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Research Note

Nasal Administration of Naloxone Is as Effective as the Intravenous Route in Opiate Addicts

N. Loimer, M.D., Ph.D.,[1] P. Hofmann, M.D.,[2] and H. R. Chaudhry, M.D.[3]

[1]*Psychiatrische Universitätsklinik Wien, Währinger Gürtel 18–20, A-1090 Vienna, Austria*

[2]*Psychiatrische Universitätsklinik Graz, Auenbruggerplatz 22, A-8036 Graz, Austria*

[3]*Fatima Jinnah Medical College, Department of Psychiatry, Punjab University, Lahore, Pakistan*

ABSTRACT

Naloxone is used intravenously in opiate addiction in emergency cases, in rapid opiate detoxification, and as a diagnostic tool. This is a study comparing the efficacy of intranasal naloxone to other routes (intravenous/intramuscular) in 17 opiate-dependent patients. The nasal drug administration of naloxone was found to be as effective as the intravenous route. The nasal drug application offers a wide margin of safety for patients and medical staff, especially in emergency situations in regard to infection risks associated with vessel puncture.

Key words. Naloxone; Opiate addiction; Nasal administration; Intravenous application

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INTRODUCTION

The pure opiate antagonist properties of naloxone (Martin, 1976) cause rapid onset of withdrawal symptoms in opiate addicts. Resnick et al. (1975) provoked these withdrawal signs by intravenous application of naloxone in order to shorten the time of detoxification. Recently this life-threatening effect of intravenous naloxone application was suppressed by short-time anesthesia (Loimer et al., 1990a). The intramuscular administration of naloxone was used as a diagnostic tool to estimate opiate dependency (Wang et al., 1974). In contrast to the findings of Creighton and Ghodse (1989), it was shown that the conjunctival administration of naloxone is not successful for assessing opiate dependency (Loimer et al., 1990b). Intravenous naloxone is recommended in the management of narcotic overdoses (Martin, 1976). Unfortunately, oral application, which is the least invasive and the most accepted method for applying a drug, is ineffective because of rapid elimination, e.g., first pass liver effect (Fishman et al., 1973; Weinstein et al., 1973). Buccal administration leads to high bioavailability and might be pharmacologically active (Hussain et al., 1987). The search for an application mode which provides the same benefits as intravenous application, e.g., rapid onset, high bioavailability, and short duration of action, without having the drawback of the risks associated with vessel puncture was based on encouraging findings in animal studies by Hussain et al. (1984).

As part of the rationale for the present study, we cite the AIDS epidemic which demands new and safer application modes of vital drugs in the high risk group of opiate addicts. A more compelling reason for establishing the efficacy of intranasal naloxone is the difficulty of finding patent vessels in chronic opioid addicts.

The aim of this study was to create a noninvasive alternative method of drug administration in intravenous drug addicts which can be used routinely for diagnostic and therapeutic purposes.

METHOD

Subjects

At the Sir Ganga Ram Hospital, Fatima Jinnah Medical College, Lahore, Pakistan, in June 1991, 17 consecutive volunteer male opiate addicted patients were investigated immediately after admission prior to routine gradual detoxification. The procedure had been explained to them by Professor Chaudhry, and they had given written informed consent. All patients satisfied DSM-III-R criteria for opiate dependence.

All patients underwent a physical examination. They were free of systemic illness and medication.

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To control drug misuse, urine samples of all subjects were screened for abusive drugs by means of Abbott Tdx.

Study Design

The study was conducted in a small sample of inpatients allocated into one or two groups, one of which was given baseline treatment (intravenous treatment) and the other intramuscular or intranasal treatment. Within each group each patient was his own control. In an open clinical, partly randomized trial, 1 mg naloxone (Naloxone CURAMED) was administered IV/IM and IV/IN within 24 hours. The naloxone nasal spray, 1 mg/400 μL, was freshly prepared by CURAMED in isotonic phosphate buffer, pH 6.5.

Three hours after intravenous naloxone administration, the patients were maintained on oral opium tablets (1 g). Three hours after intramuscular or intranasal administration, the routine gradual opiate detoxification treatment was started. The clinical ratings were carried out before naloxone was given and 1, 5, 15, 45, 90, and 180 minutes thereafter. Heart rate and blood pressure were taken at the same time. Pupillary response was assessed before naloxone was given and 5 and 45 minutes thereafter.

Measurement of Naloxone Effect

The severity of withdrawal symptoms was assessed by means of the OOWS (Objective Opiate Withdrawal Scale; Loimer et al., 1991) consisting of 11 signs related to withdrawal including the following items: uncontrollable yawning, running nose, lacrimation, profuse sweating, shivering, abdominal cramps, piloerection, hand tremors, muscular twitches, restlessness, and vomiting. These signs were rated as absent or present.

Measurement of Pupillary Responses

Pupillary response was assessed by photography by means of Polaroid photo (Type Polaroid CU-5 Land camera, USA, specially equipped with a fixed photocell pupil distance, and having a twofold enlargement) of the left eye before naloxone was given and 5 and 45 minutes thereafter. The procedure was carried out under constant conditions of reduced ambient lightening in an illuminated room (200 lux; size: 7 × 9 m) after an adaptation period of 10 minutes. This measurement was shown to be related to systemic naloxone action (Loimer et al., 1990c). Following the example of Creighton and Godhse (1989), the diameters of the iris and the pupil were measured and the iris/pupil ratio was then calculated.

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Statistics

Statistical analysis included univariant analysis of variance, the Newman Keuls test, and Duncan's multiple range test (Clauss and Ebner, 1985).

