Normal Saline and Lactated Ringers for Sepsis Fluid Resuscitation in Oncology Patients

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NURS 703B: DNP Project

Spring, 2024

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This paper is submitted in partial fulfillment of the requirements for

the Doctor of Nursing Practice degree.

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Introduction

Problem Description

Sepsis occurs when a dysregulated host response to infection causes a life-threatening organ dysfunction, possibly leading to septic shock, multiple organ failure, and death if not treated promptly (World Health Organization [WHO], 2023). Sepsis affects 1.7 million people in the U.S. and contributes approximately 270,000 deaths yearly. It is the most serious complication of infection and a leading cause of in-hospital death (National Institute of General Medical Sciences, 2021). The number of sepsis cases is predicted to rise each year, and complications of sepsis may alter patient's quality of life significantly. Oncology patients in an inpatient setting are highly susceptible to sepsis due to central line access, advanced age, hospitalization, the nature of malignancy, and high infection risk due to immunosuppression (WHO, 2023). Acutely ill septic patients require timely appropriate septic management, including fluid resuscitation, antibiotic therapy, blood tests, and imaging. However, delayed fluid resuscitation or antibiotic administration is often observed in septic patients, which is associated with increasing mortality rate (Macdonald, 2022).

Recognizing the importance of early sepsis detection and initiation of sepsis protocol, an academic hospital in the Pacific Northwest launched a nurse-initiated sepsis protocol in April of 2023. Currently, Lactated Ringers (LR) is used for all septic adult patients as a first choice of fluid resuscitation. One of the complications in cancer patients is dehydration in the setting of disease progression and chemotherapy, and fluid resuscitation plays an important role in preventing sepsis complications such as renal injury (Wang et al., 2022). However, there is no

standardization of fluid resuscitation for the septic oncology population, and LR is often changed to Normal Saline (NS) per provider order shortly after the nurse-initiated sepsis protocol is in place with LR. The change of fluid type by a provider after nurse-initiated sepsis protocol impacts and influences the comfort level of nurses to initiate early fluid resuscitation. NS is still widely used in the inpatient oncology setting as an as-needed hydration solution; the current protocol is to hydrate patients daily with 1L of NS bolus if they have <2L of oral intake in 24 hours. The use of LR for sepsis but NS for dehydration demonstrates a lack of clarity in the care of the highly vulnerable oncology population. The question of whether LR or NS is more beneficial for cancer patients remains to be determined which may affect standardization in sepsis management.

Available Knowledge

LR increases preload to the heart, therefore increasing organ perfusion in the setting of sepsis (Signh et al., 2022). The Surviving Sepsis Campaign suggests using balanced crystalloids such as LR as a preferred resuscitation solution over NS for sepsis (Evans et al., 2021). However, LR as a choice in sepsis is still debatable; the level of recommendation was weak, and the quality of evidence was low (Evans et al., 2021). According to a meta-analysis by Beran et al. (2022), a balanced crystalloid was associated with a significant reduction in the incidence of acute kidney injury (AKI) compared to NS in sepsis. This result was consistent with a randomized controlled trial (RCT) with an AKI incidence rate of 15.4% vs. 29.1% in LR and NS groups (Golla et al., 2020). However, a recent retrospective cohort analysis by Isha et al. showed no statically significant difference in sepsis patient outcomes such as mortality and hospital LOS between LR and NS (2023)

Historically, LR was avoided by many clinicians because of the misperceptions surrounding the effect of lactate in LR; clinicians previously believed there was a significant negative effect on increasing lactate level in septic patients with LR (Müller et al., 2023). However, the increases were not significant, and the benefit of LR outweighed the harm (Müller et al., 2023). LR is contraindicated in patients with liver dysfunction due to its hepatic metabolism and with cerebral edema, which requires hypertonic solution. LR is contraindicated with simultaneous blood transfusions because the calcium component in LR interacts with citrate in blood products (Signh et al., 2022). Hyperchloremia is common in critically ill patients following fluid resuscitation with NS (Hammond et al., 2020), which may lead to hyperchloremic metabolic acidosis. Cancer patients are at high risk for hyperchloremia due to dehydration in the setting of nausea and vomiting. Astapenko et al. stresses the importance of focusing on patient-specific underlying pathophysiology and clinical circumstances when choosing resuscitation therapy (2020). There is no current study comparing NS and LR for sepsis management in the inpatient oncology specific population.

Rationale

A quality improvement method, Plan-Do-Study-Act (PDSA), developed by the Institute for Healthcare Improvement (IHI), is designed to facilitate a quality improvement on a small scale and document a test of change ("Plan-Do", 2020). PDSA supported this quality improvement by providing a framework to identify a problem, to design plans, and to facilitate interventions over a short period of time. During the root cause analysis and creation of a cause-and-effect diagram, the absence of standardization of fluid resuscitation in septic cancer patients was identified.

