preterm infants ≤32 weeks are routinely transferred to tertiary centers for care after birth.[1,6,7] These tertiary care neonatal intensive care units (NICU) are located either in perinatal centers (attached with obstetric units) or freestanding pediatric hospitals. In Canada, preterm and low birth weight infants (ie, a more homogenous population) usually comprise the bulk of the admissions to NICUs attached to perinatal centers. In contrast, freestanding pediatric hospitals tend to care predominantly for neonates with complex diagnoses such as surgical, cardiac, genetic, or metabolic disorders. A relatively small proportion of preterm and low birth weight infants without complex diagnoses are admitted to these hospitals. Therefore, the expertise and experience of both medical and paramedical personnel and the practice patterns and infrastructure may differ between these two types of hospitals. This may result in differences in the care provided to these infants and their outcomes.

Subtle differences in the practices have been shown to influence certain neonatal outcomes even among perinatal centers.[8] To our knowledge, differences in outcomes of outborn preterm infants admitted to perinatal centers and to freestanding pediatric

NICU	Neonatal intensive care unit	SNAP	Score of Neonatal Acute Physiology
PDA	Patent ductus arteriosus		

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Presented at the Annual Meeting of the Pediatric Academy Societies, San Francisco, California, May 2004.

Supported by grants 40503 and 00152 from the Medical Research Council of Canada. Additional funding was provided by the B.C.'s Children's Hospital Foundation; Calgary Regional Health Authority; Dalhousie University Neonatal-Perinatal Research Fund; Division of Neonatology, Children's Hospital of Eastern Ontario; Child Health Program, Health Care Corporation of St John's; the Neonatology Program, Hospital for Sick Children; Lawson Research Institute; Midland Walwyn Capital Inc; Division of Neonatology, Hamilton Health Sciences Corporation; Mt Sinai Hospital; North York General Hospital Foundation; St Joseph's Health Centre; University of Saskatchewan Neonatal Research Fund; University of Western Ontario; Women's College Hospital.

Submitted Sep 15, 2004; revision received Dec 28, 2004; accepted Jan 13, 2005.

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0022-3476/$ - see front matter

10.1016/j.jpeds.2005.01.030

hospitals have not been described. The objective of this study was to examine whether admission hospital type (perinatal center vs freestanding pediatric hospitals) is associated with differences in mortality and morbidity among outborn preterm infants after adjustment of perinatal risks and admission illness severity (using the Score of Neonatal Acute Physiology, version II [SNAP II]).[9]

METHODS

Study Population

The Canadian Neonatal Network established a national database (including 17 hospitals with 75% of tertiary NICU beds across Canada) and collected information on all admissions over a 22-month period from January 1996 to October 1997 after approval from the research ethics board at each site. Trained research assistants prospectively abstracted relevant data from the mother's and infant's charts at each participating center on a daily basis. Details of data collection and data management have been published elsewhere.[8] Singleton newborn infants with gestational age between 24 and 32 completed weeks born outside a perinatal center and transferred to either perinatal centers or freestanding pediatric hospitals within the first 4 days of age were included in this study. Perinatal centers are centers where obstetric care is provided to mothers and where newborn infants are admitted to tertiary level NICUs. Freestanding pediatric hospitals are centers with tertiary level NICUs but no obstetric services, and all NICU patients are transferred after the birth from other hospitals. All the NICUs included in this study were tertiary level referral NICUs. Four NICUs (two perinatal centers and two freestanding pediatric hospitals) had extracorporeal membrane oxygenation capabilities. Infants with lethal congenital anomalies, who were born at <23 weeks' gestational age or who were moribund (ie, a physician, in consultation with the parents, had made an explicit decision not to provide life support at the time of the NICU admission) on admission were excluded from the analysis. The admission hospitals were divided into two groups: perinatal centers (n = 13) and freestanding pediatric hospitals (n = 4).

