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Do-Not-Resuscitate Orders and/or Hospice Care, Psychological Health, and Quality of Life among Children/Adolescents with Acquired Immune Deficiency Syndrome

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Abstract

Objective—The frequency of do-not-resuscitate (DNR) orders and hospice enrollment in children/adolescents living with acquired immune deficiency syndrome (AIDS) and followed in Pediatric AIDS Clinical Trials Group (PACTG) Study 219C was examined, and evaluated for any association with racial disparities or enhanced quality of life (QOL), particularly psychological adjustment.

Methods—A cross-sectional analysis of children with AIDS enrolled in this prospective multicenter observational study between 2000 and 2005 was conducted to evaluate the incidence of DNR/hospice overall and by calendar time. Linear regression models were used to compare caregivers' reported QOL scores within 6 domains between those with and without DNR/hospice care, adjusting for confounders.

Results—Seven hundred twenty-six (726) children with AIDS had a mean age of 12.9 years (standard deviation [SD] = 4.5), 51% were male, 60% black, 25% Hispanic. Twenty-one (2.9%) had either a DNR order ($n = 16$), hospice enrollment ($n = 7$), or both ($n = 2$). Of 41 children who died, 80% had no DNR/hospice care. Increased odds of DNR/hospice were observed for those with CD4% less than 15%, no current antiretroviral use, and prior hospitalization. No differences by race were detected. Adjusted mean QOL scores were significantly lower for those with DNR/hospice enrollment than those without across all domains except for psychological status and health care utilization. Poorer psychological status correlated with higher symptom distress, but not with DNR/hospice enrollment after adjusting for symptoms.

Conclusions—Children who died of AIDS rarely had DNR/hospice enrollment. National guidelines recommend that quality palliative care be integrated routinely with HIV care. Further research is needed to explore the barriers to palliative care and advance care planning in this population.

Introduction

National guidelines call for the integration of palliative care with disease-directed therapy for children with life-limiting conditions, including human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS).^{1–8} Although advance care planning supports health care decision-making throughout the course of illness by eliciting the values and goals of the patient and family, it is not a routine component of HIV/AIDS care.⁵ The dramatic impact of highly active antiretroviral therapy on survival and quality of life over the past decade^{9,10} has the unintended consequence of making this integration seem less relevant.⁵

Failure of HIV care programs to effectively support families in anticipating and planning for future medical complications, disease progression, or death creates missed opportunities for life closure,⁵ problems for emergency department personnel if parents/guardians are not present during health emergencies,¹¹ or conflict around end-of-life decisions within health care teams and between health providers and patient families.^{12–14} Providing choices can help families to feel effective and in control,¹⁵ and patients to maintain psychological health, even when quality of life (QOL) has decreased.^{16–18} At the end of life, decisions to limit interventions, such as cardiopulmonary resuscitation, or to seek care focused on the relief of suffering, such as hospice care, may optimize QOL for children and families, but differences in outcomes of these existing choices have not been assessed.¹⁹

HIV/AIDS disproportionately burdens black and Hispanic individuals in the United States.^{20–22} In studies of adults, ethnic differences exist in the choices that are made at the end of life. For example, African American adults want more life-sustaining treatments, yet are less likely to have discussed life-sustaining treatments with their physicians and families and have fewer advance directives than non-African Americans.²³ The reasons for this discrepancy are unknown. We do know that they are more likely than Caucasians to request life supporting treatments.²⁴ Blacks have historical experience of discrimination by health care institutions²⁵ and may interpret discussion of do-not-resuscitate (DNR) orders as euthanasia or an attempt to deny beneficial care.²⁶

The frequency of active decision-making about end-of-life care and the relationship between these end-of-life decisions and psychological adjustment are unknown for the population of children and adolescents with HIV/AIDS. We determined the frequency of reporting a DNR order or enrollment in hospice care as specific examples of advance care planning in a population of HIV-positive children/adolescents. We hypothesized that, in children/adolescents with AIDS: (1) those choosing DNR or hospice enrollment would have enhanced QOL, particularly psychological adjustment by providing choices which can help individuals feel effective and in control, compared to those without DNR/hospice enrollment and (2) blacks would be less likely to have a written DNR/hospice enrollment than other racial groups.

