End-of-life practices in seven Brazilian pediatric intensive care units

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Objective: **To evaluate the incidence of life support limitation and medical practices in the last 48 hrs of life of children in seven Brazilian pediatric intensive care units (PICUs).**

Design: **Cross-sectional multicenter retrospective study based on medical chart review.**

Setting: **Seven PICUs belonging to university and tertiary hospitals located in three Brazilian regions: two in Porto Alegre (southern region), two in São Paulo (southeastern region), and three in Salvador (northeastern region).**

Patients: **Medical records of all children who died in seven PICUs from January 2003 to December 2004. Deaths in the first 24 hrs of admission to the PICU and brain death were excluded.**

Interventions: **Two pediatric intensive care residents from each PICU were trained to fill out a standard protocol ($\kappa = 0.9$) to record demographic data and all medical management provided in the last 48 hrs of life (inotropes, sedatives, mechanical ventilation, full resuscitation maneuvers or not). Student's *t*-test, analysis of variance, chi-square test, and relative risk were used for comparison of data.**

Measurements and Main Results: **Five hundred and sixty-one deaths were identified; 97 records were excluded (61 because of brain death and 36 due to <24 hrs in the PICU). Thirty-six medical charts could not be found. Cardiopulmonary resuscitation was performed in 242 children (57%) with a significant difference between the southeastern and northeastern regions ($p = .0003$). Older age ($p = .025$) and longer PICU stay ($p = .001$) were associated with do-not-resuscitate orders. In just 52.5% of the patients with life support limitation, the decision was clearly recorded in the medical chart. No ventilatory support was provided in 14 cases. Inotropic drug infusions were maintained or increased in 66% of patients with do-not-resuscitate orders.**

Conclusions: **The incidence of life support limitation has increased among Brazilian PICUs but with significant regional differences. Do-not-resuscitate orders are still the most common practice, with scarce initiatives for withdrawing or withholding life support measures. (Pediatr Crit Care Med 2008; 9:26–31)**

Current progress in medicine has brought incontestable benefits but also some ethical and moral conflicts. In intensive care units (ICUs), excessive and inappropriate resources are sometimes used (1–4). Death as a natural progression of life is sometimes denied to patients with irreversible diseases, imposing an end of life full of suffering and not guided by the patient's or the family's preferences (5–7).

Since the 1990s, the concerns related to the end-of-life have been increasing. Life support limitation (LSL), such as do-not-resuscitate orders (DNR) or withholding or withdrawing life-sustaining treatments, has become a frequent practice in ICUs around the world (8–11).

In adult ICUs, up to 90% of deaths are preceded by LSL (8, 9). However, this incidence changes according to cultural, religious, and personal characteristics of the medical team and the institution involved (12–15). One important difficulty in evaluating LSL lies in the fact that accurate data are not always available in the medical records (16).

In pediatric ICUs (PICUs), the worldwide incidence of LSL ranges from 30% to 79% (17–19). The mortality rate in most of Latin American PICUs ranges between 7% and 15% (20–22). Depending on the region, up to 20% of these deaths occur in the first 24 hrs as a result of

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Members of the Brazilian Pediatric Center of Studies on Ethics (NEEP-BR) are included in appendix.

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acute severe and irreversible diseases. This means that 5% to 10% of all children admitted to a Latin American PICU will die after spending variable lengths of stay in the PICU and a considerable number of them will be defined as terminal patients.

Few studies have evaluated LSL involving pediatric patients in Latin America. A Brazilian study reported a progressive increment of LSL from 6% in 1988 to 36% in 2002; however, DNR orders were the prevalent mode of death (21). Moreover, limited family participation (22% to 55%) in the decision-making process as well a scarce description of an end-of-life proposal in the medical records have been observed (20–22).

In northern hemisphere countries, end-of-life care is a priority in the treatment of critically ill children (1, 7, 23–25). Immediately after the decision for LSL, life support treatments (or interventions) are withdrawn and the administration of analgesic/sedative drugs is the main therapy (26).

Most Brazilian studies about end-of-life practices had been conducted in the southern region, where an increase in LSL decisions was found (21, 22). Considering the continental size of Brazil and its regional differences, we decided to conduct a study to evaluate the incidence of LSL and identify the medical management adopted in the last 48 hrs of life of children who died in PICUs located in three Brazilian regions.

