SUMMARY AND CONCLUSION

Antimicrobial agents constitute a rapidly expanding group of drugs that are useful for treatment of various types of infections. Also it is clear that adverse drug reactions are common with these compounds. This work was done to study the histological and histochemical effects of tienam as a recent carbapenem antibiotic on the liver and kidney of sixty adult male albino rats which were divided into five groups as follows.

Group I:

Twenty rats were used as controls and each one was injected with 0.5ml of sterile normal saline solution I.M. every 12 hours.

Group II:

Ten rats, each one was injected with tienam 90mg/kg body weight/day for 4 days.

Group III:

Ten rats, each one was injected with the same dose of tienam for 7 days.

Group IV:

Ten rats, each one was injected with the same dose of tienam for 14 days.

Group V:

Ten rats, each one was injected with the same dose of tienam for 14 days, then injection was stopped for 14 days.

The animals were sacrificed at the end of the experiment and specimens of liver and kidney were obtained.

The histological methods used were Hx & E and Masson's trichrome stain to demonstrate the general architecture of the examined organs and their connective tissue content.

The histochemical procedures included:

- PAS technique to detect the neutral mucopolysaccharides in hepatocytes and uriniferous tubules.
- Sudan black method for demonstration of lipid content of hepatic cells and tubules of kidney.
- Azo dye technique for detection of acid phosphatase enzyme activity.
- Gomori calcium method for demonstration of alkaline phosphatase enzyme activity.
- Nitro blue tetrazolium method for demonstration of succinic dehydrogenase enzyme activity.
- Lead method for demonstration of adenosine triphosphatase enzyme activity.
- Alpha-naphthyl acetate for demonstration of non-specific esterase activity.

The results obtained can be summarized as follows:

<u>The Liver:</u>

Histological picture after Hx & E and Masson's trichrome stains:

Group I (control group): Showed classical hepatic lobule which was composed of a central vein and mass of liver cells, portal

tract were found at angle of hepatic lobule. Minimal connective tissue around central vein and at portal area.

Group II: Resulted in mild vacuolation of cytoplasm of hepatocytes, mild dilation of blood sinusoids with minimal cellular infiltration at portal tract. No change in amount or distribution of connective tissue.

Group III: Showed more vacuolation in the cytoplasm of liver cells also there were dilation and engorgment affecting central vein and blood sinusoids and portal vein. Mononuclear cellular infiltration and fibrous tissue streaks appeared at the periphery then the central regions of the hepatic lobules.

Group IV: Had marked vacuolation in the cytoplasm of liver cells. There were more dilation and congestion affecting central vein and blood sinusoids and portal vein. Marked mononuclear cellular infiltration and fibrous tissue streaks in portal tract and between heptocytes were observed.

Group V: Most previous changes disappeared and liver returned to the normal picture after 14 days from drug withdrawal.

Histochemical changes:

PAS reaction:

Group I (control group): Showed strong reaction in hepatocytes.

Group II: Didn't reveal any detectable changes.

Group III: Showed moderate PAS reaction in the hepatocytes.

Group IV: Showed weak PAS reaction in the hepatocytes.

Group V: Showed strong PAS reaction in the hepatocytes as control.

Sudan black B:

Group I (Control group): Showed few fat droplets in hepatocytes.

Group II: Showed increased fat content in hepatocytes.

Group III: Showed more increase in fat content in hepatocytes.

Group IV: Showed marked increase in fat content in hepatocytes.

Group V: Showed decrease in fat content distributed all over hepatic lobules.

Acid phosphatase:

Group I (control group): Showed weak reaction for acid phosphatase in liver cells.

Group II: Didn't reveal any detectable changes.

Group III: Showed moderate reaction for acid phosphatase in liver cells.

Group IV: Showed strong reaction for acid phosphatase in liver cells.

Group V: Showed a picture similar to that of control.

Alkaline phosphatase:

Group I (control group): Showed weak alkaline phosphatase activity in hepatocytes.

Group II: Didn't reveal any detectable changes.

Group III: Showed moderate increase in enzymatic activity in the hepatocytes.

Group IV: Showed marked increase in enzymatic activity in the hepatocytes.

Group V: Showed a picture similar to that of control.

Succinic dehydrogenase:

Group I (control group): Showed intense reaction for succinic dehydrogenase.

Group II: Showed strong reaction for succinic dehydrogenase in hepatocytes.

