

## Frequency of Tumor Lysis Syndrome in Aggressive and Slow Introduction Chemotherapy in Children with ALL

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### Abstract

#### Background

Tumor Lysis Syndrome (TLS) is an oncologic emergency that results from massive lysis of malignant cells. The incidence of TLS depends on the risk factors, such as baseline hyperuricemia, bulky tumor burden, elevated serum LDH, and elevated WBC. The objectives of the present study were to assess frequency of Tumor Lysis Syndrome in children with ALL in two methods of induction chemotherapy, aggressive and slow induction.

#### Materials and Methods

In this double blind randomized interventional study, the number of 60 ALL patients in the Shahid Sadoughi Hospital Yazd were studied. They randomly treated using two various methods; 30 patients by invasive and 30 by slow induction chemotherapy.

#### Results

From 60 patients, 10 cases (16.6%) developed Tumor lysis syndrome. Seven of 10 treated by aggressive chemotherapy and remaining 3 by slow chemotherapy. No significant differences were found (PV= 0.166) between them.

#### Conclusion

Based on this study there was no significant difference between Tumor Lysis Syndrome in aggressive induction chemotherapy and slow induction, but WBC and LDH levels before treatment can predict Tumor Lysis Syndrome.

#### Key words

ALL, Tumor Lysis Syndrome, Induction Chemotherapy

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## Introduction

Tumor Lysis Syndrome (TLS) is an oncologic emergency that results from massive lysis of rapidly proliferating malignant cells. TLS characterize by hyperuricemia, hyper kalemia and hyperphosphatemia, which might lead to hypocalcemia with tetanus or other potentially life threatening complications. Arrhythmias occur as a result of hyperkalemia in 5% of the patients and are the most common cause of death in TLS. TLS usually develops shortly after the start of the effective cytotoxic therapy and it may lead to acute renal failure and death. It usually happens either before or within 1-5 days of after starting specific anti-leukemia therapy (1, 2, 3).

TLS is commonly seen in tumors with a high mitotic rate such as Burkitt lymphoma or T cell leukemia. It is less common in AML and pre-B-ALL and could occur with CML with the administration of combined cytotoxic chemotherapy. It is rarely reported after single-agent corticosteroid therapy (3, 4, 5).

The incidence of TLS is 3% to 22%, which depends on the patients risk factors such as baseline hyperuricemia, bulky tumor burden (more than 10cm), concentrated acidic urine ph, elevated serum LDH, elevated WBC (more than 100000/ $\mu$ l), first course chemotherapy in patients with bulky tumor, hematological malignancies with a high proliferative index, and volume depletion (5, 6).

The prevention of TLS is as important as its diagnosis and management. The regimen of hydration (2-4 maintenance), alkalinization (to keep urine ph between 7 and 7.5) and allopurinol prevent clinically significant TLS (3).

Allopurinol could treat hyperuricemia of malignancy, but is associated with drawbacks. Rasburicase which recently become available in the united stats, provides a safe and effective alternative to allopurinol. It decreases uric acid levels and prevents uric acid nephropathy (1).

ALL is a heterogeneous disease has led to treatment directed according to phenotype, genotype, and risk. Thus, mature B cell ALL is the only subtype that is treated with short-term intensive chemotherapy (7, 8).

The goal of induction therapy is to eradicate more than 99 percent of the initial burden of leukemia cells, restore normal hematopoiesis, and a normal performance status. This treatment phase almost always includes the administration of a glucocorticoid (prednisone, prednisolone, or dexamethasone), vincristine, and at least one other agent (usually asparaginase, an anthracycline, or both). Children and nearly all young adults with high-risk ALL receive four or more drugs during induction therapy. Overly aggressive induction therapy might lead to increased morbidity and mortality (9, 10, 11).

Dexamethasone has good penetration into the central nervous system with long half-life, which provides better control in the central nervous system than prednisone or prednisolone (12, 13).

The objectives of the present study were to asses frequency of Tumor Lysis Syndrom in children with ALL in two methods of induction chemotherapy, aggressive and slow induction.

## Materials and Methods

In this double blind randomized interventional study, the number of 60 ALL patients from 2007 until the end of 2008 in the Shahid Sadoughi Hospital Yazd were studied. They randomly allocated in two groups, which one group had invasive chemotherapy and other group slow induction. The patients included 36(60%) boys and 24(40%) girls aged between 1 to 10 years old (Average 6 years old).

