

Involvement of hypothalamic pituitary adrenal axis on the analgesic cross-tolerance between morphine and nifedipine.

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Bidirectional cross-tolerance develops between opioids and Ca(2+) channel blockers relating to their antinociceptive effects; however, the role of hypothalamic pituitary adrenal (HPA) axis on this action has not been elucidated yet. We examined the analgesic cross-tolerance between morphine and nifedipine, a dihydropyridine calcium channel blocker, in intact and adrenalectomized (ADX) rats and also evaluated modification of HPA activity during this phenomenon. The tail-flick test was used to assess the nociceptive threshold. The plasma level of corticosterone, as a marker of HPA function, was measured by radioimmunoassay. Our results showed that, in sham operated rats which were chronically treated with morphine, nifedipine failed to affect nociceptive threshold but it could induce significant antinociceptive effect in ADX morphine treated animals. This effect was reversed by corticosterone replacement. Furthermore, morphine could not induce analgesic effect either in sham operated or in ADX animals that received chronic nifedipine. Chronic morphine inhibited the effect of nifedipine on corticosterone secretion but nifedipine treatment had no effect on morphine-induced corticosterone secretion. Based on these results, we can conclude that HPA axis is involved in the induction of cross-tolerance between morphine and nifedipine due to chronic morphine and not nifedipine treatment.

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