Ethical challenges with the advancement of hematopoietic stem cell transplant

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Abstract. Advancements in medical science and pediatric intensive care have significantly improved outcomes for children undergoing hematopoietic stem cell transplantation (HSCT). Critical care management of HSCT patients requires pediatric intensivists to deal with ethical issues including aggressiveness of care and futility, limiting treatment, shared decision-making with families of critically ill children, and decision-making in the context of multi-disciplinary management of complex patients. This paper will discuss the fundamental ethical principles to enable pediatric intensivists to address questions of medical decision-making. Medical futility will be explored and strategies for dealing with both the practical and emotional implications of this for the pediatric intensivist will be addressed. Another important issue related to critical care of the HSCT patient is establishing goals of care, specifically related to end of life care decisions. A framework for end of life communication with families will be provided. Finally, this paper will discuss the potential conflicts resulting from multi-disciplinary care of the HSCT patient in the pediatric intensive care unit. As medical management of the HSCT patient continues to evolve, awareness of the ethical issues surrounding their care is important for both patient and provider.

Keywords: Hematopoietic stem cell transplantation, pediatric intensive care unit, medical management

1. Introduction

This article focuses on topics relevant to the pediatric intensivist faced with caring for a critically ill child, before, during and after hematopoietic stem cell transplantation (HSCT). Questions that must be confronted by the pediatric intensivist relate to aggressiveness of care and futility, limiting treatment, and multi-disciplinary collaboration and shared decision-making with families of critically ill children.

Critical care of the HSCT patient is unique for the pediatric intensivist in three ways. First, because HSCT patients are compromised by previous aggressive treat-

ments in a quest for cure the extent of required and expected critical care support may be greater than that for a patient without cancer. This can lead to difficult decision-making about the utilization of resources for a patient who may not survive hospitalization. The ethical issues of futility and decision-making regarding limiting treatment will be discussed. Secondly, HSCT patients may be admitted to the pediatric intensive care unit (PICU) without goals of care having been established. Goals of care must be continually revised during the clinical course of the HSCT patient. End-of-life care and decision-making about withholding and withdrawing of life-sustaining treatment will be discussed. Third, HSCT patients often have long histories with the transplant treatment team and limited or non-existent relationships with the PICU prior to their critical illness. Thus, intensivists may be at a disadvantage because they must act without the context of

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patient and family history, values, and goals-factors that can very much influence decision-making. The necessity for multi-disciplinary patient care and the issues it raises for the pediatric intensivist will be discussed.

2. Decisions regarding aggressiveness of care

Critically ill HSCT patients admitted to the PICU have a significantly higher risk of mortality than the average patient. Overall PICU survival has been reported to be around 60%, with risk factors for death including mechanical ventilation, multi-organ system failure, and prior admission to the PICU [1, 2]. Improvements in overall PICU survival, especially for children requiring mechanical ventilation suggest that aggressive care for the HSCT patient can be beneficial and should be undertaken with cautious optimism. However, a discussion of medical futility can be relevant in the care of HSCT patients. The definition of futility is subjective; however, a useful definition is “an action, intervention, or procedure that might be physiologically effective in a given case but cannot benefit the patient, no matter how often it is repeated. A futile treatment is not necessarily ineffective, but it is worthless, either because the medical action itself is futile or the condition of the patient makes it futile” [3].

Medical futility should be openly and regularly addressed among the medical team, prior to and during any decision to embark on aggressive therapy. There may be conflict between the care providers and family regarding initiation or continuation of specific medical interventions. Intensivists are not obligated to offer or perform all possible treatments for patients, and treatment should be considered in the context of the overall patient condition and likelihood of achieving goals of care. Guidelines from the Society of Critical Care Medicine state that “physicians are not obligated to offer therapies that they believe cannot achieve the goals of care” [4], and the American Academy of Pediatrics published guidelines affirming that “patients or surrogates may not compel a physician to provide any treatment that, in the professional judgment of that physician, is unlikely to benefit that patient” [5]. Despite these guidelines, the medical professional’s rights and roles in determining medical futility are complex. A number of historical cases highlight the confusing picture for medical professionals regarding medical futility.