Methodology

Data were collected prospectively between September 2000 and November 2005, as part of the Pediatric AIDS Clinical Trials Group (PACTG) 219C, a recently closed observational cohort study conducted at 89 hospitals in the United States. This study was designed to evaluate the long-term effects of antiretroviral therapy (ART) and complications of HIV infection in HIV-exposed children (both HIV-infected and-uninfected). Recruitment methods, protocol history, changes in use of antiretroviral medications, and major findings of this study are well described in earlier PACTG 219C reports.^{27–29} Prior to participation, the Institutional Review Board (IRB) at each site approved the protocol. Participants gave

written informed consent/assent before enrollment. Research followed the guidelines for human experimentation by the Department of Health and Human Services and participating institutions.

Our evaluation focused on HIV-infected children enrolled in PACTG 219C with a prior CDC Class C diagnosis (AIDS) and an assessment of both QOL and DNR/hospice care. We restricted our analysis to subjects with AIDS, since it was unlikely that subjects who did not have AIDS would be candidates for a DNR or hospice care. If a subject had a DNR or hospice enrollment, then we used the QOL information from the first visit at which a DNR/hospice enrollment was reported. If a subject had no DNR or hospice enrollment, we used the most recent QOL assessment. Thus, we conducted a cross-sectional analysis of data collected as part of a prospective observational study.

Study protocol

Clinical follow-up visits were conducted every 3 months. Clinical records were abstracted to obtain medical and clinical histories, including a complete history of ART medications and clinical diagnoses. CD4 positive T lymphocyte percents (CD4⁺ %) and HIV viral loads were measured, and sociodemographic and quality-of-life information was obtained as reported by the caregiver.

QOL assessments were completed at least once each year by the parent/guardian using the General Health Assessment for Children (GHAC) QOL questionnaire developed and validated by the PACTG, based on previously validated instruments.^{30–32} These QOL measures have been used in studies of the severity of illness¹⁰ in children with HIV, for example. This QOL tool also included questions regarding whether the subject had a DNR and/or had been enrolled in hospice care. Reports of DNR/hospice enrollment were verified at each site and discrepancies were resolved by consensus. Reasonable reliability, as well as construct and discriminant validity for the domains have been reported for the GHAC.^{30–32}

The GHAC is comprised of six QOL domains: general health perception; symptom distress; physical functioning; psychological functioning; social/role functioning; and health care utilization. The first three domains above were derived from the Adult ACTG QOL form developed by Testa and Lenderking,³³ which in turn was based on measures developed for the Medical Outcomes Study.³⁴ General health perception domain is also comparable to a similar measure used in the National Health Interview Survey.³⁵ Physical functioning domain has six items rating how much the child's health has interfered with their ability to do various activities, such as walk one block.³¹ Internal consistency (Cronbach α) on physical functioning scale ranged from 0.80 to 0.87. Symptom distress domain has 18 items assessing distress related to HIV-related physical symptoms.³¹ Internal consistency (Cronbach α) on symptoms scale ranged from 0.80 to 0.88.³¹ The psychological functioning domain was based on the Behavior Problem Index adapted by Zill³⁶ from the Child Behavior Checklist.³⁷ Subscales of the psychological status domain were: anxiety/depression, antisocial, headstrong, hyperactivity, peer conflict and immaturity. Internal consistency on psychological functioning scale ranged from 0.91 to 0.93.³¹ Discriminant validity of each item with each domain was good.³¹ Scores for social/role functioning and health care utilization have not been validated, but were derived in a manner analogous to the other validated scores. We considered the number of nights hospitalized since the prior visit as a separate indicator of health care utilization.

Statistical analysis

Because of the rarity of reporting a DNR or enrolling in hospice care in the data set, we combined these occurrences for statistical analysis in order to give us sufficient power to

detect differences. We reasoned that having a DNR order or hospice enrollment suggested a deliberative decision making process about death and dying on the part of the family and health care team. We present the percentage of participants with either a DNR order or hospice enrollment with exact 95% confidence intervals based on the binomial distribution, and evaluate trends over calendar time in incidence of newly reported DNR and/or hospice after study entry based on a Poisson regression model. Predictors of DNR/hospice care were evaluated in a multiple logistic regression model including age, race/ethnicity, gender, CD4% less than 15%, HIV-1 RNA viral load greater than 400 copies per milliliter, ART use, and prior hospitalization.

