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THE EFFECT OF INTRABDOMINAL HYPERTENSION DURING PNEUMOPERITONIUM ON ENZYMATIC LIVER FUNCTIONS AND ARCHITECT THE ROLE OF CORTICOSTEROIDS, PROSTAGLANDIN'S AND ADENOSINE TRIPHOSPHATE IN PROPHYLAXIS IS: A COMPARATIVE EXPERIMENTAL CONTROLLED STUDY

By

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The pressure induced during the pnuemoperitonium in laparoscopic surgery is the main variable in most recent studies. Several studies proved that it has a deleterious effect on liver function.The cause of increase in the liver function or what is described as transaminities is considered due to the transient ischeamia and reperfusion injury which occurred as a result of obstruction of hepatic blood flow while pnumoperitoinum is performed.

In this work the role of corticosteroids, prostaglandin (PGE1) and Adenosine triphosphate (ATP) in protecting against the injurious effect of the induced pnuemoperitonium in hamsters have been studied

In our study we had 4 groups of animals each of 12 male hamsters . The 1st group was the control group where the animals received no drug. In the 2nd , 3rd and the 4th groups the animals were injected with corticosteroid, PGE1 and ATP respectivly. The animals were subjected to GA general anasthesia and pneumoperitonium was performed up to 14-mmHg pressures for up to 60 minutes . Six hamatsers of each group were sacrificed ½ an hour after release of pneumoperitonium and the remaining six animals after 24 hours . The results of this study showed that transaminites and histopathological cell damage occurred in the controle group.The transaminites and the tissue destruction in hepatocytes were also high in the 2nd group but less than the control group. In the 3rd group the enzymes and histopathological architect were less affected ½ an hr after release of pneumoperitonium, but after 24 hr it showed severe impairment. In the 4th group the transaminites were high and tissue damage were severe compared to other groups.

Corticosteroids has proven to have a promissing protective function against the excpected deleterious effect of the pneumoperitonium on liver . Prostaglandin E1 had a good intial protective effect in the immediate post operative results but after 24 hours it showed no effect at all . In this study ATP did not show any benficial protecting effect on the liver

Key words: Liver function tests, Corticosteroids, prostaglandins, ATP , IRI, experimental animals Pnuemoperitonium,IAP

INTRODUCTION

Laparoscopic surgery has gradually replaced conventional open surgery in most of the abdominal operations. The study of haemodynamic and biochemical changes as a result of increase intra-abdominal pressure due to pneuopertonium during laparscopic surgery have been extensively studied [1,2,3,4,5,6,7,8]. The deleterious effect of intra-abdominal hypertension due to pneuopertonium on liver function has been documented in humans during and after laparoscopic surgery[9,10,11].

In this study pharmacological manipulation with Corticosteroid, Prostaglandins PGE1 and Adenosine Triphosphate ATP have been tried to find out their effects on the natural course of the liver function and architect due to increase intra-abdominal tension during induced pneuopertonium in hamsters[12,13,14].

The aim of work

Is to evalute the role of the corticosteroids, the prostaglandine and adenosine triphosphate in protection of the liver against ischeamia and reperfusion injury due to induced pnuemoperitonium in hamsters.

MATERIALS AND METHODS

****Animals and experimental groups***

This study was carried out in the animal house at Theodore Bilharze Research Institute. It included fifty four animals [male hamsters weighing 150 – 200 gm], forty eight of them were divided into four main groups, each of 12 animals. Those animals were deprived of food overnight but allowed free access to water before the experiment.

Pneumoperotinum was induced in each animal for 60 minutes at 14 mmHg which exceeds the standard pressure used during expermintal laparoscopic surgery (4-7 mmHg)[15,16]. After release of pneumoperotinum, laporotomy was carried out and a venous blood sample was withdrawn for biochemical analysis and the liver was resected for histopathological examination . This was done half an hour after release of pnuemoperitonium in 6 animals and after 24 hours under GA in the remaining 6 animals in each group.

The 4 groups and the dose given are listed below .

