Prevention of Tumor Lysis Syndrome in an Outpatient Setting

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The prevention and identification of hyperuricemia are critical components in the management of tumor lysis syndrome (TLS), which is common in acute leukemias, large cell lymphomas, bulky tumors, large tumor burdens, and other cancers with high proliferation rates. Such cancers are very receptive to cytotoxic therapy because of increased mitotic rates. Lysis of their tumor cells results in metabolic abnormalities because of the release of their intracellular products. TLS is an oncologic emergency that could lead to renal failure and death; therefore, early identification of high-risk patients is vital for successful treatment outcomes. Treatment modalities include the use of allopurinol and hydration while implementing evidence-based practices for the prevention of TLS in the outpatient clinical center.

Oncology nurses need to intervene early with the proper tools and education to provide the most effective, preventive treatment of TLS. The main goals of TLS management are threefold: the identification of high-risk patients with initiation of preventive therapy, early recognition of metabolic and renal complications, and prompt supportive care with hydration and possibly hemodialysis if renal failure develops.

TLS is an oncologic emergency, with metabolic abnormalities that could lead to seizures, life-threatening arrhythmias, acute renal failure, and death (Ezzone, 1999). Acute renal failure in TLS is a result of volume depletion and hyperuricemia. Many patients with malignancies are dehydrated on diagnosis (Davidson et al., 2004). The causes are multifactorial and include nausea, vomiting, decreased oral intake, fasting for surgery, and fever (Davidson et al., 2004). According to Solh and Appel (2008), the incidence of TLS can range from 3%–22%, depending on the type of malignancy, chemotherapeutic agents used, and other risk factors. For patients with TLS, the risk of renal failure (25%–38%) and death (5%–14%) is high.

Risk Factors

TLS is common in a variety of cancers with large tumor burdens, including acute leukemias, large cell lymphomas, and other cancers with high proliferation rates (Hande, Hixson, & Chabner, 1981). TLS occurs when large numbers of neoplastic cells are killed rapidly, leading to the emission of metabolic by-products (i.e., potassium phosphate and purine nucleic acids) and, subsequently, the release of those intracellular products into the bloodstream. That rarely occurs spontaneously; however, it is seen most commonly 48–72 hours after treatment (Krishnan, 2012). Signs of TLS include hyperkalemia, hyperphosphatemia, hypocalcemia, and hyperuricemia. Additional risk factors for TLS can be present in patients with solid tumors. Comorbidities such as dehydration, hypotension, preexisting renal damage, hyperuricemia, and elevated lactate dehydrogenase (LDH) may place patients at a higher risk of TLS. According to Tosi et al. (2008), advanced age, tumor infiltration of the kidney, and obstructive uropathy are other factors known to increase the risk of TLS.

Cytotoxic therapies that predispose patients to TLS are those with cycle-specific drugs such as cytosine, arabinoside,
etoposide, and cisplatin (Tosi et al., 2008). Although TLS commonly is seen with the first cycle or within the first few days of chemotherapy, it can occur with other cancer-related treatments, including radiation therapy, corticosteroids, hormonal agents, biologics, monoclonal antibodies, intrathecal chemotherapy, and chemoembolization (Vachani, 2007).

Patient Assessment

Early identification and intervention of high-risk patients are vital for successful treatment outcomes. Identification of host-related comorbidities and disease-related complexities provides oncology nurses with patients’ hydration status and their kidneys’ ability to handle cytotoxic therapy, and demonstrates patients’ overall risk for TLS. An instrumental preventive measure of TLS for patients deemed high risk is the baseline assessment of hyperuricemia, which quantifies the metabolic abnormalities seen as a result of lysis of a tumor cell.

Rapid cell turnover releases nucleic acid purines (i.e., adenosine and guanine); those purines are then metabolized to uric acid by hepatic xanthine oxidase (Krishnan, 2012). According to Hande et al. (1981), the systemic accumulation of uric acid inundates the kidney, compromising the body’s ability to rid itself of this byproduct. The increase of uric acid causes the formation of precipitates in a crystal form that builds up in the renal tubules and causes decreased blood flow, decreased glomerular filtration, and occlusion.

Using the Cairo-Bishop grading system, Montesinos (2006) developed a predictive model for the identification of TLS in acute myeloid leukemia (AML). Montesinos (2006) discovered that only one-third of patients with AML with laboratory TLS (LTLS) developed clinical TLS (CTLS) while undergoing induction therapy. The Cairo-Bishop grading system is a classification set up to differentiate between LTLS and CTLS. The system uses an institution’s upper-level norms of biochemistry and blood counts. Any increase or decrease by 25% in two of the laboratory values determines LTLS (low risk) versus CTLS (high risk). CTLS includes the two abnormal laboratory values plus a complication such as cardiac arrhythmia, oliguria, hyperkalemia, or seizures (Montesinos, 2006).