Variable Definitions

Study variables were defined according to the Canadian NICU Network SNAP Project Abstractor Manual. Gestational age was defined as the best obstetric estimate, based on early prenatal ultrasound, obstetric examination, and obstetric history, unless the postnatal pediatric estimate of gestation differed from the obstetric estimate by more than 2 weeks. In that case, the pediatric estimate of gestational age was used instead. An infant was defined as small-for-gestational age if the birth weight was less than the 3rd percentile for gestational age according to the British Columbia provincial growth charts established by Whitfield[10] in 1992 for the Canadian population. Data are also presented for infants <10th percentile for gestational age. Prenatal care was defined as receipt of pregnancy-related care from a physician on at least one occasion (not related to a visit for diagnosis of pregnancy) during pregnancy. SNAP-II[9] is a neonatal illness severity score calculated from 6 empirically weighted physiologic measurements and made during the first 12 hours of admission to the NICU. Higher SNAP score is associated with increased risk of mortality and morbidity.[8,9] Chronic lung disease was defined as oxygen dependency at 36 weeks' corrected gestational age for an infant who was born at ≤32 weeks' gestation.[11] Intraventricular hemorrhage was defined according to the criteria of Papile[12] from head ultrasound performed before 14 days of life. Necrotizing enterocolitis was defined according to Bell criteria (stage 2 or higher)[13] and was classified as medical (clinical symptoms and signs plus evidence of pneumatosis on abdominal radiography) or surgical (histologic evidence on surgical specimen of intestine). Nosocomial infection was defined by using blood and cerebrospinal fluid culture results according to Freeman criteria.[14] Patent ductus arteriosus was defined as clinical diagnosis plus treatment with indomethacin or surgical ligation or both.

Outcomes

Death in the NICU, severe (grade 3 or greater) intraventricular hemorrhage, chronic lung disease, necrotizing enterocolitis, patent ductus arteriosus, respiratory distress syndrome, nosocomial infection, duration (days) of mechanical ventilation, duration (days) of oxygen treatment, number of transfusions, and respiratory status on day 28 (infants needing respiratory support) were compared between the two groups.

Statistical Methods

Univariate and bivariate analyses were performed to describe the characteristics of the study population and to explore the association between population characteristics and clinical outcomes. Multivariate regression analyses, including logistic, linear, and Poisson, depending on the data type (dichotomous, continuous, and counts) of each outcome, were used to compare neonatal outcomes of infants admitted to perinatal centers and freestanding pediatric hospitals after adjustment for perinatal risks, admission severity of illness (SNAP-II), and volume of admissions (number of very low birth weight infants treated at each hospital). The SPSS version 12 (SPSS Inc; Chicago, Ill) was used for data analysis.

RESULTS

A total of 3769 singleton preterm infants born at 24 to 32 weeks' gestation were admitted to 17 tertiary NICUs in the Canadian Neonatal Network during the study period of 1996 to 1997. Of these, 3164 infants were born in perinatal centers, whereas 605 infants were outborn. Two infants with lethal congenital anomalies, 102 infants born at ≤23 weeks' gestation, and 21 infants who were moribund on admission were excluded from the analyses. Of the 605

Table I. Characteristics of infants admitted to NICUs in perinatal centers (n_1 = 303) and free standing pediatric hospitals (n_2 = 302)

Infant characteristics	Perinatal centers (% of n_1)	Freestanding pediatric hospitals (% of n_2)	χ^2 (df)	*P* value
Sex				
Male	59.9	57.0	0.436 (1)	.51
Female	40.1	43.0		
Gestational age (weeks)				
20–26	25.7	26.5	1.468 (3)	.69
27–28	20.1	16.6		
29–30	22.2	24.5		
31–32	32.0	32.5		
Apgar score (5 min)				
0–3	7.7	5.0	4.321 (2)	.12
4–6	31.4	26.2		
≥7	60.9	68.8		
Small for gestational age				
3rd percentile	1.3	2.0	0.461 (1)	.52
10th percentile	5.0	8.9	3.775 (1)	.05
Delivery type				
Vaginal	65.7	58.8	3.014 (1)	.08
Cesarean	34.3	41.2		
Maternal hypertension	5.7	11.4	5.691 (1)	.02*
Presentation				
Vertex	67.6	67.0	0.367 (2)	.88
Breech	27.7	29.3		
Other	4.7	3.7		
Antenatal steroid use				
Partial	19.8	22.8	0.837 (1)	.36
Complete	6.3	12.3	6.546 (1)	.01*
Prenatal care				
None	6.2	5.8	0.025 (1)	.87
Some	93.8	94.2		
Score for Neonatal Acute Physiology (II)				
0–9	41.7	49.0	4.834 (3)	.18
10–19	29.1	26.3		
20–29	12.9	13.3		
≥30	16.2	11.3		

