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ACUTE LEUKEMIA BEFORE AND AFTER CHEMOTHERAPY WITH RESPECT TO LIVER FUNCTION TESTS

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Abstract

Background: Chemotherapeutic agents can cause hypersensitivity reactions or direct hepatic toxicity, while altered liver function can change drug metabolism and increase the risk of non-hepatic toxicity.

Methodology: Serum total bilirubin was measured with the DMSO method, while serum AST and ALT were measured using the kinetic method before and after chemotherapy doses.

Results: The results found that chemotherapy-induced hepatotoxicity in patients with acute leukaemia.

Conclusions: This study concluded that chemotherapeutic drugs cause an increase in serum total bilirubin, ALT, and AST during the treatment of acute leukaemia. Liver function tests should be performed on a regular basis while treating leukaemia patients.

Keywords: Alanine Transaminase (ALT), Aspartate Transaminase (AST), Bilirubin, Acute Leukemia , before and after Chemotherapy, Liver Function Tests and chemotherapy.

1. Introduction

Acute leukaemia is a diverse group of diseases defined by uncontrolled and clonal neoplastic proliferation of hematopoietic precursor cells, as well as impairment of normal hematopoiesis, which results in neutropenia, anaemia, and thrombocytopenia [1]. Acute myeloid leukaemia (AML) involves myeloid precursors in the bone marrow, whereas acute lymphoblastic leukaemia (ALL) involves lymphoid precursor cells in the bone marrow and other lymphoid organs. AML accounts for 15–20% of acute leukaemia cases in children and 80% in adults [2].

The hem moiety of haemoglobin and other hemoproteins breaks down to form bilirubin. Bilirubin is insoluble in water due to internal hydrogen bonding and must be excreted via enzyme-mediated glucuronidation in the liver. In normal conditions, plasma bilirubin is mostly unconjugated and tightly bound to circulating albumin. It is absorbed by hepatocytes via facilitated diffusion, stored in hepatocytes bound to glutathione-S-transferases, and converted to glucuronides by microsomal UGT1A1. [3]

Increased production, decreased uptake, and a low glucuronidation capacity in the liver can all lead to higher plasma unconjugated bilirubin levels. In patients with inherited or acquired bilirubin storage or excretion deficiencies, both conjugated and unconjugated bilirubin accumulate in the plasma. Conjugated bilirubin is less tightly bound to albumin and therefore excreted in the urine [4]. Aminotransferase levels are sensitive indicators of liver cell injury and can help diagnose hepatocellular diseases such as hepatitis. Both aminotransferases, alanine transaminase (ALT) and aspartate transaminase (AST), are typically found in serum at low levels, less than 30 to 40 U per litre (U/L).[5]

As a result, AST typically rises immediately following hepatocellular injury and initially exceeds ALT levels. If the damage is ongoing, ALT will rise above AST within 24 to 48 hours due to its longer plasma half-life. ALT is also more commonly elevated than AST in chronic hepatocellular injury; however, as fibrosis progresses, ALT activities typically decline and the AST to ALT ratio gradually increases, as is the case with cirrhosis. When the liver cell membrane is damaged, an increasing amount of both enzymes is released into the blood. The liver transaminases are regarded as the most sensitive indicator of hepatocellular necrosis (hepatitis). These enzymes contribute to gluconeogenesis by supplying amino acids for the TCA cycle. [6]

The liver is the largest and most central parenchymatous organ in the body, responsible for intermediary metabolism and balanced regulation. Chemotherapy administration presents a challenge due to strict regulations and metabolic process balance. Most drugs are lipophilic, so they are easily absorbed by the liver.[7] Up to 85% of chemotherapy patients develop liver steatosis. Steatohepatitis is the more serious event, especially if it is associated with an increase in serum bilirubin levels [8]. The primary mechanisms underlying chemotherapy-induced hepatotoxicity are based on the production of reactive metabolites caused by oxidation reactions, immunological injury, or changes in mitochondrial function. [9]

Chemotherapeutic agents can cause hypersensitivity reactions or direct hepatic toxicity, while altered liver function can change drug metabolism and increase the risk of non-hepatic toxicity. The purpose of the current study was to compare liver function tests for acute leukaemia before and after starting chemotherapy in order to raise awareness about liver function.[10]