PATIENTS AND METHODS

This observational, retrospective, multicenter study included all children who died between January 2003 and December 2004 in seven Brazilian PICUs. The PICUs selected to participate in the study are located in reference medical care centers or teaching hospitals in three Brazilian regions: a) two PICUs in the southern region: São Lucas Hospital, Pontifícia Universidade Católica do Rio Grande do Sul (PUCRS) and Hospital de Clinicas de Porto Alegre, Universidade Federal do Rio Grande do Sul (UFRGS); b) two PICUs in the southeastern region: Hospital das Clinicas de São Paulo and University Hospital, both associated with Universidade de São Paulo (USP); and c) three in the northeastern region: São Rafael Hospital, Hospital da Criança, and Ernesto Simões Filho Hospital. This study was approved by the Committees on Science and Ethics of the seven hospitals.

The seven PICUs have similar medical coverage. Medical staff consists of a medical coordinator, one or two pediatric intensivist in charge, pediatric intensive care residents, and general pediatric residents. The medical decisions are defined during two daily rounds (early in the morning and late afternoon). All seven PICUs admit children with complex diseases (congenital cardiac disease, burns, oncology, and trauma), and the southern and southeast PICU conduct transplant programs (liver, renal, and bone marrow transplant) as well.

Subjects were identified be reviewing all admission and discharge medical records of each PICU between January 1, 2003, and December 31, 2004. Patients with brain death and those who died in the first 24 hrs of PICU admission were excluded. The data and results of patients with brain death were reported in a separate study (27).

Two pediatric intensive care residents at each PICU were trained to fill out a standard protocol with data obtained exclusively from medical charts. These residents were considered adequately trained when achieving a concordance of 90% ($\kappa = 0.9$) with the main researcher when extracting data of three different medical records. In case of any doubt, they were instructed to contact the main author (PML) by phone or Internet.

The following data were extracted from the selected medical chart: a) demographic and general data (age, gender, and length of hospital and PICU stay); b) data related to death (cause of death, number of organ failures in the last 48 hrs of life, complete cardiopulmonary resuscitation maneuvers (defined as chest compressions, bag ventilation, or mechanical ventilation through tracheal tube plus intravenous epinephrine administration), and LSL decision reported in the medical chart); c) data about medical management in the last 48 hrs of life in the PICU (dose of vasopressor drugs infusion, variables of mechanical ventilation, and dose of sedative and analgesic drugs infused in the 48 hrs and 24 hrs before death and immediately before death). Multiple organ dysfunctions were classified according definition reported by Wilkinson et al. (28).

The sample size was estimated based on the records of each PICU in the previous years where an average of 400 admissions per year per unit and a mortality rate of 10% were observed. Based on these findings, a total of 560 deaths in the seven PICU would be included in a 2-yr study period. According to the previous studies, we estimated 10% for brain death and 30% for death <24 hrs in the PICU (20, 21). Therefore, we anticipated to have close to 336 medical records.

Continuous variables were expressed as mean and SD, and variables with non-normal distribution were expressed as median and interquartile range (25% to 75%). Student's *t*-test and analysis of variance were used to compare continuous variables, followed by Bonferroni *post hoc* testing in case of differences between three or more groups. The Kruskal-Wallis and Mann-Whitney U tests were used to compare variables with nonnormal distribution. *Post hoc* analysis of data with asymmetric distribution was performed with analysis of variance for rank-ordered asymmetric data and analyzed with the Tukey test. Categorical variables were expressed as percentages and compared using the chi-square and the Fisher's exact tests followed by Finner's modification of Bonferroni adjustment. An Excel (Microsoft) spreadsheet was used to collect data, which was analyzed with SPSS 11.0 software (SPSS, Chicago, IL).

RESULTS

We identified 561 deaths that occurred in the seven PICUs between 2003 and 2004. Thirty-six medical charts (6.9%) were excluded because those patients died in the first 24 hrs in the PICU, and 61 (11.6%) were excluded because of brain death (without difference between the seven PICUs). Thirty-six medical charts were not found (7% of missed documents). The study included 428 medical charts of patients who died, 121 from the south region, 111 from the southeast, and 196 from the northeast, without differences regarding age, gender, number of multiple organ dysfunctions, and sepsis as main cause of death (Table 1).

