The in vitro effect of paracetamol and five different NSAIDs on the MDA level in un-induced and iron-induced liver homogenates of the rabbit

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ABSTRACT

Background

The mechanisms behind the great interindividual variation in response to non-steroidal anti-inflammatory drugs (NSAIDs) and also behind their recent uses as chemopreventive of cancer are poorly understood. A search for a possible explanation through their effect on the oxidative status seems worthwhile. This assumption is strengthened by the existence of a wide controversy regarding their final effect as pro-oxidant or antioxidant. NSAIDs are, also, widely used in conditions where inducers of oxidative stress may accumulate such as iron in sickle cell disease.

Objective

To investigate the *in vitro* effect of paracetamol and five NSAIDs (diclofenac, indometacin, ketorolac, piroxicam and ibuprofen) on MDA level in un-induced and iron-induced liver homogenates of the rabbit.

Methodology

Paracetamol, diclofenac, indometacin, ketorolac, piroxicam and ibuprofen were evaluated in this study using *in vitro* measurement of MDA level (the main marker of lipid peroxidation) in both un-induced and iron-induced liver homogenates of the rabbit. The tested concentrations were subtherapeutic, lower therapeutic and higher therapeutic concentrations of each drug.

Results

Diclofenac decreased MDA level in all the three tested concentrations in both un-induced and iron-induced liver homogenates of the rabbit. This may point to its potential antioxidant effect. In contrast, indometacin, paracetamol, ketorolac and piroxicam, produced a potential pro-oxidant effect by increasing MDA level in both un-induced and iron-induced liver homogenates of the rabbit in each of the three tested concentrations. While ibuprofen was the only drug among these six drugs that produced pro-oxidant/antioxidant effect depending on the dose and the induction status. In contrast to the higher therapeutic concentration that produced a significant increase in MDA level in un-induced liver homogenate, subtherapeutic and lower therapeutic concentrations of ibuprofen significantly decreased MDA level in iron-induced liver homogenate with a possible antioxidant activity.

The combination of paracetamol with diclofenac, ibuprofen or aspirin in iron-induced liver homogenate increased MDA level significantly when compared with control.

Conclusion

Diclofenac and to a lesser extent ibuprofen may be preferred over other tested drugs because of their potential antioxidant effects. Also combinations of paracetamol with diclofenac, ibuprofen or aspirin can cause enhancement of pro-oxidant effect, and might be harmful in conditions of high oxidative stress when used in high doses. Differences in the effect of NSAIDs on the oxidative status could be one mechanism contributing to their great interindividual variation in response to these drugs.