2. Literature review

Chemotherapy hepatotoxicity frequently occurs unexpectedly or in an idiosyncratic manner, and prior liver disease heightens the risk16. During the treatment of acute leukaemia, serum total bilirubin, ALT, and AST levels increase in response to chemotherapy drugs.[11]

Hepatotoxicity is defined as a liver injury caused by medication exposure that impairs liver function. Hepatocellular liver injury is defined as a significant initial elevation of alanine aminotransferase, cholestatic, as evidenced by an increase in serum alkaline phosphatase levels, or mixed if both enzymes are elevated. Clinically significant abnormalities on liver tests include ALT levels that exceed three times the upper limit of normal values and total bilirubin concentrations that exceed twice the upper limit.[12]

Patients who received four or more chemotherapy drugs were at risk of developing adverse medication reactions. Post-chemotherapy liver test results were classified as drug-induced liver injury if ALT was > 3 times the upper limit of normal and total bilirubin (TB) was > 2-3 times the upper limit of normal. Chemotherapy hepatotoxicity frequently occurs unexpectedly or idiosyncratically, and prior liver disease increases the risk.[13]

Acute lymphoblastic leukaemia (ALL) can affect many organs, including the liver and kidney, through infiltration of leukemic cells or chemotherapeutic drugs used to treat ALL [14]. Acute Lymphoblastic Leukaemia can cause electrolyte and metabolic imbalances that affect the liver and kidneys. The treatment of acute lymphoblastic leukaemia is determined by the condition of the kidney and liver. If liver and renal function abnormalities can be detected earlier and appropriate management can be provided prior to the introduction of or remission therapy, the treatment outcome will be favourable.[15]

A previous study found that serum bilirubin levels were significantly higher after chemotherapy than after induction due to the toxicity of anticancer drugs used during induction of remission. It was reported that more than two-thirds of the patients had elevated SGPT levels following induction therapy.[16]

3. Methodology

3.1 Collection of blood samples:

Blood samples were collected from patients with acute leukaemia before starting chemotherapy Day 1 and after chemotherapy day 14 and 30.

Blood sample tubes were labelled and coded for identification. They were kept in a slanting position until a clot formed, then centrifuged at 3000 rpm for 5 minutes at 25˚C.

The separated serum was stored in labelled eppendorf tubes. In each eppendorf tube, 1000 µL of serum was used for total bilirubin, 100 µL for ALT, and 100 µL for AST. [17]

3.2 Analysis of blood samples:

Serum total bilirubin was measured with the DMSO method, while serum AST and ALT were measured using the kinetic method [18].

All biochemical tests were performed as early as possible.

Liver Function Tests (LFTs) normal ranges includes:

· Bilirubin (Total): 0.3 - 1 mg/dl;
· ALT (Alanine Transaminase): <45 U/L (Male), <34 (Female);
· AST (Aspartate Transaminase): <35 U/L (Male), <31 (Female).

4. Results

- On the 1 day of chemotherapy, the mean serum total blirubin level in acute leukaemia patients was (0.89 ± 0.64 mg/dl).
- On the 14th day of chemotherapy, the mean serum total blirubin level in acute leukaemia patients was 1.55 ± 1.05 mg/dl,
- At the 30th day of chemotherapy, acute leukaemia patients had a mean serum total bilirubin of 0.72 ± 0.35 mg/dl.
- On the 1 day of chemotherapy, the mean serum ALT level was (47.46 ± 15.00 U/L).
- On the 14th day of chemotherapy, the mean serum ALT level was 87.08 ± 57.45 U/L,
- on the 30th day of chemotherapy, the mean level of serum ALT in acute leukaemia patients was 37.79 ± 11.69 U/L.
- On the 14th day of chemotherapy, the mean serum AST level was 38.00 ± 7.34 U/L.
- On the 14th day of chemotherapy, the mean serum AST level was 44.96 ± 8.29 U/L.
- on the 30th day of chemotherapy, the mean level of serum AST in acute leukaemia patients was (32.29 ± 4.78 U/L).

