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Peripheral Synergistic Interaction Between Lidocaine and Lumiracoxib on the 1% Formalin Test in Rats

Interacción Sinérgica entre a Lidocaína y Lumiracoxib en la prueba de formalina 1% en ratas.

ABSTRACT

It has been shown that the association of non-steroidal anti-inflammatory drugs (NSAIDs) with analgesic agents can increase their antinociceptive activity, allowing the use of lower doses and thus limiting side effects. Therefore, the aim of the present study was to examine the possible pharmacological interaction between lumiracoxib and lidocaine at the local peripheral level in the rat using the 1% formalin test and isobolographic analysis. Lumiracoxib, lidocaine or fixed-dose ratio (1:1) lumiracoxib-lidocaine combinations were administered locally in the formalin-injured paw and the antinociceptive effect was evaluated. All treatments produced a dose-dependent antinociceptive effect. ED40 values were estimated for the individual drugs and an isobologram was constructed. The derived theoretical ED40 for the lumiracoxiblidocaine combination was 599.3 ± 58.8 µg/paw, being significantly higher than the actually observed experimental ED40 value, 393.6 ± 39.7 µg/paw. This result correspond to a synergistic interaction between lumiracoxib and lidocaine at the local peripheral level, potency being about one and half times higher with regard to that expected from the addition of the effects of the individual drugs. Data suggest that low doses of the lumiracoxib-lidocaine combination can interact synergistically at the peripheral level and therefore this drug association may represent a therapeutic advantage for the clinical treatment of procedural or inflammatory pain.

Keywords: Lumiracoxib, Lidocaine, Synergism, Nociception, Rats.

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Antinociception by Lumiracoxib-Lidocaine Combination

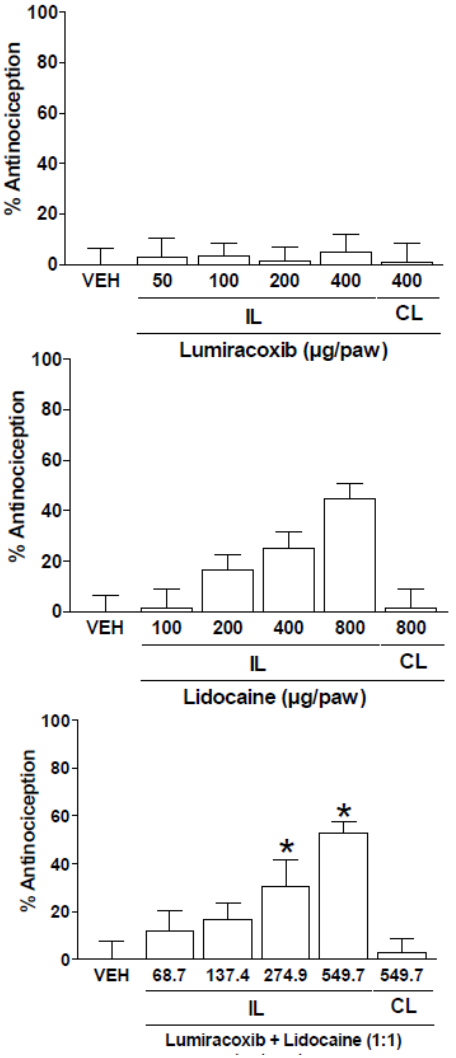

Fig. (1). Local antinociceptive effect of lumiracoxib (top), lidocaine (middle) or the lumiracoxib + lidocaine combination (bottom) in the 1% formalin test. Rats were pretreated with a local injection of vehicle (VEH), lumiracoxib, lidocaine or the lumiracoxib – lidocaine combination in a fixed-ratio (1:1) into either the right (ipsilateral, IL) or left (contralateral, CL) paw, before formalin injection. Data are expressed as the percent of antinociception on the first phase. Each point corresponds to the mean ± SEM of 6-8 animals. *Significantly different from vehicle group ($p<0.05$) as determined by ANOVA followed by Dunnett's test.

