



Original Research Article

Biochemical Changes of Liver Enzymes; ALT, AST, ALP in Patients after Surgical Operation Under General Anesthesia

Mohammed Abed Kadhim Al-Saadi Mufeed Jalil Ewadh Ahmed Ibraheem Rashid*
College of Medicine, University of Babylon, Hilla, IRAQ

*E-mail:ahmedrashid7652@yahooo.com

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Abstract

The physiologic state induced by general anesthetics typically includes analgesia, amnesia, loss of consciousness, inhibition of sensory and autonomic reflexes, and skeletal muscle relaxation. The liver function is mainly homeostasis. Alanine aminotransferase (ALT), Aspartate aminotransferase (AST) are soluble cytoplasmic and mitochondrial enzymes widely used to assess hepatocellular damage. ALP Alkaline Phosphatase is membrane associated enzyme anchored to cell membrane in particular to the biliary canaliculus. ALP is found in most tissues but is derived predominantly from hepatic cells.

Aim of this study was to evaluation of liver enzymes (ALP, ALT, AST) changes that accompany surgical operation under general anesthetic drugs.

A total of (36) patients under go surgical operations under general anesthesia. Blood samples were collected from patients just before and 24 hours after operation. The serum has been stored by deep freezing (-20°C) until used for serological tests to estimate the concentration of serum ALT, AST, ALP enzymes level. The results were significant increase in mean differences of serum ALT, AST, ALP enzymes level.

In conclusion this study showed that surgery and general anesthesia elevated serum level of ALT, AST, ALP enzymes.

Key words: General anesthesia, Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), Alkaline phosphatase (ALP), Surgery, Liver enzyme

التغيرات الكيميائية حياتية لأنزيمات ALT,AST,ALP في مرضى العمليات الجراحية تحت التخدير العام

الخلاصة

الحالة الفسلجية التي تتسبب بها ادوية التخدير العام تتضمن عدم الاحساس بالالم، نسيان، فقدان الوعي، تثبيط ردود الافعال اللاارادية والشعورية، و ارتخاء العضلات الارادية. الكبد يلعب دور مهم في التوازن الفسلجي مثل عمليات ايض الطعام والادوية، تصنيع البروتينات، ازالة سمية واخراج الكثير من المواد الضارة انزيمات Alanine Aminotransferase (ALT)، Aspartate Aminotransferase (AST) توجد في سايتوبلازم و بيوت الطاقة وتستهلك لقياس ضرر انسجة الكبد. ALP انزيم مرتبط بالغشاء الخلوي للفتوات الصفراوية وتعتبر خلايا الكبد المصدر الرئيسي لانزيم ALP في مصل الدم للانسان البالغ. تهدف الدراسة الى تقييم التغيرات في تراكيز الانزيمات بعد العملية الجراحية وادوية التخدير العام.

من مجموع (36) مريض يخضعون لعملية جراحية تحت التخدير العام، تم سحب عينات الدم من المرضى الاولى قبل العملية مباشرة والثانية بعد مرور (24) ساعة على العملية الجراحية تم سحب (5) مليلتر وبعد فصل مصل الدم تم خزنه بدرجة (-20) سليزي وبعد ذلك تمت فحوصات مستويات انزيمات (ALT,AST,ALP).

اثبتت النتائج ان هناك ارتفاع مع فرق معنوي لكل التراكيز الانزيمات ALT,AST ALP في مصل الدم بعد العملية الجراحية تحت التخدير العام (p value ≤ 0.05). استنتج الدراسة ان العملية الجراحية و التخدير العام يؤدي الى ارتفاع في مستوى انزيمات الكبد ALT,AST,ALP.

Introduction

Liver and Anesthesia; The liver plays an important role in homeostasis [1]. The liver receives 25% of cardiac output, yet, Portal vein flow is only affected by systemic hypotension and decreases in cardiac output [2,3].

Anesthetics and surgical operation affect hepatic function; conversely, liver dysfunction can affect the anesthesia and surgery. Effect of volatile anesthetics on liver blood flow and function is correlated not only to the anesthetic itself but also to the severity of liver dysfunction and abdominal surgical procedure [2].

Volatile anesthetics have an effect on liver blood flow others, including age, volume, intra-operative position, surgical operation, blood pressure, local anesthetics, hemoglobin level and oxygen level [4].

Anesthetics decrease cardiac output and then decrease portal blood flow; but they may increase hepatic arterial blood flow [3].

Total hepatic flow can be restored, Volatile anesthetics modify portal venous and hepatic arterial vascular resistance. No clinical hepatotoxicity has been found by using low and high flow sevoflurane and isoflurane anesthesia [5].