Table (1):

Group	*Drug*	*Dose*	*Pharmaceutical*
GI	Controle		
GII	Corticosteroid	0.01 mg/gm B.W.	Solucortife Upjohn Co 100mg/amp
GIII	-Postaglandins PGE1	1.5 ugm/gm B.W.	Prostavasinq 20 alprostadil
GIV	Adenosine Triphosphate	0.2 mg/gm B.W.	Adenosine 5 triphosphate magnesium Sigma Chemical 100mg/amp

[GI ,n = 12] control group in which no drug was given.
[GII,n = 12]corticosteroid (Solucortif, Upjohn Co 100 mg/amp.0.01 mg/gm body wt),
[GIII,n = 12] prostaglandin (PGE1, Prostavasine Schwarz Pharma AGX 20 mg/amp 1.5ug/gm body wt),
[GIV,n = 12].adenosine triphosphate (ATP, Sigma Chemical product Adenosine 5 triphosphate magnesium 100 mg /amp 0.2mg/gm body wt).

Each drug was injected intramuscularly before induction of penupertonium. An additional six animals were sacrficed under GA without induction of pneumperitonium and a venous blood samples were collected from IVC and their livers were resected to get the base line normal value for the animals both biochemichaly and histologicaly

****Induction of pneumoperotinum:***

Under general anesthesia with IM Thiopentanon Sodium [intraval] (0.2.mg/gm body weight), the anterior abdominal wall of the hamster was pinched away from the abdominal viscera and this fold was rolled between the thumb and the index finger of the left hand of the surgeon. The needle of the intravenous giving set [I.V. set] was inserted by the right hand of the surgeon into the peritoneal cavity through the lifted fold of the anterior abdominal wall to be directed almost horizontally to avoid visceral injury. This [I V set] was connected to the mercury scale of the manual sphignomanometer set through a trhee way tap so that insuflation of the abdomen with the rubber cuff handle pump could be done. This mechanism helped us in proper insuflation, adjusting the pressure up to 14 mmHg and controling and maintaining it for 60 minuts. At the end of the procedure the needle was disconected from its IV set and left inserted in the abdomen of the hamsters to release the pneumoperitonium and deflate the abdomen Then the needle was removed from the abdomen.(Fig 1,2).

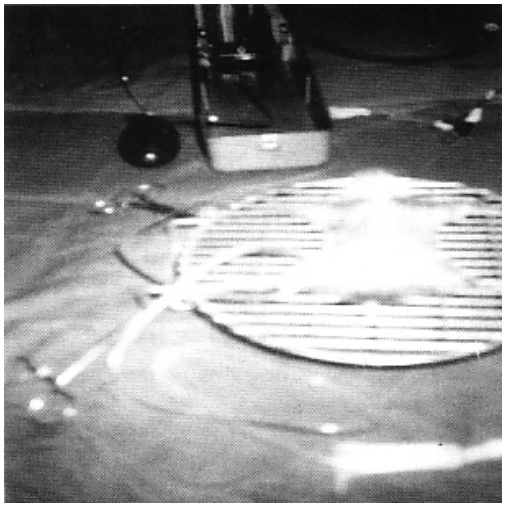

Fig (1):Showes the pressure at 14 mmHg and the 3 way tap

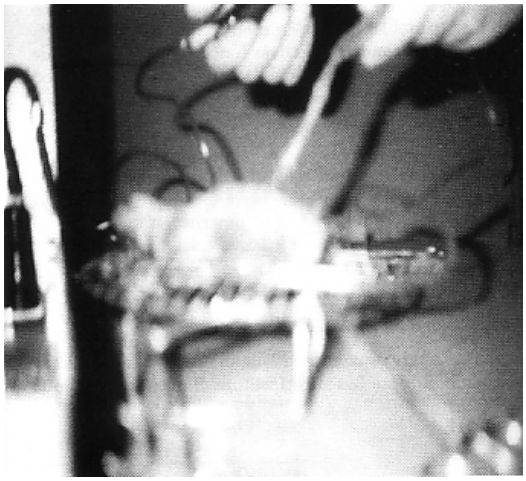

Fig (2) :Showes the method of insuflation and maintance of pressure for the whole procedure.

