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Acute Kidney Injury in the Context of Multiple Organ Dysfunction Syndrome in Severe Pediatric Patients with Oncological Disease

Jader Pereira Almeida[1]*, Scheilla Torres de Oliveira[2], Luisa Alvarenga Guerra Martins[1], Yaiza Helena Felix Fortes Tiago[1], Karina de Castro Zocrato[3]

[1]Department of Pediatric Intensive Care, Santa Casa de Belo Horizonte Hospital, Santa Efigênia, Belo Horizonte - MG, Brazil

[2]Department of Pediatric Oncology, Santa Casa de Belo Horizonte Hospital, Santa Efigênia, Belo Horizonte - MG, Brazil

[3]Department of Pediatric Nephrology, Santa Casa de Belo Horizonte Hospital, Santa Efigênia, Belo Horizonte - MG, Brazil

***Corresponding author:** Jader Pereira Almeida, Department of Pediatric Intensive Care, Santa Casa de Belo Horizonte Hospital, Santa Efigênia, Francisco Sales Avenue, 1111 - Santa Efigênia, Belo Horizonte - MG, 30150-221, Brazil

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Acute Kidney Injury (AKI) is a complication frequently found in severe children with oncological disease, being associated with longer hospital stays and higher mortality rates [1]. The discovery of more aggressive chemotherapies resulted in longer periods of immunosuppression, predisposing to the development of infections, hemodynamic shock and, consequently, renal dysfunction. The treatment of patients with tumor lysis syndrome has the kidneys as the focus of care. In addition, the use of nephrotoxic drugs during hospitalization predisposes to the development of the problem.2 Therefore, the occurrence of renal dysfunction in children with cancer is multifactorial and it has a direct implication in their prognosis [2].

Unfortunately, concern about kidney function occurs most of the time when the patient develops anuria and clinical instability due to acute kidney injury and its complications, despite being a frequent problem in children. Park et al. in their retrospective study involving 1,868 children with cancer, they identified that 53.6% of patients developed AKI during the first year of diagnosis, especially those with hematological disease [3]. When renal dysfunction is present in patients with multiple organ dysfunction, clinical management becomes more difficult, especially when renal replacement therapy is necessary. In general, the degree of organ dysfunction is directly proportional to the risk of death. Many of these patients progress with fluid overload, refractory hemodynamic shock and persistent metabolic acidosis. Thus, invasive monitoring and the use of vasoactive drugs in high doses are often necessary.

These data are confirmed in the study by Haase et al. with severe pediatric cancer patients admitted to a pediatric intensive care unit, as the mortality rate varies between 42 - 95% [4]. The fact that the kidneys are responsible for the state of body hemostasis through pressure, hydroelectrolytic and basic acid control allows us to understand why it is so important for these patients (Figure 1). In this context, avoiding the development of severe forms of kidney injury is essential for the survival. The use of current acute kidney injury scores such as Kidney Disease Improving Global Outcomes (KDIGO); pediatric Risk, Injury, Failure, Loss and End Stage Renal Disease score (pRIFLE); or renal angina is necessary for the identification and classification of the problem, defining the degree of priority in patient management. These are objective scores and the increase in the stage of acute kidney injury has a statistically significant association with mortality [5]. Its use must be performed on admission and during hospitalization, especially when exposed to risk factors. The control of diuresis must be performed at least every 6 hours. Besides that, the serum creatinine level should be estimated more frequently, as it is characterized as a late marker of acute kidney injury and its alteration needs to be identified early.

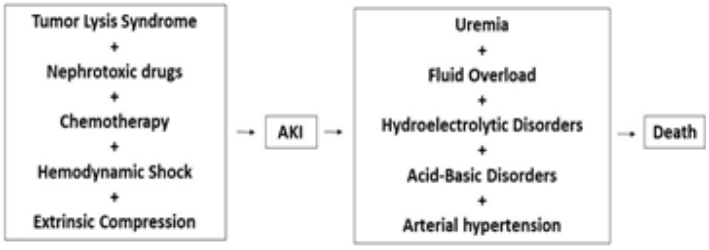

Figure 1: Risk factor for the development of acute kidney injury in pediatrc cancer patients and their complication AKI: Acute kidny injury.

One of the most critical issues in the management of critically ill children with cancer is the administration of large amounts of fluids through antimicrobials, sedatives, chemotherapy and transfusions of blood products, which can result in anasarca. Water overload is characterized as the accumulation of excess fluid in the extracellular space greater than 10% of body weight, usually associated with water supply greater than that stipulated by the Holliday-Segar formula. It can occur in the presence or not of renal dysfunction. Studies indicate that this variable is associated with increased mechanical ventilation time and increased risk of death, therefore, caution is necessary regarding the amount of fluid to be administered [6]. Medicines offered to patients should be diluted in a more concentrated manner in order to avoid over-supply and maintain the normovolemia state. The cumulative water balance must be under constant surveillance in association with clinical signs of hypervolemia (Figure 2). Furthermore, the use of lung ultrasound to identify B-line and echocardiogram to assess distensibility of the inferior vena cava are strategies that have the same purpose [7].

$$\text{Fluid Balance} = \frac{\text{Fluid in} - \text{Fluid out}}{\text{pICU dry weight}} \times 100$$

Figure 2: Accumulated water balance formula. pICU: Pediatric intensive care unit.

However, avoiding fluid overload is against one of the main therapies instituted in cancer patients, which is hyperhydration. This treatment is characterized by the administration of 2,000 to 3,000 ml/m²/day of fluid. The main indications of hyperhydration are risk of leukostasis, tumor lysis syndrome and the use of some chemotherapy drugs such as cisplatin, methotrexate and cyclophosphamide [3]. Most conventional chemotherapy drugs do not have specificity for cancer cells, resulting in organic damage in multiple systems, including the kidneys, although there is an effort among researchers in the development of chemotherapy with target therapy.

So, how do we know the amount of fluid to be administered to these patients? The answer is to individualize treatment, taking into account the patient's current volume status. Thus, patients with anasarca and fluid overload should receive less volume when compared to patients with normovolemia status. The goal of diuresis between 80 - 100 ml/m²/h in association with the acute kidney injury scores mentioned above may be good parameters in managing the volume to be administered. The use of loop diuretics can be used in the presence of fluid overload. In combination, renal replacement therapy may be an alternative, especially for critically ill patients with pulmonary congestion who have difficulty weaning from invasive mechanical ventilation.

Due to the complexity of the cases and the implications of conduct, the dialogue between the intensive care physician, nephrologist, oncologist and pharmaceutical is necessary for the proper management of patients. Multiprofessional visits at the bedside can add value in the early identification of critically ill patients at risk of renal dysfunction. In association, avoiding the use of nephrotoxic drugs and adjusting the doses of the drugs according to the glomerular filtration rate estimated by the modified Schwartz formula is imperative in clinical management [8].

Finally, the indication for renal replacement therapy should not be delayed in the presence of classic indications for this procedure, such as refractory hyperkalaemia, refractory acidosis and complications of uremia, in order to improve the survival of children with cancer.

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