More recent risk assessment scales quantify risk into three groups (i.e., high, intermediate, and low) (see Table 1). Those risk assessments facilitate the appropriate courses of treatment by differentiating the tumor types associated with the least to the greatest risk. Lohr (2008) demonstrated patient classification guidelines and management of TLS, specifically hyperuricemia. As a result of that research, healthcare practitioners are provided with an evidence-based measurement of low-risk and high-risk patient populations so that appropriate preventive therapeutic measures can be implemented to protect patients at highest risk for the emergent outcomes of CTLS.

A thorough nursing assessment must include past medical history, current medications, complete blood cell count, complete metabolic panel, urinary analysis, and LDH. Recommendations currently vary but include monitoring LDH, uric acid, sodium, potassium, creatine, blood urea nitrogen (BUN), phosphorous, and calcium levels every six to eight hours for the first 48–72 hours, every 12 hours for the first 72 hours, and every 24 hours thereafter (Tosi et al., 2008; Vachani, 2007). Regardless, in an outpatient clinical setting, preventing TLS, in particular hyperuricemia, through risk assessment is paramount when navigating patients safely through the course of cancer treatment. Standards of care need to be individualized at diagnosis and prior to the initiation of treatment. Patients must be assessed for nausea and vomiting (e.g., from dehydration, renal failure), edema (e.g., renal failure), dysrhythmias (e.g., hyperkalemia), and tetany (e.g., hypocalcemia). Hyperkalemia often is the first life-threatening abnormality and equally important for nurses to monitor.

Interventions

Xanthine Oxidase Inhibitors

Preventive treatment of TLS includes the use of allopurinol, aggressive hydration, the occasional use of loop diuretics, and urinary alkalization. Malignant cells have large amounts of nucleic acid purines and their high proliferation rates lead to ongoing DNA catabolism, which in turn breaks down more purine nucleotides, thus yielding large amounts of hypoxanthine and increasing the rate of conversion to uric acid (Davidson et al., 2004). Allopurinol is a hypouricemic agent that inhibits the enzyme xanthine oxidase, which facilitates the conversion of hypoxanthine and xanthine to uric acid (Gobel, 2002). The prophylactic intervention of allopurinol increases the excretion of xanthine, the uric acid precursor (Pui et al., 1997). Interventional use of allopurinol reduces the risk of TLS and minimizes the threat of acute renal failure and death. When initiated one to three days prior to treatment, it works to prevent the accumulation of uric acid but cannot decrease the levels of existing uric acid (Vachani, 2007). Therefore, nurses need to monitor symptoms and laboratory abnormalities associated with existing renal impairment so doses can be adjusted to reduce the risk of accumulation of xanthine that could precipitate in the kidneys, affecting an already compromised system (Held-Warmkessel, 2010).

Allopurinol is used most frequently in the prevention of hyperuricemia and can be implemented easily in an outpatient setting. Pesson, Melchionda, and Castellini (2008) recommended allopurinol 300 mg/m² three times a day for prevention of TLS in patients at low risk. The dose for a patient with a body surface area of 2 would total 1,800 mg a day, a more aggressive dose than that reported by Krakoff (1966), whose research showed that 300–800 mg caused a marked decrease in uric acid levels. To date, the recommended allopurinol dose is 600 mg prophylaxis and 600–900 mg per day, not to exceed 500 mg/m² per day for treatment of TLS (Krishnan, 2012).

Options available for the prevention and management of TLS have broadened because of the U.S. Food and Drug Administration’s approval of recombinant urate oxidase (rasburicase)
Hydration and diuresis are the cornerstone in preventing TLS. Hydration corrects electrolyte imbalances and increases intravascular volume, in turn enhancing renal blood flow, glomerular filtration rate, and urine volume, decreasing the concentration of solutes (Krishnan, 2012).

According to Del Toro et al. (2005), patients should receive fluid maintenance 24–48 hours prior to cytotoxic therapy and 48–72 hours after therapy at 3 L/m². A patient with a body surface area of 2 would require six liters of fluid in 24–48 hours, which would put the infusion rate at 250 cc per hour in a 24-hour period and 125 cc per hour in a 48-hour period. Aggressive hydration may be contraindicated in patients with compromised cardiovascular function. In such cases, hydration may be lessened or prolonged. In an outpatient setting, providing hydration two days prior to therapy and two to three days afterward allows for ongoing assessment of the patient prior to administration of cytotoxic therapy, while monitoring for TLS, urine output, and the risk of fluid overload before the completion of therapy (Held-Warmkessel, 2010).

Oliguria is a decrease in urinary output of less than 900 ml a day and a known complication increasing the risk of TLS (Montesinos, 2006). Clinical monitoring in an outpatient center can pose challenges when measuring patients’ input and output. That is of great importance when oncology nurses must assess for hyperuricemia to implement interventions for obstacles associated with aggressive volume replacement and urine output for patient populations at known risk for TLS.