*Biochemichal analysis:-

Venous blood samples were collected from IVC, centrfugated and their serum were collected and freezed for the analysis. Liver enzymes were performed by conventional laboratory method and it included (ALT, AST).

*Histopathological examination of the liver:-

Histopathological examination was done for all the removed liver specimens. They were fixed in 10% buffered formalin. Transverse multiple sections of the whole liver embedded in paraffin, sectioned and stained with Haematoxyline and Eosin stain for routine histology and studying of the central vein, the portal vein, the sinusoids, the hepatocytes, the kupffer cells and the inflammatory cells as well.

RESULTS

The hamsters tolerated pneumoperitonium well. Only one animal of the control group did not recover from anesthesia.No single case of vascular or bowel injury was recorded due to insuflation procedure.The mean serum level + SD of liver enzymes of hamsters ½ an hour and 24 hours after release of pneumoperotnium in all groups is demonstrated in (Table 2)

The serum mean (+SD) base line liver enzymes i.e. AST and ALT of hamsters in this study were 53+5 and 52+10 respectivly.

Pneumoperitonium caused an increase in Liver enzymes above the base line in all 4 groups.

In the control group the mean + SD of AST and ALT for all hamsters in each group were high ½ hr immediately after relase of pneumoperitonium then it decreased but did not reach the base line after 24hrs.

Corticosteroid injection caused a slight increase of liver enzymes above the base line but less than those of the control group both ½ hr and 24 hr after release of pneumoperitonium.

The PGE1 intial results i.e after ½ hr was better than the control group but it was even worse than the control and the Corticosteroid after 24hr

The serum liver enzymes level of the hamsters received ATP revealed a higher level than the those of the control group and of hamsters received the previous two drugs both ½ hr and 24 hr after release of pneumoperitonium.

Table (2) *Liver enzymes Mean level+SD results*

Group	*Drug*	*½ hr*				*24 h r*			
		AST		ALT		AST		ALT	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD
GI	Control	596	61.3	163	12.4	392	51.7	171	35.5
GII	Cortisone	246	54.1	156	37.7	200	41.6	147	37.3
GIII	PGE2	289	45.7	131	16.3	772	132	358	82.9
GIV	ATP	636	69.4	440	122	673	80.3	301	52.9

The results of histopathological architect of the liver resected from all animals ½ an hour and 24 hours after release of pneumoperotnium in all groups are demonstrated in (Table 3)

The liver architect showed hepatocytes, inflammatory cells, portal vein, central vein and sinsoids. The portal vein and central vein were congested and dilated in all groups. The sinsoids showed brown pigments in the base line and the four groups. The hepatocytes showed hydropic degeneration in different degrees in all groups. The control and ATP groups had severe hydropic degeneration ½ hr and 24hr after release of pneumoperitonium compared to hamsters received corticosteroids and PGE1 which showed mild to moderate degree of hydropic degeneration. The inflammatory cells in the form of histiocytes and esinophils were found in different degrees in all groups ½ hr and 24 hr after release of pneumoperitonium except in the hamsters received corticosteroids.

Table (3) *Histopathology results;hepatocytes and inflamatory cells*

Group	*Drug*	*½ hr*		*24hr*	
		HC	IC	HC	IC
GI	Control	Sever	Sever	Sever	Moderate
GII	Cortisone	Mild/Moderate	Non	Mild	Non
GIII	PGE1	Mild/Moderate	Sever	Moderate	Sever
GIV	ATP	Moderate/Sever	Sever	Moderat/Sever	Sever

HC: heptocytes , hydropic degeneration:- Sever,Moderate,Mild
IC Inflamatory cells:- Non, Mild, Moderate, Sever

DISCUSSION

The deleterious effect of increased intra-abdominal pressure on liver function tests due to pneumoperotinum in patients subjected to laparascopic surgery is documented in several studies [10,11]

It is suggested that the pneumoperetinum during laparscopic surgery causes liver ischema. This has led to ischemic reperfusion injury after deflation of the abdomen that affected liver [9]

Little is known about the prophylactic drugs which may alleviate this injurious effect to the liver during laparascopic surgery. From the ethical point of view it is illogical to try the protective effect of different drugs against this damaging disturbance of liver function due to intrabdominal pressure during laparascopic surgery in humans.