The 1994 case of Baby K [6], an anencephalic infant whose parents requested mechanical ventilation, concluded with the courts determining that the family should be the final decision maker of continuing or withdrawing treatments that were believed to be medically futile by care providers. In contrast, *Gilgunn v. Massachusetts general hospital* found in favor of physicians who argued that providing cardiopulmonary resuscitation to a patient with multi-organ system failure was futile, even though it was requested by the patient’s family [7]. One model for the resolution of futility conflicts is The Texas Advanced Directives Act (TADA). The TADA empowers physicians through a formalized process to limit life-sustaining treatments that are deemed futile by care providers. In summary, TADA requires family notification of the ethics consultation process and 48 hr notice for the family to participate in the process. If no agreement can be reached and an alternative provider cannot be found, the hospital can unilaterally withhold or withdraw life-sustaining treatment after 10 days [8]. As of 2007, 70% of the 256 cases that utilized the process found that physicians were correct in determining that the requests were medically inappropriate. In 44% of the cases where the review committee agreed with physicians, the patient died within 10 days despite continuation of life-sustaining treatment and the review process led to physician-patient/patient representative agreement to discontinue treatment. The authors suggest that these data indicate that in the former situation, physicians were likely accurate in their assessment of medical futility and in the latter, the review process persuaded patients or their representatives that the medical interventions were inappropriate [9].

The fundamental ethical principles of beneficence and non-maleficence may also provide a useful framework for making treatment decisions. Beneficence in medicine refers to the duty to act in a manner that benefits the patient. Physicians have both a responsibility to prevent harm and a moral obligation to provide care to their patients that has potential to improve their outcome. Non-maleficence means to “do no harm.” Physicians should not provide ineffective treatments to patients; exposure to risk with no possibility of benefit violates the principle of non-maleficence. In the HSCT patient, the lines between providing benefit and not doing harm are often blurred. Treatments with potential to improve the patient’s condition often cause temporary harm. In fact, HSCT itself, with the goal of cure of malignancy, metabolic condition, or

immunodeficiency, causes harm in an effort to benefit the patient in the long run.

3. Establishing goals of care

Decision-making should be based on a realistic assessment of the probable outcomes of medical treatment at the child's stage of illness. This may be curative or palliative, and may transition from one to another during a child's admission to the PICU. End of life (EOL) decision-making presents one of the biggest challenges in pediatric critical care. Regardless of the quality of communication and eliciting of patient values, there will be situations in which the physician and patient/family disagree about goals of care. Disagreement between patients/families and health care professionals about treatment decisions is among the premier ethical challenges in medicine, and the intensive care unit specifically [10, 11]. Resolution of conflict over goals and treatment plans can result in moral distress for the medical team and distrust and dissatisfaction for the patient and family. Conscientious attention to communication and conflict can help prevent or reduce conflict over goals of care.

Children who die of cancer undergo aggressive treatment prior to death and oftentimes, have poor symptom control at the EOL [12]. Ullrich et al. [13] report that children who died following a HSCT spent more days in the hospital in their last month of life, were more likely to be intubated in the last 24 hr of life, and were more likely to die in the PICU. Additionally, the interval between both physician and parental realization of no chance for cure and the child's death was significantly shorter in the HSCT patients compared to the non-HSCT patients [13]. Pediatric intensivists need to be aware of the times in a HSCT patient's PICU course when a transition might be made from curative to comfort care.

This paper suggests that EOL care for the HSCT patient in the PICU may best be provided by paying close attention to the six domains of high quality, family-centered EOL care written by the Initiative for Pediatric Palliative Care. These include; 1) support of the family, 2) communication with the child and family about treatment goals and plans, 3) ethics and shared decision-making, 4) relief of pain and other symptoms, 5) continuity of care, and 6) grief and bereavement support [14].

3.1. Support of the family

HSCT patients are often admitted to the PICU requiring intubation, pressors, or emergent imaging, following long stays on the transplant ward. During their non-intensive care unit hospitalization, they have developed a community of doctors, nurses, and other families. They are now admitted to the PICU, with physicians who are unfamiliar to the family, making rapid decisions. Pediatric intensivists must be sensitive to this issue, working to develop a relationship based on honesty, open communication, and continuity of care. Support for the family of a dying child, while ensuring appropriate medical decision-making, requires multi-disciplinary involvement; social work, chaplaincy, child life, and other supportive services should be consulted early and often.