5. Discussion

Prior to starting chemotherapy, acute leukaemia patients had a mean serum total bilirubin level in normal ranges. Previous studies have reported that conjugated hyperbilirubinemia of acute leukaemia at presentation is common and may require treatment modification and dose reduction. [19] On the 14th day of chemotherapy, the mean serum total blirubin level in acute leukaemia patients was 1.55 ± 1.05 mg/dl, which was higher than the value measured prior to starting chemotherapy (0.89 ± 0.64 mg/dl). This finding was consistent with previous studies, as it appears that induction chemotherapy results in hyperbilirubinemia. [20]. This may be due to pre-hepatic hyperbilirubinemia caused by hemolytic anaemia.

At the 30th day of chemotherapy, acute leukaemia patients had a mean serum total bilirubin of 0.72 ± 0.35 mg/dl, which was significantly lower than the pre-chemotherapy value of 0.89 ± 0.64 mg/dl. Similar findings were observed in previous studies [21] which showed that serum total bilirubin decreased on the 7th and 18th days of chemotherapy. On the 14th day of chemotherapy, the mean serum total bilirubin in acute leukaemia patients was 1.55 ± 1.05 mg/dl. There was a significant change in serum total bilirubin between the 14th and 30th days of chemotherapy (0.72 ± 0.35 mg/dl).This finding was similar to the previous study, which reported that serum total and indirect bilirubin levels significantly increased during chemotherapy compared to their levels before.

On the 14th day of chemotherapy, the mean serum ALT level was 87.08 ± 57.45 U/L, which was significantly higher than the value measured prior to starting chemotherapy (47.46 ± 15.00 U/L). This finding supported previous reports that chemotherapy-induced hepatotoxicity is a common cause of abnormal liver function tests in patients with acute leukaemia [22] It typically occurs in an idiosyncratic manner and is generally reversible and not fatal. In this study, it was observed that on the 30th day of chemotherapy, the mean level of serum ALT in acute leukaemia patients was 37.79 ± 11.69 U/L, which was significantly lower than the value measured before starting chemotherapy (47.46 ± 15.00 U/L). This observation was consistent with other studies, which showed that chemotherapy induced

The current study found that the average serum aspartate transaminase (AST) level before starting chemotherapy in acute leukaemia patients was 38.00 ± 7.34 U/L. This observation was consistent with previous studies, which reported that elevated serum aspartate transaminase (AST) is common at initial presentation of acute leukaemia due to hepatic injury from leukemic infiltrates. [23] The study found that on the 14th day of chemotherapy, the average serum AST level in acute leukaemia patients was 44.96 ± 8.29 U/L, which was significantly higher than the value measured prior to starting chemotherapy (38.00 ± 7.34 U/L). This finding was consistent with previous studies, which showed that chemotherapy-induced hepatotoxicity is common in patients with acute leukaemia

In this study, it was observed that on the 30th day of chemotherapy, the mean level of serum AST in acute leukaemia patients was 32.29 ± 4.78 U/L, which was significantly lower than the value measured before starting chemotherapy (38.00 ± 7.34 U/L). This result was consistent with previous research, which demonstrated that chemotherapy-induced hepatotoxicity is nonfatal and reversible [24]. On the 14th day of chemotherapy, acute leukaemia patients had a mean serum AST level of 44.96 ± 8.29 U/L. There was a significant change in serum ASTbetween the 14th and 30th days of chemotherapy (32.29 ± 4.78 U/L). Previous studies have found that chemotherapy-induced hepatotoxicity is reversible [25].

Chemotherapy-induced hepatotoxicity occurs frequently in an unpredictable or idiosyncratic fashion, and preexisting liver injury increases the risk. This study discovered that elevated liver function tests were caused by either leukaemia or chemotherapy. As a result, patients who have received chemotherapy must have their liver function monitored closely during treatment to determine which drugs are inappropriate and which drug doses should be adjusted.

6. Conclusions

This study concluded that chemotherapeutic drugs cause an increase in serum total bilirubin, ALT, and AST during the treatment of acute leukaemia. Liver function tests should be performed on a regular basis while treating leukaemia patients.

7. References

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