In this study laboratory finding in patients before chemotherapy and 48 and 72 hours after chemotherapy was assessed. They included potassium, calcium, phosphorus, uric acid, urea, creatinine, alkaline phosphatase, LDH, and WBC.

Statistical methods included Fisher exact and Chi square were analyzed the findings.

## Results

From 60 patients, 10 cases (16.6%) developed Tumor lysis syndrome, which 7(23%) received aggressive chemotherapy and 3 (10%) slow chemotherapy. No significant differences were found (PV=0.166) between them (table1).

**Table1:** Frequency of TLS in the two groups of patients

Group \ TLS	Aggressive chemotherapy		Slow chemotherapy		Total		P-value
	Number	Percent	Number	Percent	Number	Percent	
Yes	7	23	2	10	9	16	0.166
No	23	77	27	90	51	84	
Total	30	100	30	100	60	100	

There was no significant relation between sex and age of patients with TLS (PV>0.05).

**Table2:** Frequency of TLS in WBC and LDH groups

WBC,LDH \ TLS	Yes		No		Total		P-value
	Number	Percent	Number	Percent	Number	Percent	
WBC>100000	3	100	0	0	3	100	0.006
WBC<100000	7	12	50	88	57	100	
WBC>50000	7	58	5	42	12	100	<0.001
WBC<50000	3	5	45	95	48	100	
LDH>800	8	25	24	75	32	100	0.005
LDH<800	2	7	26	93	28	100	

The relationship between LDH and WBC before treatment with TLS, were significant (LDH =PV: 0.005, WBC= PV: 0.023) in this table.

Based on this study there was no significant difference between TLS in aggressive induction chemotherapy and slow introduction, and WBC and LDH levels before treatment could predict TLS.

## Discussion

The acute tumor lysis syndrome has been reported most commonly after combination chemotherapy, all in patients with non-Hodgkin's lymphoma. Dhingra and Newcom (1988) described an acute tumor lysis syndrome. Single agent corticosteroid treatment in a patient with non-Hodgkin's lymphoma caused renal failure 72 h after dexamethasone therapy. Sparano et al (1990) described a patient developing life threatening hyperkalemia within 12 h after 100 mg dexamethasone. Acute tumor lysis syndrome occurs rarely after single agent corticosteroid therapy, but scientists believe that prescribing corticosteroids for patients with bulky disease

non-Hodgkin's lymphoma or leukaemia should be aware of this potentially life-threatening complication and monitor the patient very closely (14).

One study suggested that an increased dose of prednisolone in the context of other intensive treatment can yield results similar to those achieved with dexamethasone (15). Imatinib mesylate, a tyrosine kinase inhibitor, has enhanced the management of leukemia with BCR-ABL fusion, especially in elderly adults. Imatinib either as a single agent or as part of combination regimens has successfully induced or consolidated remissions (16, 17). However, its capacity to improve the cure rate remains uncertain. It has clearly contributed to extend disease-free survival and improve quality of life among these patients.

The incidence of TLS can range from 3% to 22% such as Bulky tumor burden (>10cm), elevated WBC (leukemia) and elevated LDH (5, 6).

Kapoor et al defined 22% of ALL cases and 15% AML cases presented with hyperleucocytosis. They reported WBC level before treatment can predict tumor lysis syndrome(3). This is concordance with present studies. However, limited study was reported.

Michael B. Davidson et al described the metabolic and electrolyte disturbances of tumor lysis syndrome may be concurrently exacerbated by renal failure. Patients may be treated with Allopurinol, hydration, urinary alkalinization, or hemodialysis. Rasburicase was recently approved in the United States, and may be more effective than allopurinol (1).

One randomized study demonstrated more rapid control and lower levels of plasma uric acid in patients who received rasburicase compared to allopurinol that is effective alternative to allopurinol during chemotherapy (18).

Prevention of TLS is to identify patients at risk and follow them clearly by testing those 48 hours after chemotherapy. The first step in prevention of TLS is to minimize the risk factors during the high risk period, which starts from 3 days before to 7 days after chemotherapy (5).

In conclusion, based on this study there was no significant difference between tumor lysis syndrom in aggressive induction and slow induction chemotherapy, but WBC and LDH levels before treatment could predict tumor lysis syndrom.

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