Failure of Naloxone to Antagonize Metoclopramide Induced Prolactin Rise

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With 2 Figures

Received December 22, 1980

Summary

Seven subjects aged 21–54 years were investigated. Serum PRL and DBH were estimated before and at 30, 60, 90 and 120 min after the administration of 20 mg clopropamide. The same parameters were estimated a second time when 0.4 mg naloxone was associated.

PRL level increased and DBH decreased in all the patients in both investigations and no significant differences between the two occasions were detected.

It is suggested that probably the two substances do not act on identical receptors.

Introduction

Recently it has been shown that naloxone induced opiate receptor blockade affects serum concentration of prolactin (PRL) in rats (Bruni et al., 1977; Hart and Cowie, 1978; Van Vugt et al., 1978).

The reports concerning the influence of opiate blockade on PRL levels in man are equivocal. Some reports (Janowsky et al., 1979; Morley et al., 1980) found that naloxone does not influence basal levels of PRL or PRL response to certain stimuli (Quigley et al., 1980) but do change PRL response to other stimuli (Morley et al., 1980). It has been however shown that morphine raises the basal PRL levels in man (Tolis et al., 1976). Therefore it seems reasonable to believe that
opiate receptors blockade in man might influence PRL levels under certain circumstances.

In order to bring further data to these controversial findings we studied naloxone influence on PRL response to metoclopramide.

As metoclopramide increases PRL through its dopamine antagonist effect we also estimated serum dopamine-beta-hydroxylase (DBH) activity in order to see if naloxone eventually exercises its influence through the same catecholaminergic pathways.

Subjects and Methods

Seven normal female subjects aged 21—54 years, were studied. Informed consent was obtained from all subjects. Each subject was tested twice, on two different days. A needle was inserted into an arm vein between 8—9 a.m. and was kept patent with a slow infusion of physiological saline and heparine. Blood samples were drawn at 9 a.m. and 20 mg metoclopramide HCl was administered alone, one day, and associated with 0.4 mg naloxone i.v. another day. Blood sampling was carried out before and 30, 60, 90, 120 min after the drug administration. PRL and DBH activity were estimated in all the samples. PRL was determined by double antibody radioimmunoassay and DBH activity by photometric-assay (Nagatsu and Udenfriend, 1972). Maximal increments of PRL (ΔPRL) and maximal decrease of DBH (ΔDBH) were compared in the two tests and the differences between the two groups of dynamic tests were analysed by paired Student's test.

Results

The basal levels of PRL was similar in the two days of the tests: 8.4 ± 2.18 ng/ml (mean ± S.E.) and 8 ± 1.70 ng/ml (mean ± S.E.). There was an increase in the PRL levels after metoclopramide administration, either alone or associated with naloxone, in all the subjects. The average maximal increments (ΔPRL) was respectively 141 ± 26.4 ng/ml (mean ± S.E.) and 97 ± 29.4 ng/ml (mean ± S.E.). The average maximal increment was delayed (at 90 min versus 60 min) and apparently smaller in the naloxone group, but the differences were not significant (Fig. 1).

The changes in serum DBH activity paralleled the changes in the PRL levels: maximal decrease of serum DBH activity (ΔDBH) were, respectively, 18.1 ± 3.9 % at 60 min in metoclopramide treated group against 23.6 ± 2.7 % (mean ± S.E.) at 90 min in the metoclopramide plus naloxone treated group. The differences were not significant (Fig. 2).

No side effects were observed during the naloxone administration.