Of the 428 deaths evaluated, 186 (43.5%) did not receive cardiopulmonary resuscitation (CPR) (45.5% in the southern region, 54.1% in the southeastern region, and 36.2% in the northeastern region). A significant difference in the incidence of CPR was found between the southeastern and northeastern regions ($p = .0003$) (Table 1).

Compared with the nonresuscitated patients, the 242 patients receiving CPR were younger (17 vs. 31.5 months; $p = .025$) and had shorter length of PICU stay (4 vs. 9 days; $p < .001$). No differences were found related to gender, hospitalization length before PICU admission, sepsis prevalence as the main cause of death, and the time of day when death occurred (Table 2).

At univariate analysis, the DNR decisions were associated with three or more organ failures, PICU stay >5 days, and age >24 months. However, the multivariate analysis demonstrated that only length of PICU stay >5 days was associated with a DNR order (odds ratio 6.9 [1.5–31.2]) (Table 3).

Table 1. Characteristics of 428 dying children in seven Brazilian pediatric intensive care units located in three different regions

	South n = 121	Southeast n = 111	Northeast n = 196
Age, mos, mean (IQR)	18 (5–64)	46 (10.5–109,5)	13.5 (4.7–84.5)
Male gender, n (%)	68 (56.6)	56 (50.4)	110 (56.1)
Three or more organ dysfunctions, n (%)	48 (39,6)	48 (43,2)	87 (44,4)
Sepsis as a main cause of death, n (%)	38 (31.4)	32 (28.8)	71 (36.2)
CPR, n (%)	66 (54.5)	51 (45.9)[a]	125 (63.8)[a]
No CPR, n (%)	55 (45.5)	60 (54.1)	71 (36.2)

IQR, interquartile range between 25% and 75%; CPR, cardiopulmonary resuscitation.

[a] Incidence of CPR between regions: $p = .009$; After Finner-adjusted p values: south × southeast = .19; south × northeast = .14; southeast × northeast = .0003.

Table 2. Characteristics of patients who were not resuscitated vs. patients who received cardiopulmonary resuscitation (CPR)

	No CPR n = 186 (43.5%)	CPR n = 242 (56.5%)	p
Age, mos, median (IQR)	31.5 (7–105.7)	17 (5–74.3)	.025
Male gender, n (%)	101 (54.3)	131 (54.1)	.94
Hospital stay, days, median (IQR)	1 (0–7)	1 (0–5)	.258
Length of PICU stay, days, median (IQR)	9 (3–18)	4 (1–11)	<.001
Sepsis as cause of death, n (%)	106 (56.9)	130 (53.1)	.561
Death between 7 pm and 7 am, n (%)	81 (43.5)	117 (48.3)	.37

IQR, interquartile range between 25% and 75%; PICU, pediatric intensive care unit.

Table 3. Factors associated with not receiving cardiopulmonary resuscitation (CPR)

	No CPR n = 186 No. (%)	CPR n = 242 No. (%)	Univariate Analysis Mean Age, Months	Multivariate Analysis Mean Age, Months
Three or more organ failures	99 (54.1)	84 (45.9)	2.14 (1.42–3.23) <.001	0.67 (0.5–1.1) .062
PICU stay >5 days	116 (53.0)	103 (47.0)	2.24 (1.48–3.37) <.001	6.9 (1.5–31.2) .01
Age >24 mos	102 (50.2)	101 (49.8)	1.7 (1.13–2.54) .007	0.3 (0.1–1.3) .10

PICU, pediatric intensive care unit.

The decision to not perform CPR was recorded clearly in the medical chart for only 98 of 186 patients (52.7%) who were not resuscitated, with significant differences between the regions. The interval between LSL decision and a patient's death was 2.8 days (median 2 days, interquartile range 1–3 days). In two patients, the DNR decision was recorded in the medical charts >30 days before death (34 and 37 days).

In just four (2.5%) of the 186 patients who did not receive CPR, inotropic/vasoactive drugs were discontinued and mechanical ventilation variables (respiratory rate, positive inspiratory pressure, and fraction of inspired oxygen) were reduced in the last 48 hrs of life. On the other hand, for 90 (48.3%) patients who did not receive CPR, mechanical ventilation variables were increased in the 48 hrs before death without difference between the regions (Table 4). For 123 (66.1%) patients, the dose of inotropic drugs was maintained or increased in the last 48 hrs of life, without differences between the three regions: 43.6% in the southern region, 66.7% in the southeastern region, and 83.1% in the northeastern region.