3.2. Communication with the child and family about treatment goals and plans

Establishment of family's goals should occur with any change in a child's clinical condition. When specific goals are rendered unachievable because of a deteriorating illness, the intensivist must be direct and open. New achievable goals must be established to ensure that the family is able to make decisions that benefit the child's overall well being. When survival is not likely, redirecting care to optimize comfort should be addressed. Communicating bad news to children and families, while difficult, should be done as soon as that information is available to the medical team. The SPIKES protocol was developed to facilitate breaking bad news to oncology patients and demonstrated increased confidence in the ability to disclose unfavorable medical information to patients among oncologists, oncology fellows, and medical students (Table 1) [15]. Utilization of this protocol and similar techniques has demonstrated improved patient satisfaction with communication [16].

Despite sound communication, disagreement may arise when the family requests medical interventions that the medical team considers non-beneficial. Two strategies for resolution of this conflict may include; 1) offering and seeking a second opinion and 2) consultation with the institutions ethics committee. A second opinion may assist patients or families who need reassurance, more certainty, or have a conflict with their physician. Many institutions require a second opinion in cases of conflict over medical futility. A second

Table 1
Components of the SPIKES protocol

SPIKES categories [15]	Components of the protocol
Setting up the interview	Arrange for privacy, involve significant members, and sit down
Assess the patients perception	Use open ended questions to probe family understanding “What have you been told about your child’s medical situation so far?”
Obtain the patient’s invitation	Query family’s interest/preferred method of receiving information “How would you like me to give the information about your child?”
Giving knowledge and information to the patient	Warn patient/family of bad news Use vocabulary at the level of the patient/family Use non-technical words Avoid bluntness
Addressing the patients emotions	Observe emotions Identify and communicate the emotion Identify the reason for the emotion Communicate an understanding of the emotion “I can see that this is upsetting news for you”
Strategy and summary	Share responsibility for decision-making Ask patients about specific goals and frame hope in regards to these goals

opinion may also provide support to staff by affirming the decision against non-beneficial treatments. Additionally, utilization of the ethics consultation process can be critical in resolving conflict over goals of care. In the intensive care unit, ethics consultations have been shown to reduce hospital and intensive care unit days and life-sustaining treatments believed to be non-beneficial by the medical team [17]. Ethics consultations can assist in resolving difficult cases, improving communication between the medical team and families, and provide institutional support in the rare occasion when the conflict cannot be resolved.

3.3. Shared decision-making

Shared decision-making is the model of medical decision-making most respectful of patient autonomy. It represents the gold standard for assisting patients in making difficult choices about treatment plans. The three components are; 1) discussion of clinical information (scientific evidence about the treatment choices, treatment options, and the risks/benefits of the options), 2) clarification of the patients’ values in the context of the decision, and 3) guidance and communication about treatment decisions that synthesize the clinical information with patient values. Shared decision-making for an HSCT patient occurs throughout a child’s transplant but is critical when EOL care questions arise. Input and recommendations from providers are important to families in making decisions, and most families prefer to have decisional authority when it comes to making value-laden

decisions related to withholding and withdrawing life-sustaining treatment [18]. The establishment of good communication and an understanding of the values important to a particular family will enable intensivists to guide decisions that are appropriate for the patient.

3.4. Relief of pain and other symptoms

Pain and symptom control are important needs for critically ill HSCT patients in the PICU. The inclusion of palliative care, for appropriate patients, is a recommended standard practice [19]. Improved symptom control eases the suffering of the patient and reduces stress for the family. Palliative care practitioners have expertise in symptom management, communication, and facilitating discussion of transition from curative to EOL care and should be considered a critical part of the PICU team for HSCT patients. Perceived impediments to the inclusion of palliative care in the PICU include conflict over provider roles, concern that the family will misinterpret palliative care involvement as “giving up”, and lack of available palliative care teams on a 24/7 basis [20]. Intensivists should strive to overcome these barriers and include palliative care practitioners early on in the PICU course.