Total QOL domain scales were calculated by summing multiple items and transforming to a 0–100 range, such that higher scores indicate better QOL. There was no overlap in items included in different domain scores. Occasionally, caregivers responded to the majority of questions within a domain, but failed to respond to one or more item. In these cases, which occurred in less than 3% of domain scores overall, the mean of nonmissing items within a domain was computed as the score for the missing item.

QOL domain scores were compared between those with and without DNR/hospice care using general linear regression models, controlling for disease severity and potential confounders. A separate model was fit for each domain, and estimated means and standard errors for those with versus without DNR/ hospice care were calculated. Means for symptom distress and physical functioning were adjusted for gender, age, race/ethnicity, and ART. The remaining four domains were also adjusted for CD4%, HIV-1 RNA viral load, or previous hospitalization. A sensitivity analysis was conducted for all domains excluding the 17 patients missing ART information. Two-sided p values < 0.05 were considered statistically significant. The normality assumption for QOL scores was empirically assessed, and tests of DNR/ hospice care status were validated with nonparametric Wilcoxon rank sum tests.

Based on the number of subjects with and without DNR/hospice care, we calculated that comparison of QOL scores between groups would have 80% power to detect a difference of approximately 0.64 standard deviations, or 11 points in QOL on a scale from 0–100 with SD = 18.

SAS version 9.1 (SAS Institute, Inc. Cary, NC) was used to conduct all analyses.

Results

Of the 2850 HIV-infected children enrolled in the PACTG 219C study as of November 2005, 726 (25.5%) had an AIDS diagnosis prior to their QOL assessment. Of these, 16 reported DNR decisions and 7 hospice care enrollment (2 with both a DNR and hospice care), yielding a total of 21 subjects (2.9%, 95% confidence interval: 1.8%, 4.4%) with a DNR and/or hospice care. Demographic and other characteristics of the children with AIDS at the time of their QOL assessment are summarized in Table 1. Most were perinatally infected (93%), with 51% male and 60% black and non-Hispanic. Average age was 12.9 years (SD = 4.5; range, 2–21). Sixty-seven percent had been hospitalized prior to relevant QOL evaluation. Five of the 21 subjects with DNR/hospice care were 18 years or older, and all five of these subjects had prior hospitalization. A few sites had 2 to 3 participants with DNR/hospice, while many very large sites had none.

Forty-one deaths occurred, with 8 deaths among the 21 DNR/hospice care patients (38%), and 33 deaths among the 705 non-DNR/hospice care patients (5%). There were no differences by age, gender, race/ethnicity, or source of transmission between children with and without DNR/hospice care (Table 1). However, those with DNR/hospice care were

significantly more likely to have been previously hospitalized than those without DNR/hospice care (90% versus 66%, $p = 0.02$), to have CD4% less than 15% (43% versus 17%, $p = 0.002$), and to not be on ART (33% versus 14%, $p = 0.04$). These associations were maintained after adjustment for gender, age at QOL assessment, race/ethnicity, and viral load level in a multiple logistic regression model. In the final model, those with CD4% less than 15% (odds ratio [OR] = 3.1, 95% CI [1.1–8.9], $p = 0.04$), no current ART use (OR = 2.8, 95% CI [1.1–7.2], $p = 0.04$), and prior hospitalization (OR = 4.2, 95% CI [0.95–18.4], $p = 0.06$) were more likely to have DNR/hospice care. Although viral load was marginally associated with DNR/hospice care in univariate analysis (Table 1, $p = 0.07$), there was no association after adjustment for the above covariates ($p = 0.74$). Although the number of events was low, we found a significant increase in the rate of newly reported DNR orders/hospice enrollment after study entry over calendar time, with an incidence rate per 100 person years follow-up time of 0.5 for 2001, 0.7 for 2002, 0.9 for 2003, 0.7 for 2004, and 3.3 for 2005 ($p = 0.03$ for increasing trend based on a Poisson regression model).