This project aimed to improve the quality of sepsis care by eliminating unnecessary variation in fluid resuscitation protocol. Collecting baseline data to approach harmonization of sepsis management may help clinicians better understand appropriate resuscitation fluids in septic oncology patients, which may contribute to improving health outcomes and decreasing sepsis-related mortality. This quality improvement project may contribute to new recommendation on current guidelines or confirm the existing recommendation as best practice in sepsis management. It may also impact other settings, such as the emergency department, where cancer patients seek their first line care for the onset of neutropenic fever and often receive fluid resuscitation.

Specific Aims

The aim of this quality improvement project was to recommend a standardized resuscitation solution for inpatient oncology patients in a hospital. The results may reduce sepsis-related complications and mortality in cancer patients with appropriate fluid standardization in sepsis care.

Methods

Context

This quality improvement project was a retrospective review of three months data from June 2023 to August 2023 gathered from the Epic Electronic Health Record. The settings were all the units including the medical/surgical and Bone Marrow Transplant (BMT) units in a single hospital setting in the Pacific Northwest. The analysis only included patients with greater than or equal to one cancer diagnosis. Patients without a cancer diagnosis were excluded. The identified adult oncology patients with sepsis were included if they had received ≥ 30mL/kg of either NS,

LR, or both during the first six hours of sepsis management. The time of sepsis management initiation was determined by either time of a lactic acid draw, antibiotic administration, or nurse-initiated sepsis protocol. Excluded were patients who were under 18 years old at the time of sepsis management initiation, had no cancer and sepsis diagnosis, or if they had received <30ml/kg of each fluid type during first six hours.

Interventions

Utilizing Medical Record Numbers (MRNs) of patients with sepsis, patients' charts were manually reviewed to determine the type of fluid given for sepsis management. Patients' lactate level, vital signs, kidney function, ICU transfer rate, length of hospital stay, and mortality were reviewed and analyzed to compare the effectiveness of each solution in cancer patients.

Study of the Interventions

According to U.S. Food and Drug Administration (FDA), Real-World Evidence (RWE) provides clinical insights and requires assessment and validation of current clinical practice (2023). There is often a difference between what is expected to happen and what really happens in clinical practice: a gap between research and everyday practice in health care. This quality improvement project analyzed Real-World Data (RWD) on cancer patients' outcomes with LR or NS, to create RWE on effectiveness of each fluid resuscitation. The aim is to standardize current sepsis fluid resuscitation practice and protocol. RWE empowered by RWD analysis may contribute to improvement in overall cancer patient care by reducing sepsis-related complications and mortality.

Measures

The primary outcome measure for this project was what type of fluid resuscitation was given to patients for sepsis management. The secondary outcomes included vital signs (blood pressure, heart rate, respiratory rate, and temperature), lactate level, BUN, and serum creatinine level (sCr), hospital LOS, in-hospital mortality, and ICU admission after receiving resuscitation fluid(s).

Analysis

A retrospective analysis was performed to identify the oncology patients' outcomes with LR and NS for sepsis. This improvement project collected three months of data from June 2023 to August 2023 in the EPIC system, with analysis occurring September 2023 through March 2024. With the help of the sepsis report system, identified patients' charts were manually reviewed to determine the use of LR or NS for sepsis management, change in vital signs, lactate levels, BUN, and serum creatinine. Additional data was pulled from the hospital mortality dashboard and from nurse-initiated sepsis protocol team documentation for ICU transfer rate, in hospital mortality, and hospital Length of Stay (LOS). Data was mainly categorized by LR and NS with outcomes for each solution and additionally by solid tumor and blood malignancy diagnosis to compare impact of each fluid resuscitation in differences cancer type.

Ethical Consideration

This quality improvement project began after obtaining approval by the Institutional Review Board (IRB) with a waiver and included a letter of support from the agency. Non-identified patient data was used for this project. Direct patient contact or participation was not required; therefore, informed consent was not required. Patients included in this project were

coded by age, sex, diagnosis, and medical prognosis, not by name, demographic information, or occupation. Patients were anonymized, and their information was confidential to minimize physical, social, and psychological harm. Due to the retrospective approach of this project design, potential for physical harm was not identified. Information about the medical team who contributed to the patient care was not shared.

Results

A total of 427 adult patients were diagnosed with or treated for sepsis between June and August 2023; those who had no cancer history and sepsis onset in this three-month period were excluded. From 22 oncology patients with sepsis diagnosis, further exclusions included patients receiving less than 30 ml of fluid resuscitation per their admission weight (kg) in the first six hours as sepsis management. Ultimately, this retrospective analysis included a total of five patients; of these, four (80 %) received LR, none received NS (0%), and one (20 %) received both NS and LR as the sepsis resuscitation fluid.

