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Title: NALOXONE DOES NOT CHANGE SENSORY INTENSITY OR AFFECTIVE MAGNITUDE OF EXPERIMENTAL PAIN STIMULI

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Introduction. The role of endogenous opiates is still uncertain and there is existing controversy regarding the effect of naloxone on human pain perception (1,2,3,4) and the mood (1,2). Careful review of the literature revealed that all the previous studies concerning the effect of naloxone on human pain perception were performed using methods which are not very reliable. Recently, however, a new and a reliable method of experimental pain study, which provides ratio scale measurement, has been described (5). This method provides independent measurements for both the sensory intensity and the affective magnitude (unpleasantness or pleasantness) of experimental pain stimuli (EPS). The purpose of this study is to evaluate the effect of naloxone on both sensory intensity and affective magnitude of EPS using this validated ratio scale measurements. This may solve the existing controversy regarding this point.

Methods. This study was carried out in two parts. Part I: Thirty normal human volunteers (with informed consent and approval by the Research Committee) in the age group 23-32 years and with body weight 55-75 kg (mean = 69 kg - S. D. = ± 3.9) participated in this part. The thirty subjects were divided into different groups (each of ten subjects) in a double blind study. The first group received 0.4 mg of naloxone hydrochloride, the second group received 0.8 mg of naloxone hydrochloride, and the third group received placebo saline injection. The three types of injections were prepared in equal volumes (each of 2 ml). Considering the recommended dose of naloxone as antagonist of opiate analgesia (6) and stimulation produced analgesia (7,8) is, 0.4 mg or less, thus, 0.4 or 0.8 mg of naloxone seem to be the appropriate doses for blocking the effect of endogenous opiate on pain perception and therefore were used in this study. Perception of EPS (45,47, 49 and 51°C) was rated using the visual analogue scale (VAS) for both the sensation intensity (how intense the sensation feels) and the affective magnitude of pain perception (how unpleasant or pleasant the stimulus feels). This pain test was performed before and after injection by 5 min and 20 min and each test lasted for 2 - 4 min. Thermal pain stimuli were delivered by a thermode system which is identical to that describe previously by other authors (9).

Part II: Six normal subjects (with informed consent and approval by the Research Committee) in the age group 24-30 years and with body weight of 63 - 70 kg (mean = 64 - S. D. = ± 2.8) participated in this study. Each group received three different injections (0.4 mg naloxone, 0.8 mg naloxone and saline), each of an equal volume (2 ml) and on a separate session. These three sessions were randomized in a double blind study. Subjects were asked to rate (VAS) for the unpleasantness (affective magnitude) of four EPS (45,47,49 and 51°C) before and 5 min after each injection. Each test lasted 2 - 4 min.

Results. Data analysis using ANOVA revealed no change (P > 0.05) in rating the sensation intensity of EPS following either 0.4 mg or 0.8 mg naloxone injection. There was a significant effect (P < 0.05) on the rating of the affective magnitude of EPS following the injection of 0.4 mg but not 0.8 mg of naloxone in Study I. In Study II however, there was no change in the rating of the affective magnitude of EPS (P > 0.05).

Discussion. The finding that 0.4 mg naloxone reliably affected affective responses to experimental heat pain but a higher dose (0.8 mg naloxone) was ineffective is perplexing and may reflect the presence of a type I error. Therefore, we decided to attempt to replicate this effect in another 6 subjects. On attempting to replicate the effect of naloxone (0.4 mg and 0.8 mg on the unpleasantness of EPS, it was clear that neither does has a significant effect (P > 0.05). Hence, we conclude that naloxone (0.4 mg and 0.8 mg) has no effect on either sensory intensity or affective magnitude of experimental pain.

References.