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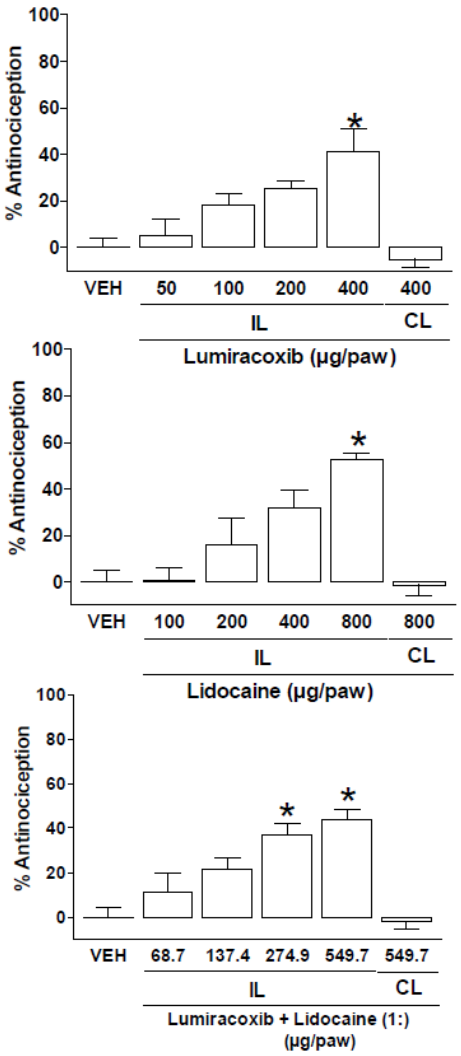

Fig. (2). Local antinociceptive effect of lumiracoxib (top), lidocaine (middle) or the lumiracoxib + lidocaine combination (bottom) in the 1% formalin test. Rats were pretreated with a local injection of vehicle (VEH), lumiracoxib, lidocaine or the lumiracoxib – lidocaine combination in a fixed-ratio (1:1) into either the right (ipsilateral, IL) or left (contralateral, CL) paw, before formalin injection. Data are expressed as the percent of antinociception on the second phase. Each point corresponds to the mean ± SEM of 6-8 animals. *Significantly different from vehicle group ($p<0.05$) as determined by ANOVA followed by Dunnett's test.

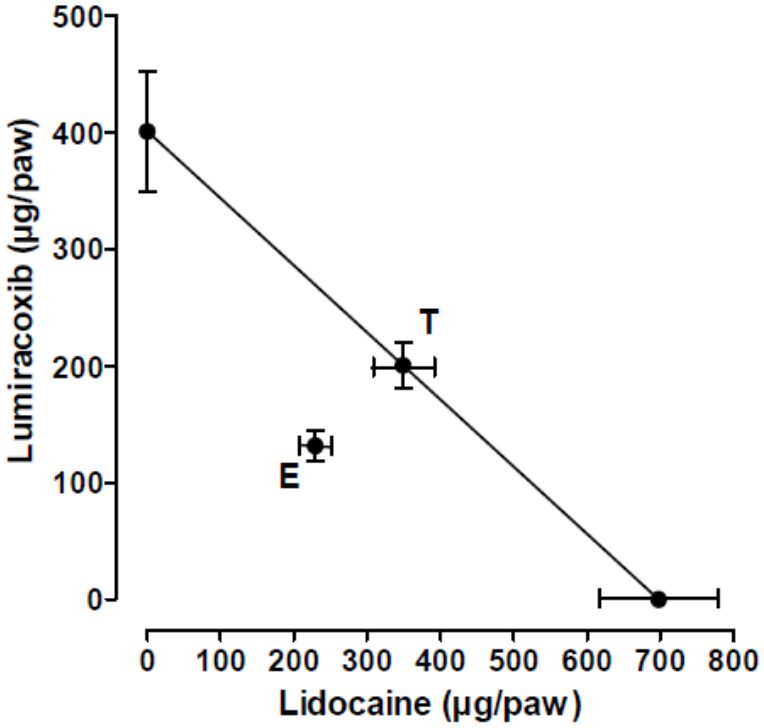

Fig. (3). Isobologram showing the peripheral interaction between lumiracoxib and lidocaine (fixed-dose ratio 1:1) at ED40 level of effect in the formalin test. The oblique line, between the x and y axes, is the theoretical additive line. The point in the middle of this line, denoted by "T", is the theoretical additive point calculated from the individual drug ED_{40} values. The experimental point, denoted by "E", is the actual observed ED_{40} value for this combination. Horizontal and vertical bars indicate the SEM.

CONCLUSION

Clinical outcomes of the lumiracoxib-lidocaine co-administration could include greater analgesia and probable attenuation of adverse reactions. The efficacy and benefits of this combination in clinical situations await supplementary validation.

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