*$P < .05$.

eligible outborn infants, 303 infants were admitted to perinatal centers and 302 infants were admitted to freestanding pediatric hospitals. There was no significant difference in the gestational age distribution of patients admitted to the two types of hospitals (percentage of babies born at ≤26 weeks, 27 to 28 weeks, 29 to 30 weeks, and 31 to 32 weeks were 26%, 20%, 22%, and 32%, respectively, for perinatal centers; and 26%, 17%, 25%, and 32%, respectively, for freestanding pediatric hospitals). The mean (±SD) number of infants ≤32 weeks' gestation that were admitted per center (including inborn and outborn infants) were 256 (±122) patients for the 13 perinatal centers and 110 (±76) patients for the 4 freestanding pediatric hospitals during the study period.

Baseline characteristics (Table I) of infants admitted to perinatal centers and freestanding pediatric hospitals were similar, with the exception of maternal hypertension and administration of a complete course of antenatal corticosteroids, which were more prevalent among infants admitted to freestanding pediatric hospitals. Bivariate analysis (Table II) showed that the nosocomial infection and oxygen dependency at 28 days of life were higher among infants admitted to freestanding pediatric hospitals, whereas patent ductus arteriosus was more prevalent among infants admitted to perinatal centers. There was a trend toward increased mortality rates and decreased incidence of chronic lung disease among infants admitted to the freestanding pediatric hospitals; however, it did not reach statistical significance in bivariate analysis.

Multivariate regression analyses (Table III) revealed that outborn infants admitted to freestanding pediatric hospitals were at higher risk of death (adjusted odds ratio [OR], 2.25; 95% confidence interval [CI], 1.20, 4.20), nosocomial infection (adjusted OR, 2.48; 95% CI, 1.64, 3.73), and oxygen dependency at 28 days of age (adjusted OR, 1.77; 95% CI, 1.14, 2.75) and at lower risk for development of patent ductus arteriosus (PDA) (adjusted OR, 0.46; 95% CI, 0.30, 0.69), even after adjustment for perinatal risks and admission illness severity. Volume of admission was not a significant predictor. Male sex was predictive of death (adjusted OR, 2.10; 95% CI, 1.15, 3.85) but not other outcomes. Lower gestational age was predictive of all adverse outcomes. Small for gestational age and antenatal corticosteroids (partial) were only predictive of nosocomial infections. Higher admission illness severity was predictive of death but higher SNAP-II scores were not significantly predictive of PDA, nosocomial infection, or oxygen dependency at 28 days of life. The latter probably is due to the small numbers of patients with high SNAP-II scores in the cohort. Diagnostic plots showed no departure from model assumptions.

We also examined the issue of nonlinearity and categorization of SNAP scores. When SNAP-II is fitted as a linear variable, the residuals indicate a nonlinear effect. Categorizing SNAP-II into 0 to 9, 10 to 19, 20 to 29, and 30+ groups accommodates nonlinearity; the categories also enable a sufficient number of observations in the cells. If we fit the logistic model with SNAP-II as a continuous polynomial term, the likelihood ratio statistics is equal to 203.7 on 12 degrees of freedom. Refitting the model with the categorized SNAP-II instead gives a likelihood ratio statistic equal to 202.5 on 13 degrees of freedom. This shows that categorizing SNAP-II in the given categories eliminates nonlinearity.

