

Evaluation of Serum Levels of AST, ALT, Total Bilirubin, Glucose, Urea and Creatinin in Mice after Administration of Tc-99m MIBI

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Abstract: Tc-99m MIBI methoxyisobutylisonitrile (MIBI) is a lipophilic cationic agent which is widely used for myocardial perfusion imaging and also for the detection of various tumors. In present study, for evaluation of serum level of AST, ALT, Total bilirubin, FBC, Urea and Creatinin, 25 mice, respectively were selected and they were divided in 5 groups. 0.3 mC/kg of drug was injected to 4 groups via tail vein. In the control group, before beginning of the investigation bleeding was done. Twenty four hours after injection from the 2nd group, 48 h later from the 3rd group, one week later from the 4th group and two weeks later from the 5th group bleeding was done respectively and the levels of Glucose, Urea, creatinin, ALT, AST and T-bilirubin, respectively were measured using spectrophotometr (Biowave S2100 made in England) and diagnostic kits (made in bio-chemistry company, Iran). In Comparison to control group, results had significant differences in serum level of Urea, Creatinin and total bilirubin after 24 and 48 h of administration ($p < 0.05$). Also there were insignificant differences in serum ALT and AST level and Glucose after 24 h of administration in all groups ($p < 0.05$). Results shows that more care is needed for administration of drug in diabetic, renal and hepatic patients.

Key words: Tc-99m MIBI, Glucose, AST, ALT, Bilirubin, Urea, Creatinin, Mice

INTRODUCTION

Tc-99m MIBI methoxyisobutylisonitrile (MIBI) is a lipophilic complex with positive charge that oxidation degree of technetium in that is +1 (Beller and Sinusas, 1990; Boucher, 1990). This complex rapidly will be cleared from peripheral blood circulation after intra venous injection (with 4.3 min half-life, only 1% of that connects to plasma protein) and looks like one-capacity cation, thallium -201, it is absorbed in live cardiac tissue (7) (Braat *et al.*, 1990; Charles, 1994). In the evaluation of ischemic heart disease only MR imaging seems to have the potential to assess myocardial perfusion, function, and coronary morphology on a single instrument (Bremerich *et al.*, 1997). The amount of cardiac absorption of Tc-99m MIBI depends on cardiac partial circulation that the major part of that is $1.5 \pm 0.04\%$ during exercise test and 1% during rest. This complex will be cleared slowly, it has 6h half-life and it has not redistribution (Chilton and Witcotski, 1986; Gopal, 1998; Charles, 1994). Absorption mechanism of Tc-99m MIBI, unlike thallium-201, is not related to Na/K adenosine 3 phosphatase (Na/K-ATPase) so it uses Passive diffusion

from plasma and mitochondrial membranes (Yakup and Unak, 2005); near 80% of activation in myocyte connects to negative charge of cytosole. The major activation is observed in cardiac cells, spleen and pulmonary cells respectively (Rajagopalan *et al.*, 1988). The main clearance way of the drug after first hours of injection is hepato-spleen pathway. Activation of gall bladder will appear in lumens (Balon *et al.*, 1992; Gibbons *et al.*, 1989). Therefore to accelerate the activation of hepatic and biliary system exertion, milky or fatty diet should be given to patient (Grégoire and Théroux, 1990; Isakandrian *et al.*, 1989). In addition to hepato-biliary system, about 27% of activation in 48h is excreted via urine; the amount via hepato-biliary is 37%. But it does not seem that absorption is not under control of TSH (Kiat *et al.*, 1989) (17, 19). The objective of this study is evaluated the effect of Tc-99m MIBI on serumal levels of AST, ALT, Total bilirubin, Glucose, Urea and Creatinin in mice.

MATERIALS AND METHODS

This experimental study was carried out in Research Center of Islamic Azad University at 2011, and all the

Table 1: Effect of Tc-99m MIBI on blood glucose level and serum markers of liver and kidney tissue injury at different periods of the experiment (mean±SEM)

	Control	24 h	48 h	1 week	2 weeks
Glucose	72±15.1	158.66±3.52*	66.66±4.40	74.00±3.05	65.67±4.70
AST	66.50±1.66	117.66±1.45*	141.96±1.66*	129.6±0.33*	127.5±1.20*
ALT	56.70±2.88	129.70±1.60*	128.8±1.85*	107.66±1.45*	103±1.52*
UREA	47.50±1.45	80±1.52*	60.66±0.32*	50.30±0.22	50.60±0.88
CREAT	1.66±0.03	2.40±0.5*	2.10±0.02*	1.00±0.05	1.15±0.02
T-bilirubin	0.43±0.03	1.52±0.17*	1.33±0.03*	0.46±0.03	0.43±0.01