3.5. Continuity of care

Families in the PICU interact with a number of different providers on a regular basis. These providers bring different beliefs, insight, and opinions about the patients’ prognosis and care. Critical events can occur

at any time, and the need for conversations about how to proceed with life-sustaining treatments and EOL care may occur at 3 A.M. with an intensivist the family has never met. For this reason, the primary intensivist caring for the patient should ensure that his/her colleagues are aware of the treatment plan, conversations regarding potential decisions that need to be made, and the family's goals of care. This will ensure a smooth transition between intensivists, and the family will be reassured that the PICU acts as a "team."

3.6. Grief and bereavement support

Unfortunately, more than half of HSCT patients admitted to the PICU will die in the PICU. It is incumbent upon intensivists to ensure, through inclusion of palliative care, social work, chaplaincy or spiritual support, that the families of children who die are provided with bereavement support services. Families should be offered time to be alone with their child and hold their child, access to private space, and the opportunity to express their emotions, and create mementos of their child [21]. Expression of compassion by caregivers, building a trusting relationship with the team, honest communication about the child's impending death, and the recognition of the child as a human being with social worth are all needs of parents experiencing the loss of a child in the PICU [22].

4. Providers of care

Most intensivists can relate to the situation of receiving a phone call from the transplant ward about a HSCT patient who is in respiratory distress and needs to be emergently transferred to the PICU. The patient arrives, requiring aggressive resuscitative care. Oftentimes, there is limited information about the patient and family wishes for treatment. The intensivist, a "stranger" to this family, must now engage in an involved conversation, under time pressure, and with a very limited relationship with the family. Provider roles should be established and communicated to the family so that there is clarity about how, and by whom, the treatment decisions will be made.

From a practical standpoint, collaboration between the PICU and HSCT teams is crucial for improved survival among HSCT patients. When a patient is transferred to the PICU, they are co-managed by the PICU and HSCT teams at the majority of high volume

HSCT centers in the US and Canada [23]. Collaboration between teams and earlier admission of patients with impending respiratory failure has led to improved outcomes by allowing for mechanical ventilation earlier in the disease process [24, 25]. Communication about patients on the HSCT ward who are worsening, and early admission to the PICU, with co-management by both teams, is important and necessary for improved survival. Realistically, disagreement over decision-making between intensivists and the transplant team can be a source of ethical conflict in the PICU. Relevant to the discussion of provider roles and decision-making is the moral distress experienced by those caring for critically ill HSCT patients. Intra-team conflict is a commonly reported source of distress among intensive care unit physicians and nurses [11].

Because of the extent and nature of illness among HSCT patients, and the multi-disciplinary decision-making, PICU providers may initiate or continue therapies that may not be beneficial, or conversely, may withhold or withdraw therapies that have the potential to be life saving. Moral distress occurs when providers are aware of the ethically appropriate action to take but are unable to act upon it or act in a manner contrary to their personal and professional values. Lower job satisfaction and lower satisfaction with quality of care are reported for providers when moral distress increases [26]. Frank discussion and acknowledgement of the moral distress associated with caring for HSCT patients is the critical first step toward resolution. Systematic methods for reduction of intra-team conflict include regular multidisciplinary team meetings, the identification of primary decision-makers amongst the various services caring for the patient, and the inclusion of the ethics committee in discussions about treatment goals and conflicts.

In conclusion, pediatric intensivists confront ethical issues in the care of HSCT patients. The main sources of ethical conflict relate to medical decision-making and EOL care. Based on the multidisciplinary nature of caring for transplant patients and the extent to which aggressive therapies are provided, the pediatric intensivist caring for these patients must be cognizant of the ethical principles surrounding decision-making and futile medical care. Establishing clear goals of care, with both the family and the transplant team, is necessary to ensure that patients receive the medical treatment that is most likely to benefit then without causing undue harm or morbidity. Utilizing colleagues with expertise in ethical analysis of medical decisions

will reduce the burden on the pediatric intensivist. As technologies and medical care of the critically ill HSCT patient continue to evolve, so must direct communication about ethical concerns and moral distress.

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