DISCUSSION

We report that outborn preterm infants have better outcomes if they are admitted to perinatal centers compared with freestanding pediatric hospitals. Previous reports documented that regionalization of perinatal care improved the outcome both for the mother and infant. McCormick et al[6] reported a decline in neonatal mortality rates after regionalization of perinatal care, which emphasized delivery of high-risk and preterm infants ≤32 weeks' gestation at perinatal centers. Truffert et al[7] showed a similar trend among infants 31 to 32 weeks' gestational age in France, with the use of an established neonatal transport team attending birth when feasible. The Victoria Infant Collaborative Study Group[2] in Australia reported an increase in the number of intrauterine transfers and survival of neonates over time (1979 to 1992), accompanied by an increasing gap between survival rates of inborn and outborn preterm infants. It is speculated that regionalization results in better outcomes because high-risk pregnancies are transferred in an orderly manner to facilities with the appropriate expertise and facilities for ongoing surveillance and timely intervention. Although Canada has a highly regionalized perinatal care system, Chien et al[1] reported that in 1996 to 1997, approximately 20% of preterm infants were born outside perinatal centers, mostly due to emergent circumstances that prevented in utero transfer to a tertiary center.

Previous authors reported variations in outcomes of tertiary NICUs and suggested that hospital and patient characteristics may affect outcomes. Lee et al[8] reported significant variation in mortality, morbidity, and resource use among tertiary Canadian NICUs. Horbar et al[15] reported that mortality rates among very low birth weigh infants admitted to the NICU were affected by factors such as volume of patients and whether the NICU was an academic hospital. Phibbs et al,[4] in a large population-based study in California, reported significantly lower-risk adjusted neonatal mortality rates (OR, 0.62; 95% CI, 0.47, 0.82) for neonates born in a perinatal center with a level 3 NICU with an average NICU census of >15 patients per day compared with hospitals without NICUs. Risk-adjusted neonatal mortality was not different among smaller level 3 NICUs, level 2 NICUs, and hospitals without NICUs and was significantly higher than large level 3 NICUs. Lee et al[16] reported that NICU mortality rates were higher if the patient volume was low, the infant was admitted at night, and the in-house medical staff were inexperienced. However, outcomes of outborn infants admitted to NICUs associated with perinatal centers and freestanding pediatric hospitals have not been previously compared.

We speculate that there might be several possible reasons for our finding that perinatal centers had better NICU outcomes than freestanding pediatric hospitals. Note that only outborn preterm infants were included in this study, to ensure comparability of findings. First, the NICUs in freestanding pediatric hospitals had lower patient volumes (especially preterm infants) than the perinatal centers (mean admissions per NICU during the study period were 110 and 256). Lee et al,[16] Horbar et al,[15] and Phibbs et al[4] reported a relation between lower patient volumes and poorer outcomes. Second, proportionately more patients with surgical problems, congenital heart disease, and complex congenital anomalies were admitted to freestanding pediatric hospitals than to perinatal centers because the former were more often designated for care of infants with these conditions. Infants with predominant surgical problems are at increased risk of infections and treatment with multiple antibiotics, and this may predispose to cross-infections and resistant organisms. Although adjustment for admission illness severity using SNAP-II minimizes the impact of patient differences, it is possible that SNAP-II may not completely compensate for differences in referral patterns. Third, clinical practices and hospital infrastructure and organization may vary because of

Table II. Crude mortality and morbidity rates among the infants admitted to perinatal centers and freestanding pediatric hospitals

Outcome	Perinatal centers (%)	Freestanding pediatric hospitals (%)	Odds ratios (95% CI)
Death in the NICU	12.9	18.3	1.52 (0.97–2.37)†
Severe intraventricular hemorrhage (≥grade 3)	15.0	18.5	1.29 (0.81–2.06)
Chronic lung disease	24.4	18.6	0.71 (0.46–1.08)
Necrotizing enterocolitis	5.6	3.4	0.59 (0.26–1.33)
Patent ductus arteriosus	33.7	29.7	0.51 (0.35–0.75)†
Respiratory distress syndrome	84.3	78.5	0.68 (0.45–1.08)
Infection			
Primary	0.3	2.3	7.17 (0.88–58.6)
Nosocomial	18.2	34.1	2.33 (1.60–3.40)†
Number of blood transfusions (mean ± SD)	3.2 ± 2.6	3.6 ± 3.3	0.45 (−0.24–1.13)*
Oxygen-dependent at 28 d	78.5	86.6	1.77 (1.15–2.72)†
Ventilator-dependent at 28 d	92.4	96.0	1.98 (0.97–4.05)

*Using Poisson regression model.
†Outcomes for which regression models were created.