Adjusted mean QOL scores presented in Table 2 and Figure 1 show significantly lower mean scores for those with DNR/hospice care than those without for all domains except psychological status ($p = 0.95$) and health care utilization ($p = 0.17$). When this analysis was repeated excluding those with missing ART information (sensitivity analysis), the results remained essentially unchanged. Table 2 and Figure 2 also illustrate that the adjusted mean QOL psychological subscale scores showed no significant differences between groups. Children with DNR/hospice care spent significantly fewer nights hospitalized since the last visit (mean = 5.1 versus 5.9, $p < 0.001$), although their overall health care utilization did not differ significantly from those without DNR/hospice care.

Poorer psychological status correlated with higher symptom distress ($p < 0.001$), even after controlling for potential confounders, but not with DNR/hospice enrollment after adjusting for symptoms ($p = 0.19$). Psychological status was not associated with physical functioning ($p = 0.16$). A few sites had two to three participants with DNR/hospice care, while many very large sites had none.

Discussion

In our multicenter prospective study, 5.6% of children and adolescents with AIDS died, less than 1% enrolled in hospice. This is a much lower frequency than the less than 5% of all dying children in the United States who use hospice care.^{1,19} Hospice enrollment increased over time, consistent with the increase in the number of pediatric palliative hospice programs nationwide.³⁸ Our understanding of these findings is limited because we do not know if our patients received palliative care consultations, nor do we know if families were offered DNR/hospice care and declined. Although there were fewer hospitalizations since the last visit in the DNR/hospice care group, we do not know if these patients received fewer unwanted medical interventions. The clustering of DNR/hospice care by sites suggests differential expertise or comfort with these conversations, but other factors may have played a role as well. Predicting end-of-life in this population has become more difficult as many children with a history of AIDS-defining diagnoses experience dramatic clinical improvement with currently available antiretroviral therapy and thus are not appropriate candidates for DNR/hospice care.^{5,9} Furthermore, the prognosis for children with AIDS is variable and dependent on many factors including the timing of diagnosis, when ART was started, the child's response to therapy, their adherence to therapy, and their most recent CD4%.¹⁰ Almost all subjects with DNR/hospice care had prior hospitalization.

Inclusion of patients who reported either a DNR decision or hospice enrollment accounted for only 2.9% of patients with AIDS. Four times as many children with AIDS died with no

documentation of DNR or hospice care. Although not directly comparable, Klopfenstein and colleagues³⁹ in a review of 95 medical records of children with cancer who died from progressive disease found that 53% had a DNR at the time of death, suggesting a much higher frequency of DNR use.

That all five subjects 18 or older with DNR/hospice care had prior hospitalization may reflect the impact of the Patient Self-Determination Act,⁴⁰ a requirement for hospitals to ask adults about Advance Directives at hospitalization, which may include signing a DNR. However, we cannot confirm whether the hospitalizations were before, after or coincident with choosing DNR.

We did not find a correlation between psychological QOL and DNR/hospice status. However, psychological health was preserved in the DNR/hospice group despite lower QOL in other domains suggesting that DNR/hospice care does not cause psychological distress. DNR/hospice status was strongly associated with lower QOL scores in the domains of general health perception, symptom distress, physical functioning, and social/school functioning. These associations make sense given the physical illness experienced by children with AIDS and its impact on daily living.

There were no racial differences in prevalence of having a DNR order or hospice enrollment. This differs from findings in adults,^{23–26} among whom blacks were less likely to have a written DNR or hospice enrollment than non-blacks and more likely to want aggressive treatment.

The very low number of patients with DNR/hospice care makes any conclusions tentative at best. In addition, only one measure of QOL, adapted for individuals living with HIV/AIDS, was used. Other limitations of our study include the cross-sectional nature of the analysis, which only allows statements of association. We do not know if poorer prognosis, poorer quality of life, or distressful symptoms resulted in a DNR/hospice enrollment.