Intravenous anesthetics can affect liver function; thiopental and etomidate decrease hepatic blood flow, propofol increases portal and hepatic arterial blood flow. But intravenous anesthetics have not demonstrated effect on postoperative hepatic function [6].

The effect of central neuroaxial blocks on liver function is still unclear. Administration of anesthesia reduces blood flow to the liver during all surgical operations. In normal liver function, the decrease in blood flow can cause a symptomatic elevation in the results of serum liver biochemical tests postoperatively; in patients with compromised liver function preoperatively, hepatic decompensation can occur intra- and postoperatively, leading to morbidity and mortality [7].

The majority of surgical operation, whether performed under general or regional (spinal or epidural) anesthesia, are followed by minimal changes of serum liver biochemical tests [8].

Minor postoperative increase of serum aminotransferase, alkaline phosphatase, or bilirubin levels in patients without primary cirrhosis are not clinically significant [9]. Anesthetic drugs may reduce hepatic blood flow by 30% to 50% following induction. Animal data suggest, however, that isoflurane (along with desflurane and sevoflurane, which are believed to be similar) causes less perturbation in hepatic arterial blood flow than other inhaled anesthetic agents and therefore is preferred for patients with liver disease [10].

Other factors that may lead to decreased hepatic blood flow intra-operatively include hypotension, bleeding, and vasoactive drugs. Intermittent positive pressure ventilation and pneumo-peritoneum throughout laparoscopic surgery mechanically decrease hepatic blood flow [11].

Intravenous induction drugs together with sedatives, narcotics, are usually well tolerated in patients with compensated hepatic disease but must be used with care in patients with liver dysfunction, because they may precipitate hepatic encephalopathy [1]. High first-pass extraction by the liver of narcotic drugs, increase as hepatic blood flow decreases. Elimination of benzodiazepines that undergo glucuronidation (e.g., oxazepam, lorazepam) is unaltered by hepatic disease, whereas the elimination of those that do not undergo glucuronidation (e.g., diazepam, chlordiazepoxide) is postponed in liver disease [12].

Benzodiazepines and narcotics should be avoided in these patients; yet, when necessary, remifentanyl is the favored narcotic and oxazepam is the preferred sedative, because the metabolism of these agents is unaffected by liver disease [13].

Anesthesia: The physiologic state caused by general anesthetics classically includes amnesia, analgesia, loss of consciousness, inhibition of sensory and autonomic reflexes, and skeletal muscle relaxation. The extent to which every specific anesthetic agent can produce these effects depends on the specific drug, the dosage, and the clinical circumstances [14].

Alanine aminotransferase (ALT), Aspartate aminotransferase (AST)

Soluble cytoplasmic and mitochondrial enzymes widely used to assess hepatocellular damage. AST is found in all tissues, especially heart, liver, and skeletal muscle. ALT is present primarily in liver and, to lesser extent in kidney and skeletal muscle, making it more liver specific. AST and ALT are responsible for transferring of amino groups from aspartate and alanine to alpha-ketoglutarate respectively [15,16].

Both enzymes are present in high concentration in the liver, ALT is solely cytoplasmic, but AST is located in the cell cytoplasm and mitochondria. In acute inflammatory condition of the liver, ALT elevation frequently being higher than that of AST and tends to remain elevated longer due to its half-life in serum [17].

Alkaline Phosphatase (ALP)

Membrane associated enzyme anchored to cell membrane in particular to the biliary canaliculus. ALP is found in most tissues but is derived predominantly from hepatic, osseous, and intestinal cells. The liver cells are the major source of ALP in the serum of healthy adult [18].

ALP is secreted into bile and an elevation may be the first clue to intrahepatic or extrahepatic cholestasis. It is also elevated in most disorders of bone. ALP is belonged to a group of enzymes that catalyze the hydrolysis of a wide variety phospho-monoesterase in alkaline PH. It is a non-specific enzyme capable of reacting with many different substrates [19].

The aim of this study is for evaluation of liver enzymes (ALP, ALT, AST) changes that accompany surgical operation under general anesthetic drugs.

Materials and Methods

Patients

A total of (36) patients under go surgical operations consisting of (16) females and (20) males were involved in this study. The patient's age ranged from (22-51) years. The case information sheet was taken from each patient includes; name, age, sex, marriage, residence, history of chronic diseases, history of drugs intake, smoking history, type of operation. These patients were admitted to Hilla Teaching Hospital, Hilla-Iraq during the period from November (2013) to March (2014). Patients with suffering from other chronic diseases were excluded.