Table III. Risk factors predictive of death, patent ductus arteriosus, nosocomial infection, and oxygen dependency at 28 days (odds ratio; 95% confidence interval)

Variables	Death in NICU	Patent ductus arteriosus	Nosocomial infection	Oxygen dependency at 28 d
Freestanding pediatric hospitals	2.25 (1.20–4.20)	0.46 (0.30–0.69)	2.48 (1.64–3.73)	1.77 (1.14–2.75)
Male	2.10 (1.15–3.85)	NS	NS	NS
Gestational age				
≤26 wk	8.00 (3.45–18.52)	7.95 (4.12–15.3)	5.89 (3.23–10.7)	NS
27–28 wk	1.51 (0.53–4.30)	10.9 (5.63–21.2)	5.05 (2.72–9.37)	
29–30 wk	0.58 (0.16–2.04)	2.88 (1.45–5.72)	2.49 (1.37–4.54)	
Apgar score (5 min)				
0–3	3.61 (1.37–9.53)	NS	NS	NS
4–6	2.14 (1.11–4.13)			
Small for gestational age (10^{th} percentile)	NS	NS	2.37 (1.16–4.87)	NS
Antenatal steroid				
Partial	NS	NS	1.98 (1.24–3.15)	NS
Complete	NS	NS	1.15 (0.57–2.31)	NS
Admission SNAP-II				
10–19	1.80 (0.73–4.44)	1.78 (1.07–2.94)	1.79 (1.12–2.87)	2.21 (1.24–3.92)
20–29	6.43 (2.58–16.02)	3.34 (1.81–6.15)	1.20 (0.65–2.24)	1.78 (0.86–3.70)
≥30	11.7 (4.67–29.28)	1.50 (0.78–2.87)	0.36 (0.17–0.75)	0.81 (0.45–1.44)

The reference group is perinatal centers, Apgar ≥7, gestational age 31 to 32 weeks, female, not small for gestational age, no antenatal steroid use, and SNAP-II 0 to 9.

the differing patient types and volumes in perinatal centers and freestanding pediatric hospitals. Increased emphasis on larger infants with complex medical conditions may be less conducive to care for the small preterm infant. Indeed, although the mortality rate was 50% higher among preterm infants ≤32 weeks' gestation at birth when they were admitted to freestanding pediatric hospitals compared with perinatal centers, we found no evidence that this was due to higher illness severity. Practice differences (eg, fluid management) might also explain the decreased risk of PDA among infants admitted to freestanding pediatric hospitals. Since the mortality rates and morbidity risks are highest among the very preterm infants <26 weeks' gestation at birth, these infants are at greatest risk of adverse outcomes if admitted to freestanding pediatric hospitals.

Our results could be confounded by the lack of information regarding socioeconomic status, reasons for transfer, timing of maternal admission, resuscitation of infants, treatment given during and after birth, and transport stabilization. However, there were no differences in the perinatal risks and admission illness severity scores among outborn infants admitted to either type of hospitals, thus making it unlikely that there were any major baseline differences among the infants. Our results were derived from regionalized NICUs serving 75% of the Canadian population and are generalizable to NICUs in Canada and potentially worldwide.

CONCLUSIONS

We recognize that we had only four freestanding pediatric hospitals in our study, further studies involving more units are needed before firm recommendations can be made. However, if the results hold true, this could have significant potential implications for regionalization planning and resource utilization. If our findings are replicated in other studies, it would suggest that when in utero maternal transfers are not possible, efforts should be made to transfer outborn preterm infants to perinatal centers. This is particularly true for infants ≤28 weeks' gestation, when the risk for adverse outcomes is greatest.[16] Alternatively, changes in the treatment of preterm infants admitted to freestanding pediatric hospitals may be warranted. Further research is needed to determine risk factors in freestanding pediatric hospital NICUs that are associated with good or poor outcomes and that might be amenable to intervention.

APPENDIX 1

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