Tumour lysis syndrome (TLS) is an important metabolic disorder frequently encountered in the management of a variety of cancers including lymphoma, leukemia, neuroblastoma and small cell lung cancer. The acute tumour lysis syndrome (ATLS) may be a dramatic complication of anticancer therapy. It occurs mostly in haematological malignancies and less commonly in solid tumours. Spontaneous tumour lysis syndrome (STLS) has been reported more frequently in Burkitt’s lymphomas than in other haematological tumours and exceptionally in solid tumours like small-cell lung carcinoma and germ-cell tumours. Delayed recognition can result in biochemical abnormalities resulting in life-threatening complications such as renal failure, arrhythmias and seizures. Identification of high-risk patients and early recognition of the syndrome is crucial in early institution of appropriate prophylaxis and treatment.

**Metabolic abnormalities**

In patients with myeloproliferative diseases or hematopoietic malignancies, nucleic acids are catabolised as a result of increased turnover of malignant cell populations. This results in an increase in purine catabolism, leading to hyperuricemia. Aggressive cancer chemotherapy, radiotherapy or immunotherapy causes an increase in cell lysis and release of intracellular molecules (potassium, phosphorus and nucleic acid) into the bloodstream and results in four metabolic abnormalities: hyperuricemia, hyperphosphatemia, hyperkalemia and hypocalcemia. The large amounts of intracellular contents released cannot be processed and excreted by the kidneys. When renal excretory capacities are exceeded, patients develop acute renal failure secondary to precipitation of uric acid in the renal tubules. Hyperuricemia is the leading disorder responsible for TLS and its consequences (Table 1).

**Hyperuricemia**

Uric acid is a weak organic acid (pKa 5.8), and poorly water soluble at acidic pH. It derives partly from diet and partly from endogenous biosynthesis and it is eliminated by enteric (25-35%) and renal (65-75%) ways. Hyperuricemia (uric acid blood level over 8 mg/dl or 4.76 μmol/l), in fact, is considered its biochemical hallmark, because the precipitation of uric acid is possible when uric acid exceeds the limit of solubility (about 4.20 μmol/l at 37°C). It is already present at the diagnosis or it develops within 48-72 hours after the neoplastic treatment. The impact of hyperuricemia and deposition of monosodium urate (tophi) is widely felt because it may cause pathologic consequences in several organs, such as kidney, brain, subcutaneous tissues or joints. Kidney is one of the most involved organs in case of hyperuricemia, because it is the main site of uric acid excretion. Its impairment may be of different types. Hyperuricemia is a cause of urolithiasis. Calculi, predominantly composed of uric acid, represent around 13 percent of human kidney stones. It is also possible in acute urate nephropathy, due to dramatic and rapid increase of uricemia and renal handling of uric acid and urate. The crystals precipitate and obstruct tubules of distal nephrons and collecting ducts, where pH is acidic. The result is a tubular necrosis and acute renal failure (ARF) because of internal obstruction of urinary flow. After the disruption of tubules, crystals start to accu-

<table>
<thead>
<tr>
<th>Table 1: Metabolic imbalance in TLS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperuricemia</td>
</tr>
<tr>
<td>Hyperphosphatemia</td>
</tr>
<tr>
<td>Hyperkalemia</td>
</tr>
<tr>
<td>Hypocalcemia</td>
</tr>
</tbody>
</table>
Crystallisation is worsened by volume depletion (frequently in neoplastic patients owing to vomiting, diarrhea and fever), that compromises glomerular filtration and increases urate concentration in distal tubule. Also, low urine pH reduces uric acid solubility, worsening crystallisation.

The most frequent causes of ARF are the cytostatic therapies in patients with cancer or blastic crisis in acute leukaemia. The consequent massive cellular lysis exceeds the renal excretory ability. ARF is reversible with early treatment. Calculi are rarely described in this kind of renal damage. When uric acid exceeds renal capacity of elimination, it precipitates into renal tubules. So, a vicious circle is created because the consequent renal functional impairment worsens hyperkalemia and hyperphosphatemia; phosphorus and calcium bind themselves and precipitate within kidneys. Hyperuricemia and hyperphosphatemia severely worsen renal functionality; hyperkalemia and hypocalcemia compromise regular cardiac rhythm causing arrhythmias, sometimes mortal, and neuromuscular function, with potential tetany, convulsion and cramping. Being the clearance of uric acid, potassium, calcium and phosphate mainly renal, kidneys are overloaded, until their excretion ability is saturated with great difficulties to eliminate electrolytes, toxic substances and drugs, with consequent risk of accumulation and toxicity.