In this study we have described a simple technique to induce and maintain a controled pneumoperotinum for establishing an animal model of hamster with increased

intra abdominal pressure almost similar to that occurring in humans during laparscopic surgery.

The serum liver enzymes and histopathological changes of the liver had been studied to demonstrate the effect of pneumoperotinum

The animals were injected with different drugs which claimed to have a protective effect against liver ischemia and reperfusion injury namely corticosteroid, prostaglandlin and ATP.[12,13,14]

In this study the induced pneumoperotinum proved to cause damaging effect on the liver cells. These changes in liver cells reflected on the serum level where serum AST and ALT were increased . These results may suggest that during pneumoperitonium and after its release in any laparoscopic procedure we should monitor the liver function for early detection of the expected impairment that might occur particularly in patients having compansated compromised liver. These results agreed with that recorded by other before [17,18,19].

In the animals that received corticosteroid (G II) the damaging effect on liver cell and the disturbance of liver function test were less than that of control group (GI) ½ an hour and 24 hours after release of pneumoperotinium. These experimental results might support the suggestion of studying of corticosteroid as a protective drug against the injurous effect of pneumoperotinium on liver function during laparscopic surgery particularly in those patients having a compromised liver but with no contraindication to corticosteroid use e.g. hypertension, peptic ulcer, severe infection and uncontrolled Diabetes. These results were similar to those recorded in a previous studies before.[20,21].

In our study, the third group (GIII) where the animal received (PGE1), the intial results after ½ hr revealed a better protective effect to the liver than corticosteroid but the 24 hours results was disappointing, as the liver function test and the histopathological finding were worse than corticosteroid (G II) and even the control group (GI) which received no drug. This intial effect of the PGE1 in the present study was simmiler to that obtained before by other investigators in dogs. In their study they used I.V. PGE1 before induction of Ischeamia by total clamping of hepatic blood inflow [14].They revealed a better incidence of survival in the treated animals than those received no drugs. This could explain our latent deleterious results using PGE1 in our study.

In our study we did not reach an exact explanation for such a latent reversal effect of PGE1 but further experimental studies is needed to find out its effect regarding the type of prostaglandin, re-evaluation of the dose, rout of adminsteration and its frequency, or if there might be a hepatotoxic metabolitis of the drugs which can be dealt with.

It was obvious in the histopathological results that the increase of intraabdominal pressure due to pneumoperitonium induces some degree of inflammation among the liver architect in all groups of the present study except in those hamsters received corticosteroids which did not show any inflammatory cells ½ hr and 24 hr after release of pneumoperitonium . These findings may explain why liver enzymes were less affected in animals of (GII) received corticosteroid before induction of pneumoperitonium. These results agreed with other previous studies which proved a protective effect of corticosteroids against liver ischeamia by total clamping of hepatic inflow vasculature[13].

In this study ATP in group (G IV) showed no beneficial effect as a protective drug against the damaging effect of abdominal hypertension due to induced pnuemoperitonium in experimental animals. These results disagreed with those of the previous studies where ATP was used to protect the liver tissues in shocked animals [12]

CONCLUSION

Corticosteroid proved to be a promising prophylactic drug against the expected injurous effect of the liver due to increased intra abdominal pressure during induced pneumoperotinium in hamsters.

These experimental results might recommend further clinical studies to find out such effects of corticosteroids in patients who have no restriction to its use.

PGE1 has an initial encouraging results in protection but unfortunately, the 24 hours results were exceedingly disappointing. These results suggest that further experimental studies is needed to explain and try to modify this strange action of PGE1. In this study, ATP did not show any signficant beneficial effect in this aspect.

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