*: There is meaningful difference with control group (p<0.05)

procedures and works on animals was conducted under Animal Rights Monitoring Committee of Islamic Azad University Research Center. Investigations using experimental animals were conducted in accordance with the internationally accepted principles for laboratory animal use and care as found in the United States guidelines (United States National Institutes for Health publication no. 85-23, revised in 1985), and our Ethical committee on animal care approved the protocol. In present study, 25 healthy male mice have selected and divided into 5 groups. After body-weighting of each group by digital balance, all animals were kept in individual cages during the whole experimental period, under strict hygienic conditions and fed with standard ration for rat ad libitum, in lightning for 12 h and darkness for the same hours in 25°C to adaptation to the environment. Mice were divided in 5 groups, one group was as control and other 4 were as treatments. 0.3mc of Tc-99m MIBI were injected via tail vein to all 4 treatment groups. Blood sampling was done from control group before injection via tail vein. Twenty four hours after injection blood sampling of second group, after 48h sampling of third group, after a week sampling of fourth group and after 2 weeks sampling of fifth group was done. Biochemical parameters such as urea, creatinin, ALT, AST, Urea, Creatinin and T-bilirubin, respectively were measured using spectrophotometr (Biowave S2100 made in England) and diagnostic kits (made in bio-chemistry company, Iran). All biochemical results were expressed as mean±S.D. significant differences amount the groups were determined by one-way analyses of variance (ANOVA) followed by student t-test using the statistical analysis software (SPSS) Ver. 14, under windows XP. Statistical significance was considered at p<0.05.

RESULTS AND DISCUSSION

The results of this study are listed in Table 1. Glucose level in the 24 h group was higher than 4 groups and the results showed statistically significant increases with the other group (p<0.05).

The Mean levels of AST and ALT in the 24, 48, 1 and 2 week groups were higher than the control group and showed significant increases (p<0.05). The creatinine, Urea and bilirubin levels in the 24 and 48 h group were higher than other group and showed significant increases (p<0.05).

One of the most important and common diagnostic methods in heart disease is thallium scan. Nowadays instead of thallium, Tc-99m MIBI is used more which is useful for detection of cardiovascular tissue perfusion. It will absorb by cardiac tissue after entering the blood and excrete via hepatic and renal system from body. Technetium-99m-MIBI may be a useful agent in the localization of recurrent medullary thyroid carcinoma (O'Driscoll *et al.*, 1991). Technetium-99m-MIBI may be useful in the assessment of disease activity and monitoring response to treatment in patients with lymphoma (Scott *et al.*, 1992).

Results showed an increase in serum glucose level in 24 h after administration which may be due to stress of administration, or in other hand, probably this drug have made a disorder in insulin discharge that needs farther evaluation. The serum levels of creatinin and urea had significant increase in comparison to treatment groups in 24 and 48 h after administration. Urea is an excreting substance that is produced in protein metabolism. creatinin is an excreting substance that is produced in creatin metabolism in a nonenzemetic pathway. Increasing in urea and creatinin may be due to pre renal or post renal disorders (Mojabi, 2005; Duncan *et al.*, 2001). Pre renal problems may happen during dehydration and diseases and cardiovascular disorders that the amount of renal perfusion decreases (Amouoghli *et al.*, 2008); while in this study water consumption was in normal range all mice were clinically health. The increase may happen due to renal or glomerular or tubular plexus disorders. The hypothesis is that excreting metabolites may have adverse effects on renal tissue that were cause of disorders that need more researches. Overlay consumption in diabetic and renal failure patients should be under more medical care. ALT (SGPT) and AST (SGOT) are two aminotransfrase enzymes that transfer amino group in a single columnar alpha acid. Most ALT functionality is in hepatocells and less in other cells. ALT is a cytoplasmic enzyme however AST is a mitochondrial one that has isoenzyme in other cells beside hepatocells such as myocardial cells, muscles, kidney, and etc. increase enzyme content after 24 h of drug consumption may be due to direct drug action or other active metabolites of drug in hepatocells. As it metabolizes in hepatocells, may has adverse effects there. Another important factor in HFP (hepatic function test) is bilirubin which is an excretional metabolite of RBC which excretes in bile. Twenty four

hour Bilirubin content had crease and was increasing in 48 h that may be due to drug action or excrete of material that needs conjugated and non-conjugated bilirubin assay.

CONCLUSION

This study demonstrated that Tc-99m MIBI administration resulted in elevation of serum biomarkers of liver and kidney tissue injury and blood glucose level.

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