PHARMACOLOGICAL STUDIES ABOUT THE INTERACTIONS BETWEEN ETORICOXIB RESPECTIVELY TRAMADOL ASSOCIATED WITH ENALAPRIL

ADRIANA IONITOIU1, O. POPESCU2

1Emergency Clinical County Hospital Tg. Mures, 2Clinical Ophthalmology Hospital Tg. Mures

Abstract: The purpose of this study was to verify the influence of antinociceptiv effect by associating an opioid drug respectively a NSAID with an angiotensin converting enzyme inhibitor. We also tested the analgesic effect of each drug used and we compared the results. Material and method: We used 5 groups of 10 mice Swiss breed and device Tail Flick Unit, standardized assessment to analgesics activities in animal experiments. The 5 groups were treated as follows: Group I: Tramadol; Group II: Etoricoxib; Group III: Enalapril; Group IV: Tramadol and Enalapril; Group V: Etoricoxib and Enalapril. Subsequently each animal from the lots above were exposed to pain stimulus 0, 15, 30, 60 and 90 minutes after treatment. Results: The mice from each lots had the maximum analgesic point at 30 minutes after the treatment administration. Among the 5 groups at the same time (T 30) animals in group I had the lowest sensitivity to pain stimulus (p < 0.0001) followed by the animals in group II, III respectively group V. Conclusions: Among all the treatments done, the most effective was for the group treated with tramadol, although the measurements done at T 60 and T 90, its analgesic effect was matched by Etoricoxib. We observed a decrease in analgesic effect when we associated tramadol respectively Etoricoxib with Enalapril. Between the two was the more effective combinations that I used along with Enapril Tramadol to all measurements (p < 0.05), although the group treated with enalapril had a mild analgesic effect measurements made at 15’, 30’, 60’ and 90’ compared with the time T0 (p < 0.05).

Keywords: Etoricoxib, Tramadol, Enalapril, interactions, pharmacological studies

THE AIM OF THE STUDY

The purpose of this study was to verify the influence of antinociceptiv effect by associating an opioid drug respectively a NSAID with an angiotensin converting enzyme inhibitor. We found frequently in the medical literature the association between Etoricoxib and Enalapril or other anti hypertensive agents in studies for patients with rheumatologic disease who had the associated hypertension pathology [1,2,3]. These studies have shown that this combination will produce an increase in blood pressure. Because COX inhibition is associated with antinatriuretic and vasoconstrictor effects mediated through the inhibition of the actions of prostaglandin E2 and prostacyclin [4,5]. The first 2 studies that evaluated the effects of NSAIDs on BP demonstrated that mean arterial pressure could rise by as much as 5 to 6 mm Hg in a population of patients with hypertension [6]. The

Corresponding Author: Adriana Ionitoiu, 12/10, 22 Decembrie 1989 street, Tg Mures, România; e-mail: adriana_ionitoiu@yahoo.com; tel +40-0745612149

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The greatest effects of NSAIDs on BP control were observed in patients on monotherapeutic regimens of β-adrenergic blocking drugs, diuretics, or angiotensin-converting enzyme (ACE) inhibitors [7,8,9].

MATERIAL AND METHOD
We used 5 groups of 10 mice Swiss breed and device Tail Flick Unit, standardized assessment to analgesics activities in animal experiments.

The 5 groups were treated as follows:
- Lot I: Tramadol (1 mg/kg of bodyweight/mouse)-ip;
- Lot II: Etoricoxib (2 mg/kg of bodyweight/mouse)-po;
- Lot III: Enalapril (0,5 mg/kg of bodyweight/mouse)-po;
- Lot IV: Tramadol (1 mg/kg of bodyweight/mouse)-ip and Enalapril (0,5 mg/kg of bodyweight/mouse)-po;
- Lot V: Etoricoxib (2 mg/kg of bodyweight/mouse)-po and Enalapril (0,5 mg/kg of bodyweight/mouse)-po.

Subsequently each animal from the lots above were exposed to pain stimulus 0, 15, 30, 60 and 90 minutes after treatment.

RESULTS AND DISCUSSIONS
We followed the variation of analgesic point depending on the time elapsed from administration of therapy for each lot. Thus all groups had an analgesic point within 30 minutes after treatment and the other times we got this effect antinociceptiv for each group:

At 15 minutes after the all the treatments, the more effective analgesic effect appeared at the animals treated with Tramadol. Between this group and the others studied wasn’t statistical difference (p <0.05) except the group treated with Enalapril. The effect of this 2 substances (Enalapril and Tramadol) wasn’t additive, on the contrary the association had a noticeable decrease in analgesic effect. Observation is emphasized by the statistical calculation. Between the groups treated with Etoricoxib, Enalapril and Enalapril - Tramadol wasn’t statistical difference (p > 0.05). Again, Etoricoxib with Enalapril combination had a lower analgesic effect. The minimum antinociceptiv effect was at this association (Fig.1).

At 30 minutes after medication administration the groups treated with Tramadol and Etoricoxib have resisted the longest time after exposure to pain stimulus. However it should be noted that animals treated with Tramadol had an effect antinociceptiv lower than the measurement did at the time T 30. The group treated with Etoricoxib instead has maintained constant the analgesic effect at the measurement made at time T 60 (p> 0.05). Unlike the first time, respectively time T 90 when we made the measurements, when the combination of Tramadol and Enalapril were statistically lower in terms of analgesic effect compared with the group treated with Tramadol, when we made the measurements at time T 60 there wasn’t statistical differences between the 2 groups. On the other hand the association between Etoricoxib and Enalapril compared with the group treated only with Enalapril, it was maintained a better antinociceptiv effect for the monotherapeutic treated group. The groups with the lowest analgesic effect were those which were treated with Enalapril respectively the combination between Enalapril and Etoricoxib, between this two groups there was no difference in statistical terms (p <0.05) (Fig.3).
At 90 minutes after administration of medication were kept the same algesimetric values that we presented for time T 90, with the exception mentioned above related to the analgesic differences between Tramadol and Tramadol associated with Enalapril-treated group. It should be emphasized that at the time T 90, the group treated with Enalapril associated with Etoricoxib was the only one which hasn’t a statistical difference with their control T 0 in terms of antinociceptive effect (Fig.4).

Figure no. 4. Variation of the analgesic effect of different drugs at 60 min after drug administration

CONCLUSIONS

Among all the treatments done, the most effective was for the group treated with tramadol, although the measurements done at T 60 and T 90, its analgesic effect was matched by Etoricoxib. We observed a decrease in analgesic effect when we associated tramadol respectively Etoricoxib with enalapril. Between this two, the more effective combinations was for the group treated with Tramadol and Enalapril at all measurements we did (p<0.05), although the group treated with Enalapril had a slight analgesic effect on measurements made at T 15', T 30', T 60', and T 90' versus time T 0 (p<0.05).

BIBLIOGRAPHY