EFFECT OF INTERACTION BETWEEN FUROSEMIDE AND OXYTERCYCLINE ON BLOOD UREA AND CREATININE IN RATS

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INTRODUCTION

Recently Seegers et al, (1979) reported that concurrent administration of paracetamol with aspirin resulted in decreased gastric acidity indueed by aspirin in rats, this effect is due to stimulation of endogenous production of prostaglandins produced by paracetamol. The work of Seegers et al. (1979) was based on the observations of Bobak et al. (1978) and Mc Donald et al., (1979) that paracetamol could stimulate the prostaglindin sythetase of bovine seminal vesicles in vitro.

The antagonism of paractamol to the gastric hyperacidity, may be accompanied by an antagonism to the therapeutic efficacy of aspirin but, on the other hand, paracetamol has pharmacological properties which are similar to those of aspirin and might thereforefore augment the therapeutic efficacy. In the present work the interaction between paracetamol and aspirin with regard to their analgesic and anti anflammatory activities were studied in rats.

MATERIAL AND METHODS

Drugs Used :

Paracetamol (Abimol tablet - ABI) and aspirin tablet - Bayer) were suspended in 4% Tween - 20 and administered orally by using gastric tube. The dosages of both paracetamol and aspirin were 250mg/Kg, because Seegers et al., (1979) found that this dose of aspirin Produced considerable gastric damage that was reduced significantly by the same dose of paracetamol.

Animals Used :

80 albino rats of both sex weighing 100 - 200 gm were used in the

present study. They were divided into 10 groups each group consists of 8 rats. The first 5 groups were used to study the effect of paracetamol on the analgesic activity of aspirin while the other 5 groups were used to study the effect of paracetamol on the antiinflammatory activity of aspirin. Each drug was given daily for one week.

Assessment of Analgesic Activity :

The analgesic activities of the drugs were measured according to the method of Takesue et al., (1969).

Assessment of Anti- inflammatory Activity :

Paw oedema test (Winter et al., 1962) was used for the assessment of anti - inflammatory activities of the drugs.

RESULTS

Table (1) shows that both drugs alone or in combination with each other produced significant increase in the pain threshold as compared with the control group.

The combination of paracetamol with aspirin, on the contrary, resulted in significantly lower pain thresholds than expected on adding the single drugs (antagonism).

As regard the anti - inflammatory activity, it was found that paracetamol or aspirin alone reduced significantly the carrageenin - induced paw oedema as compared with the vehicle - treated group. The combination of paracetamol with aspirin had about the same anti - inflammatory activity as was expected on simply adding the single drug doses (Table 2).

DISCUSSION

The results of this study indicate that simultaneous administration of paracetamol and aspirin resulted in simple addition in the anti - inflammatory test (Table 2). However, the analgesic test seems to indicate an antagonism between paracetamol and aspirin (Table 1). This antagonism may be due to differences in the mode of action.

Aspirin probably exerts its analgesic and anti- inflammatory activity by inhibiting the biosynthesis of inflammation mediating prostaglandins (Vane, 1971). On the other hand, the exact mechanism of action of paracetamol is not yet clear, it may act by reducing noxious lipid peroxides (Sobanski et al., 1976), by reducing prostaglandin

endoperoxides (Kuehl et al., 1977), or by indirectly blocking prostaglandin synthesis (Lands, 1981).

Perhaps paracetamol affects the inflammatory reaction in the same way as asprine, but influences the pain reaction in such a way that it antagonizes the analgesic effect of aspirin.

This antagonism is not too serious for a possible clinical application of the combination, as the analgesic activity of aspirin, which is antagonized by paracetamol, is less important than its anti - inflammatory action when aspirin is used in treatment of inflammatory diseases. Moreover, the combination of aspirin with paracetamol resulted in analgesic effects which were not substantially lower than those of the single drugs.

As mentioned above the anti - inflammatory effect of aspirin and paracetamol add to each other. Considering this and the protection which paracetamol may offer against gastric damage produced by aspirin (Seegers et al., 1979) a combination of these drugs imght be of value in analgesic anti - rheumatic therapy.

SUMMARY AND CONCLUSION

Since some workers reported that paracetamol can antagonize the toxic effect of aspirin on the gastric acidity in rats, the present work was done to study the effect of paracetamol on the analgesic and anti - inflammatory activity of aspirin in rats. It was found that the anti - inflammatory effect of paracetamol and aspirin additive. Although antagonism was observed in the analgesic test, the effect of the combination was not inferior to that of paracetamol alone.

In light of the present study and reports of other workers on experimental animals, it may be concluded that although paracetamol antagonized the analgesic effect of aspirin, yet the protection which paracetamol offer against gastric damage produced by aspirin make the combination of both drugs mightbe of value in antirheumatic therapy.

Table (1) : The influence of paracetamol on the analgesic effect of aspirin, using analgesymeter test, in rat.

Drug	Dose	Analgesic Effect (Wt. in grams ± S. E.)
Control group receiving saline.	o. 5 ml / day for 7 days	130 ± 3. 81
Control group receiving 4 % tween - 20	0.5 ml / day for 7 days	130 ± 4. 91 (P : N . S.)
Paracetamol	250 mg / kg / day for 7 days	195 ± 6. 22 (P'< O. O5)
Aspirin	250 mg/ kg / day for 7 days	210 ± 5. 99 (P' < 0.05)
Paracetamol + Aspirin	250 mg / kg / day + 250 mg / kg / day	194 ± 7.1 (P' < 0. 05) (P" <o.o5)

P : Significance of difference between saline group and 4 % tween - 20 group.

P` : Significance of difference between 4 % tween - 20 group and the tested drugs.

P`` : Significance of difference between aspirin and the combined drugs.

N. S. : Non - significaut.

Table (2) : The influence of paracetamol on the antiinflammatory effect of aspirin, using paw oedema test, in rats.

Drug	Dose	Anti-inflammatory effects (Thickness of paw in cm. ± S. E.).
Control group receiving saline.	o. 5 ml / day	3.9 ± 0.12
Control group receiving tween - 20	0.5 ml / day	3.8 ± 0.08 (P : N. S.)
Paracetamol	250 mg / kg / day	3.1 ± 0.03 (P' < 0.05)
Aspirin.	250 mg/ kg / day	2.8 ± 0.01 (P' < 0.05)
Paracetamol + Aspirin	250 mg / kg / day + 250 mg / kg / day	2.2 ± 0.073 (P' < 0.05) (P'' < 0.05)

All drugs were given orally for 7 days.

P : Significance of difference between saline group and 4 % tween - 20 group.

P` : Significance of difference between 4 % tween - 20 group and the tested drugs.

P`` : Significance of difference between aspirin and combined drugs.

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