Implications for Nursing

Before choosing treatment modalities, healthcare practitioners must include baseline laboratory tests that indicate kidney function and hydration status. A patient’s BUN, creatine, phosphorus, calcium, potassium, sodium, LDH, uric acid level, and urinalysis should be obtained. Those will help the nurse to gauge the patient’s ability to tolerate cytotoxic therapy and identify patients at higher risk for TLS.

Research has established evidence-based treatments available for the management of TLS to rid the body of excess uric acid and protect renal function. Prophylaxis, the focus of those guidelines, provides healthcare practitioners with the appropriate tools to safely treat the outpatient population. The protocols include xanthine oxidase inhibitors, loop diuretics, hydration, baseline laboratory measurement tools, and guidelines to determine low-risk versus high-risk patient populations.

Prior to the implementation of the prescribed treatment, the oncology nursing staff must understand directives regarding appropriate hydration, administration of allopurinol,

Table 1: Classification of Patient Risk and Treatment of Tumor Lysis Syndrome

<table>
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<tr>
<th>Risk</th>
<th>Identification</th>
<th>Treatment</th>
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<tr>
<td>Low</td>
<td>ALL with WBC greater than 50 K/mcl, AML with WBC greater than 10 K/mcl, CLL with WBC greater than 10 K/mcl, indolent NHL, and other malignancies</td>
<td>Clinical judgment and monitoring</td>
</tr>
<tr>
<td>Intermediate</td>
<td>ALL with WBC 50–100 K/mcl, AML with WBC 10–50 K/mcl, CLL with WBC 10–50 K/mcl and treated with fludarabine, diffuse large B-cell lymphoma, and other malignancies with rapid proliferations and expected rapid response to therapy</td>
<td>Prevention: hydration and allopurinol prior to and during the course of treatment</td>
</tr>
<tr>
<td>High</td>
<td>ALL with WBC greater than 100 K/mcl, AML with WBC greater than 50 K/mcl, B-cell ALL, Burkitt lymphoma, lymphoblastic lymphoma, monoblastic AML</td>
<td>Hydration and rasburicase in an inpatient setting</td>
</tr>
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ALL—acute lymphoblastic leukemia; AML—acute myeloid leukemia; CLL—chronic lymphocytic leukemia; NHL—non-Hodgkin lymphoma; WBC—white blood cell count.
Implications for Practice

- Assessment and identification of patients at high risk for tumor lysis syndrome (TLS) are vital to successful treatment outcomes in an outpatient setting.
- Preventive measures for TLS can be pharmacologic or nonpharmacologic, and must be implemented prior to treatment.
- Oncology nurses play a pivotal role in the care and management of all patients at high risk of TLS.

and caution with urinary alkalinization and loop diuretics. Those should be made available to the nursing staff as part of the healthcare practitioner’s plan of care. Krishnan (2012) provided standards that focus on history, workup, treatment, medications, and follow-up care. Those evidence-based standards are the guiding system for oncology nurses to ensure that the most important aspects of the management of TLS are in place, including identifying patients at greatest risk for TLS and having preventive measures of hyperuricemia in place prior to beginning treatment.

Nurses must assess patients’ and families’ levels of understanding prior to the education process. Based on the level of comprehension, education can be provided through verbal, written, and visual materials to ensure an in-depth knowledge about the diagnosis, treatment, and prevention of TLS. Prior to the initiation of cytotoxic treatment, instructions regarding appropriate hydration, the administration of allopurinol, and symptoms associated with TLS need to be given to patients and families. Education helps ensure patient adherence, which plays an important role in the implementation of preventive measures, ultimately improving efficacy and safety for this patient population.

Management of hyperuricemia is important in the treatment of TLS; however, prevention and identification of risk factors associated with TLS are of greater importance in the protection against hyperuricemia, acute renal failure, and death. Oncology nurses are the front line of defense and must confirm the patient’s risk status (e.g., high, intermediate, low) to facilitate appropriate and safe treatment.

Conclusions

Evidence-based treatments for the prevention and management of TLS have been established through research. That research has provided resources to differentiate between low and high risk of TLS, creating a pathway for the healthcare team to base their treatment protocols.

The protocols include xanthine oxidase inhibitors, loop diuretics, hydration, baseline laboratory guidelines, and measurement tools to distinguish between high- and low-risk patients. Allopurinol and IV hydration remain the standard of care in treatment of TLS in the outpatient setting. To ensure safe passage through cytotoxic therapy, those and other preventive measures must always be implemented prior to treatment. Uropathy prevention is vital in outpatient clinical settings that often contain fewer resources to quickly reverse uric acid.

Oncology nurses play an essential role in keeping patients at high risk for TLS safe. Performing comprehensive assessments of patients’ past medical histories, medications, and renal function is crucial. A patient that presents with compromised renal function or other risk factors must be reassessed for LTLS versus CTLs and possibly treated in an inpatient facility, based on the assessment findings. That safety feature allows for the individualization of treatment, ultimately decreasing the incidence of TLS and improving the efficacy of treatment outcomes. The end result ultimately will improve patients’ quality of life, allowing for safe passage into recovery and remission.

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References


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