RESULTS

According to the study protocol, the patients were randomly divided into two group:

Group A: intravenous vs intramuscular; $n = 7$

Group B: intravenous vs intranasal; $n = 10$

Subject Characteristics

No significant differences could be detected between Groups A and B in age [mean: 31.4 years (SD ± 11.3) vs 31.1 years (SD ± 8.6), $t = 0.068$, $p = .94$], in body size [mean: 169.8 cm (SD ± 7.3) vs 167.8 cm (SD ± 6.3), $t = 0.57$, $p = .57$], in body weight [mean: 59.6 kg (SD ± 9.8) vs 59.3 kg (SD ± 23.0), $t = 0.038$, $p = .96$], and the reported dose of daily heroin intake [mean: 1.6 g (SD ± 0.8) vs 1.6 g (SD ± 0.7), $t = 0.072$, $p = .94$]. Significant differences were found in the history of heroin addiction [mean: 6.5 years (SD ± 3.4) vs 2.6 years (SD ± 0.7), $t = 2.8$, $p = .011$).

Outcome

Significant differences between baseline and the ratings 1, 5, and 15 minutes after intravenous administration were calculated. On the day following intramuscular administration of 1 mg naloxone, significant differences in the severity of withdrawal signs were found between baseline, 15 minutes, and 45 minutes.

In the clinical rating within Group B, significant differences between baseline and the ratings 1, 5, 15, and 45 minutes after intravenous administration were calculated. On the day following intranasal administration of 1 mg naloxone, significant differences in the severity of withdrawal signs were found between baseline, 5 minutes, 15 minutes, and 45 minutes.

As mentioned above, differences of statistical significance were evaluated in clinical rating within the groups (Fig. 1). No significant differences could be found by comparing the vital signs (blood pressure and heart rate) of the groups (Figs. 2–4). Measurement of the iris/pupil ratio showed no significant changes throughout the observation period in the IM sample (Fig. 5). In both Groups A and B, pupil dilatation reached statistical significance after IV and IM appli-

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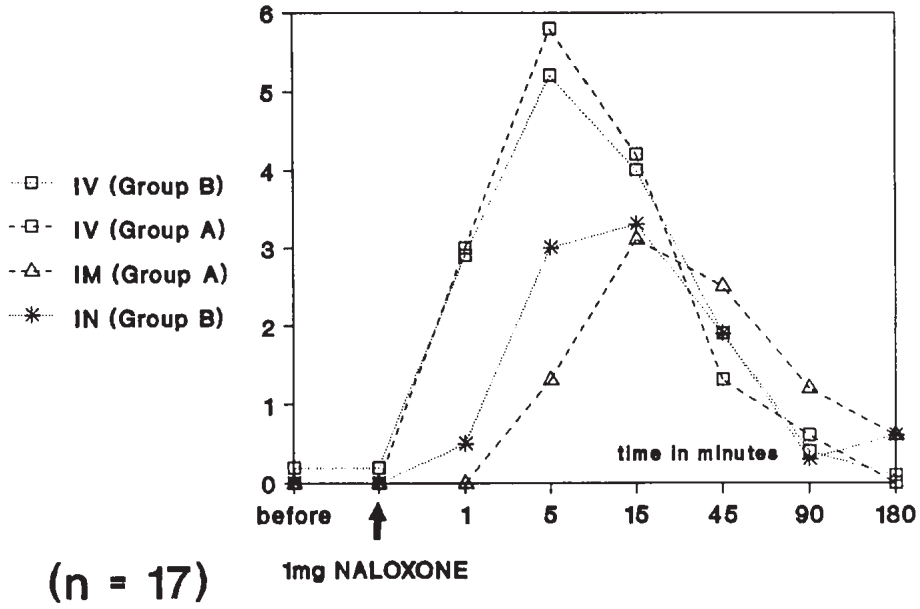

Fig. 1. Rating of withdrawal distress after administration of naloxone IV; IM; IN.

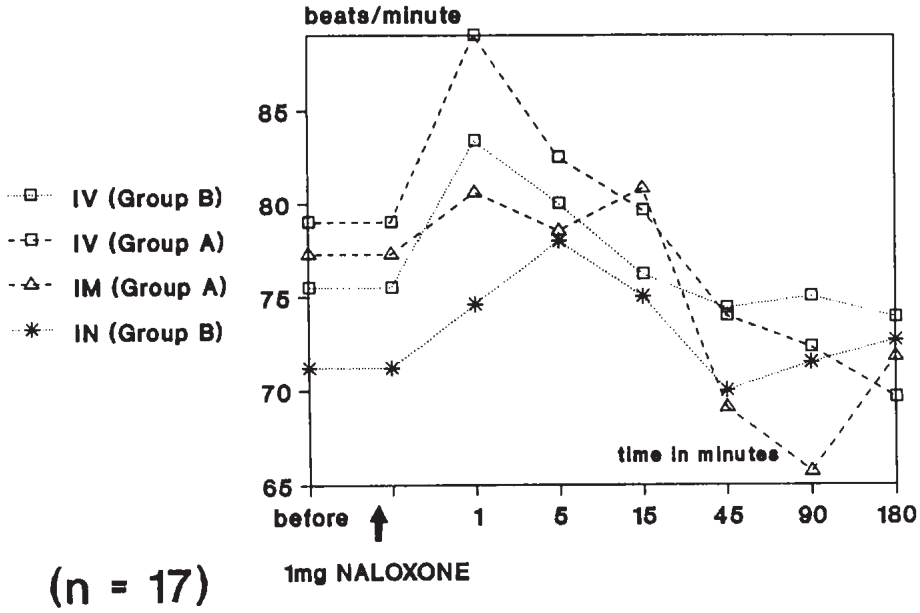

Fig. 2. Heart rate response to the administration of naloxone IV; IM; IN.

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