Conclusion

Policy and research implications

This is the largest evaluation of DNR/hospice care enrollment in children/adolescents with AIDS and one of the few large-scale hypotheses driven studies in the pediatric palliative medicine literature. Yet, it generates more questions than it answers. In a world where millions of children and adolescents live and die with HIV/AIDS (www.who.int/hiv/pub/surveillance/en/), in-depth qualitative study is recommended to examine the physical, psychological, and social underpinnings for these findings. Purposive sampling by demographics (age/gender/ethnicity/socioeconomic status), access to ART (country of residence/access to AIDS clinical trials/access to ART programs), settings (home/hospital), caregivers (professional/personal), health care centers (presence/absence of palliative program), education, and cultural belief systems, as well as to provide a rigorous framework for conducting this important work.

In the United States, there is now consensus among professional organizations on the domains and preferred practices of quality palliative care.^{4–5} Implementing preferred practices requires collaboration among health care institutions, insurers, health professionals, patients, and families. Patients should have distressing physical and psychological symptoms evaluated and treated.^{4–6} Interdisciplinary teams should work with patients and families to articulate values and goals in order to continuously update care plans as conditions change. Many health professionals hesitate initiating such discussions for fear that they provoke anxiety and sadness in families.⁴¹ But evidence supports the fact that

families are willing to discuss end-of-life decision-making.^{42,43} Furthermore, framing conversations about end-of-life care as supportive care,⁴⁴ may help families make decisions based on the best interest of the child.

Health care professionals are also often uncomfortable,⁴⁴ inconsistently trained,⁴⁵ or in need of support to reduce their own suffering⁴⁶ when their patient is dying. Interventions to help relieve the suffering of professionals who work in pediatric palliative care should be implemented as standard hospital practice. Education and training are key interventions that can be provided in a variety of formats and settings.

Communication and decision-making are key factors affecting dying children and families.⁴⁶ Although no peer-reviewed, evidenced-based, family-centered program currently exists to help families of adolescents with life-threatening illnesses speak directly and honestly about end-of-life care,⁴⁷ family centered advance care planning is being piloted with HIV positive adolescents and their families to close this gap.

In settings with access to antiretroviral therapy, HIV/AIDS has become a chronic, incurable illness with increased long-term survival and deaths increasingly due to non-HIV related illnesses.⁹ Integrating quality palliative care with family-centered HIV care from the time of a child's diagnosis provides the best opportunity to maximize both the length and the quality of that child's life.

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FIG. 1.

Adjusted quality of life domain scores by do-not-resuscitate (DNR)/hospice care status, means and 95% confidence intervals for each domain adjusted for gender, age, race/ethnicity, and antiretroviral therapy (ART) regimen, and except for symptom distress and physical functioning also adjusted for CD4% (<14%, 15%–24%, >25%), HIV-1 RNA viral load (400, >400 copies per milliliter), and previous hospitalization (yes, no). EOL, end of life; QOL, quality of life.

FIG. 2.

Adjusted quality of life psychological subscale scores by do-not-resuscitate (DNR)/hospice care status, means and 95% confidence intervals for each domain adjusted for gender, age, race/ethnicity, CD4% (<14%, 15%–24%, >25%), HIV-1 RNA viral load (<400, >400 copies per milliliter), previous hospitalization (yes, no), and antiretroviral therapy (ART) regimen. EOL, end of life; QOL, quality of life.

Table 1
Characteristics of Seven Hundred Twenty-Six Children with AIDS, by DNR/Hospice Enrollment