Hyperkalemia
Hyperkalemia is the most dangerous immediate consequence of TLS. It results in cardiovascular, neuromuscular and GI irritability and leads to delayed cardiac conduction and repolarisation. These changes can lead to atrioventricular block, ventricular tachycardia, ventricular fibrillation, or asystole. The cardiac effects of hyperkalemia can be exacerbated by hyperuricemia and hypocalcemia. The neuromuscular effects of hyperkalemia include muscle weakness and irritability, cramps, twitching and paresthesias in the form of tingling and burning.

Hyypocalcemia
The inverse relationship between calcium and phosphorus, hypocalcemia results from increased phosphorous binding to the calcium in the bloodstream, forming calcium phosphate salts.

Laboratory determinations
The prevention and early detection of metabolic abnormalities related to TLS include assessment of both laboratory data and symptoms related to elevated levels of uric acid, potassium, phosphorous. Close monitoring of metabolic parameters includes serum electrolytes (Na⁺, K⁺, Ca²⁺, Cl⁻, P), uric acid, LDH and renal function studies, including BUN and creatinine. Monitoring of laboratory values should take place every 6 to 8 hours during the first 72 hours after induction chemotherapy. TLS is defined as the presence of at least two of the following laboratory data: hyperuricemia, hyperkalemia, hyperphosphatemia and secondary hypocalcemia as described by Cairo-Bishop criteria (Table 2).

Nursing management
▪ Identify at-risk patients, including those in whom tumour lysis syndrome may develop up to 1 week after therapy has been completed (Tables 3 - 5).
▪ Institute essential preventive measures (e.g., fluid hydration and allopurinol). Close monitoring for fluid overload must be carried out by evaluating intake and output and daily weights and by assessing for oedema. The need for diuresis may be demonstrated by distended neck veins, shortness of breath, cough and rales on auscultation.
▪ Assess patient for signs and symptoms of electrolyte imbalances.
▪ Assess urine pH to confirm alkalisation. In addition to Allopurinol and hydration, urinary alkalisation is important to prevent uric acid crystals by
maximising its solubility in urine. Once the hyperuricemia has been corrected, urinary alkalisation should be stopped (i) to prevent phosphate precipitation in the renal tubules because phosphates are not soluble in alkaline urine, and (ii) to prevent alkalosis, which may predispose the patient to neuromuscular irritability by exacerbating hypocalcemia.

- Monitor serum electrolyte and uric acid levels for evidence of fluid volume overload secondary to aggressive hydration.
- Instruct patients to report symptoms indicating electrolyte disturbances.

Recent advances in the understanding of urate metabolism, development of new urate lowering drugs and application of biomarkers, calculation method and prognostic models to identify high risk patients will pave the way for improving the management of tumour lysis syndrome.

References

Table 3: Risk factors for tumour lysis syndrome
- High white blood cell count
- Impaired renal function
- Hyperuricemia
- Sepsis
- Elevated lactate dehydrogenase(LDH)
- Dehydration

Table 4: Early signs of TLS
- Diarrhoea
- Lethargy
- Nausea and vomiting
- Weakness
- Paresthesias

Table 5: Clinical manifestations

Renal Problems
- Decreased urine output
- Elevated blood urea nitrogen and serum creatinine
- Elevated serum uric acid
- Uric acid crystallization in renal tubules
- Acute renal failure

Cardiac Arrhythmias
- Atrioventricular block
- Ventricular tachycardia
- Cardiac arrest

Neuro-muscular Irritability
- Tetany
- Carpopedal spasm
- Muscle cramp
- Confusion, delirium, hallucination
- Seizures
- Digital and perioral paresthesias

Gastrointestinal Effects
- Nausea and vomiting
- Anorexia
- Intestinal colic
- Diarrhoea
- Hyperphosphatemia


THE NURSING JOURNAL OF INDIA 268

Dec 8 ’09