We identified only 14 patients (7.5%) who died without attempts to perform airway access or provide mechanical ventilation support; 71% of them did not receive inotropic drugs, and only 22% received sedative or analgesic drugs. For 10 of these 14 children, the decision for not performing CPR was reported in the medical chart.

Comparing the CPR group with the no-CPR group regarding inotropic drug infusions in the last 48 hrs of life, dopa-

Table 4. Medical data for children in whom cardiopulmonary resuscitation (CPR) was not performed before death

	South n = 55 No. (%)	Southeast n = 60 No. (%)	Northeast n = 71 No. (%)	Total n = 186 No. (%)		Finner-Adjusted p
DNR decision reported in the medical chart	35 (63.6)	29 (48.3)	34 (47.9)	98 (52.7)	.24	
Inotropic infusion (48 hrs): increased or no change	24 (43.6)	40 (66.7)	59 (83.1)	123 (66.1)	.01	S × SE = .019 S × NE < .001 SE × NE = .029
No tracheal access or MV at death	9 (16.4)	2 (3.3)	3 (4.2)	14 (7.5)	.01	S × SE = .11 S × NE = .11 SE × NE = .99
Increased MV variables	26 (47.3)	32 (53.3)	32 (45.0)	90 (48.3)	.62	
Decreased MV variables	1 (0.8)	1 (1.7)	2 (2.8)	4 (2.5)	.54	
Sedative, analgesic drugs: increased or no change	34 (61.8)	44 (73.3)	54 (76.6)	132 (71.0)	0.19	

DNR, do-not-resuscitate; MV, mechanical ventilation; S, south region, SE, southeast region; NE, northeast region.

Table 5. Comparison of children receiving full cardiopulmonary resuscitation (CPR) with those who were not resuscitated before death (No CPR): Cardiovascular drug infusion and oxygen administration

	Dopamine	Dobutamine	Adrenaline	FIO_2
CPR, n (%)	135 (55.8)[a]	140 (57.9)[a]	132 (54.5)[a]	229 (94.6)
Mean ± SD	15.2 ± 5.2	14.7 ± 5.4	2.1 ± 1.8	0.82 ± 0.24
No CPR, n (%)	81 (43.5)	81 (43.6)	48 (25.8)	171 (91.9)
Mean ± SD	15.1 ± 5.0	14.7 ± 5.8	2.8 ± 2.3[b]	0.78 ± 0.28
Chi-square	.01[a]	.003[a]	<.001[a]	.26
Student's *t*-test	.888	.96	.028[b]	.209

[a] Percentages were statistically different calculated with chi-square test; [b] means were statistically different calculated with Student's *t*-test. Values for drugs given as μg/kg/min.

mine was infused more frequently in the CPR group (55.8% vs. 43.5%; $p = .01$) but without difference related to the mean doses. For dobutamine and adrenaline, the results were quite similar. However, the adrenaline infusion dose in the no-CPR group was extremely high (2.8 ± 2.3) and significantly greater ($p = .28$) (Table 5).

For 71% of the patients who were not resuscitated, medications to provide comfort (morphine, fentanyl, or midazolam) were continued or increased in the last 48 hrs, but the mean dose infused was similar to the group of patients who received complete CPR.

DISCUSSION

In this collaborative study that involved seven Brazilian PICUs, we analyzed 428 deaths that occurred during 2 yrs, and the following aspects were of note: a) CPR maneuvers were not performed before death in >40% of children dying in these PICUs, confirming the trend observed in previous studies in South America (20–22); b) the decision for not performing CPR was significantly associated with the length of PICU stay; c) DNR decisions recorded in the medical chart are still infrequent (close to 50% in the no-CPR group) as described in other studies in the same region (20–22); d) end-of-life practices related to LSL (inotrope infusion, sedation, and mechanical ventilation support) in Brazil are still far from what is recommended in North America and northern European countries (24, 25, 29–31).

The incidence of patients who did not receive resuscitation (43.5%) was higher than described in previous studies in Latin America (30% to 36%) and confirms a regional trend toward an increment of LSL decisions before death in a PICU (19, 21, 22, 24, 25). Length of PICU stay >5 days was the only factor associated with the decision for not performing CPR, as observed in other regional end-of-life studies (21, 22). We speculate that this finding may be associated with the need for more time to define terminality, for medical discussions to reach a consensus, and for communication with families and their participation in the decision-making process. This is the opposite of what has been seen in adult ICUs: Patients with LSL orders stay in the ICU for a significantly shorter time than those who receive full life support, because the decision to limit life support is made earlier (32).