<i>Characteristic</i>	<i>Total n = 726</i>	<i>EOL care n = 21</i>	<i>No EOL care n = 705</i>	<i>p value^a</i>
Male	373 (51%)	9 (43%)	364 (52%)	0.51
Perinatally acquired HIV	675 (93%)	20 (95%)	655 (93%)	0.78
Age (years)				0.52
Mean $\pm$ SD	12.9 $\pm$ 4.5	13.0 $\pm$ 4.6	12.9 $\pm$ 4.5	
<5	34 (5%)	0	34 (5%)	
5–11	233 (32%)	6 (29%)	227 (32%)	
12	459 (63%)	15 (71%)	444 (63%)	
Race/ethnicity				0.49
Black	435 (60%)	16 (76%)	419 (59%)	
Hispanic	179 (25%)	3 (14%)	176 (25%)	
White	107 (15%)	2 (10%)	105 (15%)	
Other	5 (<1%)	0	5 (<1%)	
CD4 T-lymphocyte percent				0.002 ^b
Median	27	19	27	
<15%	127 (17%)	9 (43%)	118 (17%)	
15%–24%	174 (24%)	5 (24%)	169 (24%)	
25%	425 (59%)	7 (33%)	418 (59%)	
HIV RNA (copies/mL)				0.07
Median	612	9231	567	
400	338 (47%)	6 (29%)	332 (47%)	
401–5,000	120 (17%)	4 (19%)	116 (16%)	
5001–50,000	140 (19%)	3 (14%)	137 (19%)	
>50,000	128 (18%)	8 (38%)	120 (17%)	
Antiretroviral regimen				0.04
HAART with PI	540 (74%)	13 (62%)	527 (75%)	
HAART without PI	64 (9%)	0 (0%)	64 (9%)	
Not on HAART	105 (14%)	7 (33%)	98 (14%)	
Missing/Unknown	17 (2%)	1 (5%)	16 (2%)	
Ever hospitalized	484 (67%)	19 (90%)	465 (66%)	0.02
Death	41 (6%)	8 (38%)	33 (5%)	<0.001

^a *p* value by Fisher's exact test for binary outcomes and by Pearson's χ^2 test for characteristics with more than 2 levels.

^b Wilcoxon rank sum test based on actual CD4%, rather than CD4% category.

AIDS, acquired immune deficiency syndrome; DNR, do not resuscitate; SD, standard deviation; PI, protease inhibitor; HAART, highly active antiretroviral therapy; EOL, end of life.

Table 2
DNR/Hospice Enrollment Adjusted Mean QOL Domain and Psychological Subscale Scores and 95% Confidence Intervals, Adjusted for Other Covariates^a

	End-of-life care (n = 21)		No end-of-life care (n = 705)		p value ^b	
	n	Mean	95% CI	Mean		95% CI
QOL domain						
General health perception	706	67.2	(58.7–75.7)	79.0	(76.2–81.9)	0.006
Symptom distress	721	77.8	(72.8–82.8)	90.0	(88.3–91.6)	<0.001
Psychological status	669	80.6	(73.8–87.5)	80.8	(78.5–83.1)	0.95
Physical functioning	672	49.8	(36.3–63.2)	79.1	(74.7–83.5)	<0.001
Social/school functioning	720	59.5	(51.0–68.0)	71.8	(68.9–74.6)	0.004
Health care utilization	709	88.8	(84.5–93.1)	91.8	(90.3–93.2)	0.17
Psychological subscale						
Anxiety/depression	672	75.4	(67.5–83.2)	79.8	(77.1–82.4)	0.26
Peer Conflict	669	90.9	(83.6–98.3)	89.9	(87.5–92.4)	0.79
Immaturity	668	74.5	(64.3–84.8)	80.0	(76.5–83.5)	0.29
Antisocial	672	89.9	(81.9–97.8)	85.1	(82.4–87.8)	0.23
Headstrong	672	78.1	(68.1–88.1)	74.1	(70.7–77.4)	0.42
Hyperactivity	669	72.6	(62.6–82.6)	77.6	(74.2–81.0)	0.33
Health care utilization						
Nights in hospital	712	5.1	(4.8–5.4)	5.9	(5.8–6.0)	<0.001

^a Means and confidence intervals for all domains (except symptom distress and physical functioning) and psychological subscales are adjusted for gender, age, race/ethnicity, CD4% (<14%, 15–24%, >25%), HIV-1 RNA viral load (<400, >400 copies/mL), previous hospitalization (yes, no), and ARV regimen; means and confidence intervals for symptom distress and physical functioning are adjusted for gender, age, race/ethnicity, and ARV regimen.

^b p value for EOL status from General Linear Model fit separately within each domain/psychological subscale, adjusting for covariates noted above.
DNR, do not resuscitate; QOL, quality of life; CI, confidence interval; ARV, antiretroviral.