At the time of sepsis management, all five patients presented with decreased BP and increased HR, compared to previous vital signs regardless of fluid types. All of the patients' Mean Arterial Pressure (MAP) increased after fluids and trended downward six hours after fluid resuscitation. After receiving fluid, three patients' heart rate decreased, and heart rate of one patient with LR and one patient with NS/LR continued to increase after receiving fluids. When the NS/LR patient switched fluid type from NS to LR, the patient's heart rate continued to increase; there are no other vital signs available after receiving LR due to death. One patient with LR presented with fever (≥38 °C) before sepsis resuscitation. A decrease in temperature was observed in all five patients after sepsis resuscitation. SpO2 decreased at the time of sepsis diagnosis in all five patients from their baseline; three of LR patients had increased SpO2 after

fluid resuscitation. The other two LR and NS/LR patients had no change in SpO2 after receiving fluids. Other factors that may have improved SpO2 were not observed. All patients' SpO2 remained ≥ 94% before, during, and after fluid resuscitation. One patient with LR had decreased RR at the time of sepsis diagnosis which increased after receiving fluid. The rest of the patients had increased RR from previous values at the time of sepsis diagnosis and decreased RR after fluid resuscitation.

Initial lactate levels ranged from 1.2 to 3.6 mmol/L with a mean value of 2.25 mmol/L. Two patients with LR had decreased lactate levels after receiving fluid resuscitation. One LR patient had a slight increased lactate level after receiving fluid. One LR patient did not have a repeat lactate level. One patient with NS/LR had an increased lactate level after receiving NS but a significantly decreased level after switching to LR. At the time of sepsis diagnosis, all five patients' creatinine levels had increased from baseline, and one LR patient's creatinine level continued to increase after receiving fluid. The other four patients (three LR and one NS/LR recipients) had decreased creatinine levels after fluid resuscitation. Three patients (two LR and one NS/LR recipients) had decreased BUN after fluid resuscitation, and the other two patients who received LR had increased BUN levels after fluid resuscitation.

Hospital length of stay ranged from three to 51 days and ICU stay from one to 46 days. The patient who received both NS and LR had the shortest hospital stay (three days) without ICU transfer due to death. Three in-hospital deaths during the same admission and one later admission were observed among the five patients. Sepsis management in one LR recipient was initiated by RN delegation protocol.

The five patients in this quality improvement project were white and averaged 69.6 years old. Four patients were male (80%), and one was female (20 %). Three patients (60%) had a

history of blood cancer, and two patients (40%) with solid tumor. Staging of cancer or previous cancer treatment and medications were not identified in this project.

Summary

This quality improvement project was conducted to evaluate types of fluid resuscitation in septic oncology patients and to compare the difference in patients' outcomes with different types of fluid. A total of five patients was included in this project of four patients received LR and no one received solely NS, and one patient received both NS and LR as fluid resuscitation for sepsis management. There was improvement in BP and HR after receiving adequate fluid resuscitation, consistent with national trends. There was not sufficient data to identify the superiority of LR or NS based on outcomes of four patient with LR and one with NS/LR.

Interpretation

This quality improvement project showed that most oncology patients received LR as a sepsis resuscitation fluid, which is per sepsis guideline recommendations. It also revealed that the use of NS as an initial resuscitation fluid still occurs in oncology patients with sepsis. The reason for choosing initial NS in this one patient was unclear.

Given the small sample size and the absence of a strictly NS group, this project was not able to show the difference in outcomes with LR compared to NS for sepsis resuscitation. Patients who received LR as sepsis resuscitation had positive outcomes in improving BP and HR, but again this quality improvement project is not able to support benefits of LR to improve hemodynamics in septic patients given the small sample size. Likewise, a positive or negative renal effect of NS versus LR solution cannot confirm studies that showed an association between use of NS and worsening of renal function (Beran et al., 2022; Golla et al., 2020).

This quality improvement project noted that the patient who had both NS and LR died on the same day of sepsis diagnosis, and he had the shortest hospital stay without ICU LOS. An outcome connection cannot be made because the death was likely the main factor of the shortened hospital stay. It was unclear if the patient's hospital death shortly after fluid resuscitation was related to the types of resuscitation the patient received. This project initially had 22 septic adult oncology patients, with 17 excluded because they received less than 30 ml/kg resuscitation fluid in the first six hours as sepsis management. Further investigation is needed to clarify why many oncology patients with sepsis did not receive > 30ml/kg in the first six hours of fluid resuscitation.

Limitations

There are several limitations of this project. The main limitation was the small sample size. This project did not include previous fluid administration status, and fluid resuscitation was determined only after either time of a lactic acid draw, antibiotic administration, or nurse-initiated sepsis protocol. Data collection from a single hospital setting and for only a short period (three months) is another limitation of this project. Additionally, there may be unidentified underlying conditions that could make patients more susceptible to failure or success with fluid resuscitation. For example, those who previously received antibiotics or continuous fluid prior to the sepsis management may show better outcomes than those who did not. Patients' baseline kidney functions, their types and stage of cancer, and previous drug therapy could also significantly alter patients' outcomes with sepsis fluid resuscitation. Additionally, predominantly white male patients were included in this project which limits generalization of the outcomes.

Conclusions

This quality improvement project was not able to compare significant outcome differences of NS and LR as sepsis resuscitation in oncology patients due to inadequate sample size. This project showed the evidence that most providers followed the guideline recommendation on using LR as a first choice over NS in sepsis resuscitation. Despite the limitations, the project confirms the use of the guideline recommendation on the type of fluid resuscitation for sepsis and spurs additional quality improvement projects to validate the outcomes of fluid resuscitation type for septic oncology patients.

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