In this study, end-of-life decisions were reported in only 52% of patients' charts. Similar findings were reported in previous studies conducted in Brazil, Argentina, and southern Europe (18, 19, 21, 22). These results were very different from what was reported in North American, Canadian, and northern European studies, where the LSL decision is reported in near 100% of the medical charts (1, 19, 26). We speculate that medical staff in South America still have some difficulty in assuming the LSL decision, which could be related to a) legal concerns; b) lack of knowledge about medical and ethical aspects for handling terminal patients; c) failure to fully discuss the decision by the medical team and, consequently, lack of consensus; and/or d) lack of family involvement in the decision-making process, as recommended in most of end-of-life care guidelines (29–31). These factors probably could explain the different incidence of CPR between southeast PICU and northeast PICU (46% vs. 64%).

An intriguing aspect of our study is that 48% of patients in the no-CPR group had mechanical ventilation variables increased, and inotropic drug infusions were maintained or increased for 66% of them in the last 48 hrs of life. These results demonstrate some incoherence between the final decision (to not provide CPR) and the subsequent medical attitude in the 48 hrs before death. What ethical or moral reason could motivate medical staff, after a decision is made to not resuscitate some dying child, to maintain full life support until the occurrence of cardiopulmonary arrest?

Although there is no single correct manner for LSL (8, 10), the final aim should be the patient's quality of life (1, 6). We believe that maintaining full life support in a terminally ill child until the development of cardiopulmonary arrest does not provide for the patient's well-being. This medical approach only prolongs the dying process and increases the suffering of patients and their families (14).

On the other hand, we could identify some small signs demonstrating that end-of-life care for dying children in Brazilian PICUs is moving in another direction: a) There were 14 cases of death without tracheal intubation or mechanical ventilation support; and b) in 63 cases (34%) in the no-CPR group, inotropic drug infusions were reduced. These results, described at the first time in our country, indicate incipient changes for adopting proactive measures in the management of end of life in PICU.

Regarding sedation and analgesia, the average doses for patients who were not resuscitated were not greater than for patients receiving full CPR. Because the patients in our study were not evaluated individually, it is difficult to classify such results as a disregard for pain and anxiety, because the sensory systems of some of these children might have been compromised. Most authors suggest that the terminal patient should have a peaceful death without suffering (30, 33). Many physicians may be afraid of side effects of sedative and analgesic medication, but their use is justified when the main objective is to ensure that patients have a dignified death (9, 33).

This is the first multicenter study to evaluate medical care of dying children in different regions of Brazil, and like most retrospective studies based on medical chart reviews, it has limitations related to methodology: Definitions and medical terms were not uniform, the evaluation instruments were not validated, and the medical chart data were not always objective or complete (26). Although these facts may have added some bias to data collection, we believe that our findings

are consistent and could be comparable to similar studies conducted in other countries.

Our results confirm old problems associated with death in the Brazilian society. This topic receives little attention in the general population as well as in the medical community. Moreover, physicians and a reasonable number of healthcare providers are unaware of the ethics and legal concepts associated with death and end-of-life care (34). The infrequent participation of families and patients in the decision-making process for dying children contributes to the fact that measures of full life support are maintained even when the situation is irreversible and the disease is incurable (20–22, 34). Recently, the Brazilian Federal Council of Medicine, aware of such problems, issued a resolution (35) that reinforces the responsibility of Brazilian physicians to involve families and explain end-of-life care and appropriate LSL measures to patients defined as irreversible.

This study draws attention to the fact that end-of-life care provided for dying children in Brazil is still far from what we desire (36). Attitudes of healthcare providers need to change regarding end-of-life care, and the civil society must be included in this discussion. We believe that the recent resolution issued by the Brazilian Federal Council of Medicine brought at least two great advances on this matter: The council dismissed some legal concerns the existed in part of the medical community and extended end-of-life discussions to the general community as well as healthcare providers. We strongly believe that these two actions will in the near future bring substantial change to the management of end-of-life in Brazilian PICUs.

APPENDIX

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