Group III: Showed weak reaction for succinic dehydrogenase in hepatocytes.

Group IV: Showed negative reaction for succinic dehydrogenase in the hepatocytes.

Group V: Showed slight return of the enzymatic activity in many hepatocytes.

Adenosine triphosphatase:

Group I (control group): Showed moderate ATPase activity in the hepatocytes.

Group II: No obvious change was observed in the ATPase activity.

Group III: Showed weak ATPase activity in the hepatocytes.

Group IV: Showed negative ATPase activity in the hepatocytes.

Group V: Showed moderate ATPase activity in the heptocytes (as control).

Non specific esterase:

Group I (control group): Showed weak enzymatic reaction in the hepatocytes.

Group II: Showed moderate enzymatic reaction in the hepatocytes.

Group III: Showed strong enzymatic reaction in the hepatocytes.

Group IV: Showed intense enzymatic reaction in the hepatocytes.

Group V: Showed weak a picture similar to that of control.

The Kidney:

Histological picture after Hx & E and Masson's trichrome stains:

Group I (control group): Showed renal corpuscle, proximal and distal convoluted tubules and loop of Henle.

Group II: Showed swelling of epithelial cells lining of some proximal convoluted tubules.

Group III: Showed swelling of epithelial cells lining of most of proximal convoluted tubules.

Group IV: Showed focal necrosis of proximal convoluted tubules.

Group V: Some of proximal tubules were regenerate, the others were still necrotic.

There was no change in the amount or distribution of collagen fibers in the kidney with drug injection.

Histochemical changes:

PAS reaction:

Group I (control group): Showed strong PAS reaction in proximal convoluted tubules.

Group II: Didn't reveal any detectable changes.

Group III: Showed moderate PAS reaction in proximal convoluted tubules.

Group IV: Showed weak PAS reaction in proximal convoluted tubules.

Group V: Showed a picture similar to that of control.

Sudan Black B:

Group I (control group): Showed few fat droplets in tubules but no fat in glomeruli.

Group II: Showed increase in fat content in tubules but no fat in glomeruli.

Group III: Showed more increase in fat content in tubules.

Group IV: Showed marked increase in fat content in tubules.

Group V: Showed decrease in fat content in tubules.

Acid phosphatase:

Group I (control group): Showed moderate reaction for acid phosphatase enzyme in tubules as well as glomeruli.

Group II: Didn't reveal any detectable changes.

Group III: Showed strong reaction for acid phosphatase enzyme in tubules and moderate in glomeruli.

Group IV: Showed weak reaction for acid phosphatase enzyme in tubules and moderate in some glomeruli and strong in others.

Group V: Showed a picture similar to that of control.

Alkaline phosphatase:

Group I (control group): Showed moderate reaction of alkaline phosphatase in tubules and negative in glomeruli.

Group II: Didn't reveal any detectable changes.

Group III: Showed increased enzymatic activity in the tubules and negative reaction in the glomeruli.

Group IV: Showed marked increase in the enzymatic activity in the tubules with negative reaction in the glomeruli.

Group V: Showed a picture similar to that of control.

Succinic dehydrogenase:

Group I (control group): Showed intense reaction for succinic dehydrogenase in tubules and negative in glomeruli.

Group II: Showed strong reaction for succinic dehydrogenase in tubules and a negative in glomeruli.

Group III: Showed moderate reaction for succinic dehydrogeanse in tubules and a negative one in glomeruli.

Group IV: Showed weak reaction for succinic dehydrogenase in tubules and negative in glomeruli.

Group V: Showed a slight return of the enzymatic activity in tubules.

Adenosine triphosphatase:

Group I (control group): Showed strong ATPase acivity in glomeruli and tubules.

Group II: Didn't reveal any detectable changes.

Group III: Showed moderate ATPase activity in tubules and weak in glomeruli.

Group IV: Showed weak ATPase activity in tubules and weak in glomeruli.

Group V: Showed a picture similar to that of control.

Non specific esterase:

Group I (control group): Showed weak reaction in glomeruli as well as tubules.

Group II: Showed moderate reaction in tubules and weak reaction in glomeruli.

Group III: Showed strong reaction in tubules and weak reaction in glomeruli.

Group IV: Showed intense reaction in tubules and weak reaction in tubules.

Group V: Showed a picture similar to that of control.

The results of this work attract our attention to restrict the use of tienam for short duration and urgent indications and it must never be used in renal impairment or liver dysfunction.