Blood Samples

Blood samples were collected from patients and before and 24 hours after operation a volume of five milliliters of venous blood was withdrawn by disposable syringe under aseptic technique (Lewis *et al.*, 2001). Each blood sample placed in a sterile plane tube and allowed to clot, and then serum was separated by centrifugation at (3000) rpm for (10) minutes. The serum has been stored by deep freezing (-20°C) until used for serological tests to estimate the concentration of (ALT, AST, ALP) enzymes by technique according to the instructions of manufacturer company kit (Randox).

Results

Distribution of Patients by Socio-Demographic Characteristics

The patients involved in this study had an ages range from (22-51) years that mean they were in young and middle age groups this may be due to selection of patients by inclusion and exclusion criteria.

Exclusion of patients with chronic diseases such as hypertension, ischemic heart diseases decreased the number of older

patients. Thus we found that the overall mean age of patients was (36.96±8.67) years old.

The sex distribution of patients revealed that the number of male patients was higher than female, but there was no great difference between them. The percent (56.0%) of patients were males and (44.0%) were female.

The distribution of patients by marital status, occupational status and residence showed that the married patients (32) which was significantly more than the single

patients (4), also about two-third of the patients were employed (24) whereas (12) patients had been found unemployed.

There was no great difference regarding the residence of patients whether urban or rural areas. Table 3.1 shows the distribution of patients by marital status, occupational status and residence, majority (88.0%), (68.0%) and (54.0%) of patients were married, unemployed and belong to rural area, respectively.

Table 1: Distribution of patients by marital status, occupational status and residence

Variable	Frequency (%)
Marital status	
Married	32 (88.0%)
Single	4 (12.0%)
Occupational status	
employed	24 (68.0%)
Unemployed	12 (32.0%)
Residence	
Urban area	16 (46.0%)
Rural area	20 (54.0%)

Effect of General Anesthesia on Serum ALT, AST and ALP Enzymes levels

The results of current study showed significant elevation of serum activity of all enzymes when compared their levels pre- and post- general anesthesia.

There were significant mean differences of ALT, AST, and ALP for patients' readings pre and post general anesthesia, p value ≤ 0.05 is significant. Table 2

Table 2: Mean Differences of serum ALT, AST and ALP for Patients Pre and Post General Anesthesia

Parameter	Mean	S.D	t-test	P value	
ALT	Paired	9.28	1.33	6.247	<0.001*
	ALT pre anesthesia	8.58	1.95		
	ALT post anesthesia	13.10	4.43		
AST	Paired	9.22	1.92	5.867	<0.001*
	AST pre anesthesia	8.15	1.60		
	AST post anesthesia	11.77	2.99		
ALP	Paired	8.43	2.26	21.857	<0.001*
	ALP pre anesthesia	8.30	2.19		
	ALP post anesthesia	18.99	1.98		

Regarding the current study results the significant elevation of enzymes activities level were all within the normal spectrum values i.e we can said there were no clinical withdrawals or symptoms occurs to these patients.

Discussion

Effect of Anesthesia on Serum ALT, AST and ALP Enzymes levels

The results of current study showed significant elevation of serum activity of all enzymes when compared their levels pre- and post- general anesthesia.

The liver cell is liable to damage because of its function of taking up and dealing with many metabolites, drugs, toxins etc. [20]

The serum ALT, AST activities indicated liver cell membrane damage rather than function [21].

ALP is a membrane bound enzyme and it is widely distributed in several tissues of the body such as liver, bone, kidney, intestine and placenta [22].

ALP is secreted into bile and is released when the canalicular membrane is damaged that lead to cause biliary obstruction [23]

Regarding the current study results the significant elevation of enzymes activities level were all within the normal spectrum values i.e there were no clinical withdrawals or symptoms occurs to these patients.

There was mild changes in postoperative serum levels of ALT, AST, were significant and that propofol and isoflurane anesthesia have a comparable minor effect on liver function after an elective posterolateral thoracotomy [24] and this result agrees with current study.

There were elevated liver enzymes occurs with prolonged propofol anesthesia for craniotomy. Liver enzymes were elevated (peak ALT) but returned to nearly normal within 5 days. [25] The current study agreed but the enzyme level changes did not reach these very high levels however, in both studies they had no clinical effect.

It was found in cohort study of trauma patients that some of these patients had abnormal post-operative liver biochemistry potentially attributable to volatile anesthetic and thus concluded that volatile anesthetic drug-induced liver injury in adult trauma patients may be significantly more common than previously noted. [25] The current study indicated these biochemical changes .

It was found after studying both general and spinal anesthesia there was slight to moderate increases above normal were observed for ALT, AST, and gamma-GT both groups differ with respect to enzyme levels during the postoperative course. So concluded that interpret these changes to indicate a reaction of the liver to the stress of operation and to the mode of anesthesia. [27].

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