

SUMMARY

In the present study, the acute and short term chronic toxicity of two anti-inflammatory drugs (Piroxicam and piroprofen) given alone or in combination with the anabolic compound (methyl androstenedione acetate) were investigated. Besides, valuable knowledge about their toxicities were obtained.

Acute toxicity studies:

The results of the study revealed the following results:

Piroxicam was more toxic to female rats than males on acute basis, since the LD₅₀ and LD₅₄ of females were about one third those of males. Its acute toxicity was not antagonized by the anabolic drug.

Piroprofen was equally toxic to male, female, adult and immature rats. Its acute toxicity was reduced by about 25% in adult male rats by the anabolic drug.

Short term chronic toxicity studies:

These studies were done on 100 adult normal male albino rats divided into 10 equal groups each comprising 10 rats. The obtained results indicated that the anabolic

drug (methyl androstenediolone acetate) reduced the mortality rate of pirprofen on chronic administration by 5 folds. On the other hand, the anabolic agent had no effect in the case of piroxicam.

The two anti-inflammatory drugs reduced the growth rate, while the body weight was constant. The anabolic drug improved the harmful effect of pirprofen but this effect was not observed in case of piroxicam.

Both the anti-inflammatory drugs caused a noticeable reduction in the weight of the spleen but the other internal organs were constant. This effect was not modified by the anabolic drug.

Serum biochemical studies:

Serum glucose level was not affected by the anti-inflammatory drugs.

Serum total proteins, albumin, globulin and albumin to globulin ratios were not modified in response to chronic toxicity of the anti-inflammatory drugs.

Piroxicam (1.8 and 5.4 mg/kg) as well as pirprofen high dose level markedly elevated serum bilirubin by 71.25%, 82.5% and 44.94%, respectively. This effect was

abolished by the anabolic drug treatment.

Serum transaminase (GOT and GPT) activity was not pathologically affected by the antiinflammatory drugs.

Both the antiinflammatory drugs induced marked increment in serum alkaline phosphatase activity. The effect was more pronounced in case of piroprofen (82.33%) than piroxicam. The anabolic was able to antagonize the effect of piroxicam than that of piroprofen. The increase of serum alkaline phosphatase along with the increment of serum bilirubin is an indicator of drug induced cholestatic jaundice.

The renal excretory function was not effected by the two antiinflammatory drugs, since serum creatinine and urea were not elevated. However, serum urea level was decreased to 60.46% in response to piroprofen. The effect was related to slight depression in liver function and this amount of nitrogenous compound may be directed to protein biosynthesis. This effect was not corrected by the anabolic agent.

The estimation of serum prostaglandin confirmed that the anabolic compound may enhance the medical effects of the antiinflammatory drugs or at least shall not

antagonize them.

Liver biochemical studies:

Piroxicam elevated liver triglyceride content. This result indicates that a degree of liver fatty deposition occurred. This effect was not antagonised by the anabolic drug.

Hepatic ribonucleic acid content was elevated in response to both piroxicam and piroprofen by 17% and 19%, respectively. This effect is probably related to the increment requirement of proteins needed for drug protein binding and biosynthesis of enzymes. Therefore, the protein percentage of liver has been increased. The anabolic antagonized the effect of the piroxicam while did not affect on the piroprofen. Hepatic DNA was not affected by the antiinflammatory drugs.

Liver lysosomal studies indicated that chronic toxicity of both piroxicam and piroprofen is related to excessive labilization of lysosomes. This toxic effect was minimized to a great extent by the anabolic drug.

Blood haematological studies:

Blood haematological studies showed that both piroxicam and piroprofen caused agranulocytosis phenomenon.

This toxic effect was not accompanied by any degree of anaemia. The anabolic agent was not able to correct this effect.

Finally, it is recommended that determination of serum bilirubin and haematological examination of leucocytes should be done during prolonged therapy with piroxicam and pirprofen. The concurrent administration of anabolic steroid is also very much advisable. Future studies are recommended to investigate the use of anabolics in combatting toxicity of other types of drugs and its action mechanism.