Acute Effects of Pentazocine, Naloxone and Morphine in Opioid-Dependent Volunteers

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ABSTRACT
The purpose of this study was to evaluate the agonist and antagonist properties of pentazocine, an opioid mixed agonist-antagonist analgesic, in relation to prototypic opioid agonist and antagonist drugs in opioid-dependent human subjects. Pentazocine (45 and 60 mg), naloxone (0.1 and 0.2 mg), morphine (20, 40 and 60 mg) and saline placebo were administered intramuscularly to six male volunteers maintained on methadone (30 mg/24 hr p.o.), following a double-blind, randomized block order design. Drugs were administered 20 hr after the last dose of methadone. Subject-reported and physiological measures were collected before drug administration and during 4 hr postadministration. Morphine produced significant dose-related increases in subjective measures characteristic of mu agonist effects, decreased pupil diameter and was classified as an opioid agonist. Naloxone precipitated a dose-related opioid withdrawal syndrome which was measurable on several subject-rated measures, and significantly increased pupil diameter. Subjects consistently identified naloxone as an antagonist. Pentazocine precipitated a withdrawal syndrome, but the effects were not dose-dependent, and produced symptoms of confusion and dysphoric changes that were not observed after naloxone administration. Pentazocine was classified as an antagonist by some individuals, and as alcohol or hallucinogen by others. The results of the present study indicate that pentazocine acts in humans as a partial mu agonist with a non-mu component of activity.

Pentazocine is a mixed agonist-antagonist opioid that appears to be 3 to 6 times less potent than morphine in analgesic efficacy (Brogden et al., 1973; Jaffe and Martin, 1990). Pentazocine inhibits the binding of mu and kappa opioid receptor ligands and has been classified as either an antagonist or partial agonist at mu receptors with agonist activity at kappa receptors (Martin, 1983). In the non-dependent chronic spinal dog, pentazocine acted as a weak mu agonist, whereas it precipitated a withdrawal syndrome and failed to suppress morphine abstinence in the morphine-dependent chronic spinal dog (Gilbert and Martin, 1976); in contrast, pentazocine suppressed abstinence in the cyclazocine-dependent withdrawn dog. Although the effects of pentazocine in humans are generally consistent with those observed in animal species, the opioid receptor activity of pentazocine in man has not been fully ascertained. It has been shown that in nondependent subjects, low doses of pentazocine produced morphine-like effects, but a ceiling effect was observed as the doses increased; moreover, dysphoria and sedation emerged at doses higher than 40 mg s.c., resembling the effects produced by nalorphine (Jasinski et al., 1970). In another study, pentazocine (90 mg i.m.) also caused dysphoria and sedation which were not observed at lower doses (Preston et al., 1987b). Pentazocine failed to suppress abstinence in morphine-dependent withdrawn humans (Fraser and Rosenberg, 1964; Jasinski et al., 1970), and precipitated a withdrawal syndrome in subjects dependent on 240 mg of morphine s.c. per day. Furthermore, doses of pentazocine up to 140 mg produced disturbing psychotomimetic effects that were interpreted as a lack of cross-tolerance to nalorphine-like subjective effects of pentazocine in morphine-dependent subjects (Jasinski et al., 1970). However, no direct comparisons of withdrawal syndromes precipitated by either pentazocine or the pure antagonist naloxone have been made.

The inclusion of volunteers maintained on a constant dose of methadone has been shown to constitute a good model of opioid physical dependence in which to evaluate antagonist effects (Kanof et al., 1992). In previous studies, the effects of the opioid mixed agonist-antagonist analgesics butorphanol and nalbuphine and the partial mu agonist buprenorphine have been assessed using this model (Preston et al., 1988, 1989b; Strain et al., 1992). In the present study, we compared the subjective and physiological effects of acute doses of pentazocine, naloxone and morphine in methadone-maintained sub-
jects. Naloxone served as standard comparison for opioid-precipitated withdrawal and morphine as positive control for mu agonist effects. For these purposes the methods originally developed in the U.S. Public Health Service Addiction Research Center for the abuse liability evaluation of opioid drugs (Jasinski, 1977; Jasinski and Henningfield, 1989) have been adapted to a non-English-speaking sociocultural context.

Methods

Subjects. Six adult white male volunteers enrolled in a methadone maintenance program took part in the study. The demographic data of the participants are summarized in table 1. The subjects were recruited from a methadone clinic (Centre de Dispensació de Metadona, Generalitat de Catalunya, Barcelona, Spain). On the basis of anamnesis, physical examination, 12-lead electrocardiogram, blood tests and urinalysis, all participants were found to be in good health, and without significant medical and psychiatric disorders other than drug dependence. Minor abnormalities of laboratory tests judged by investigators not to be relevant to the study outcome did not constitute an exclusion criterion. Four subjects were HIV seropositive. Before entry in the study, the dose of methadone was progressively adjusted to that of a daily oral dose of 30 mg. All subjects were taking this dose for at least 10 days before the beginning of the study and throughout the study period.

Subjects were provided with written information about the purposes and methods to be followed. They were told that the purpose of the study was to evaluate the effects of several classes of opioid drugs in methadone-maintained volunteers and that during the experimental sessions they would experience effects resembling those of opioid agonists (such as heroin or methadone) and/or opioid withdrawal symptoms. Subjects were given no other information about what they might expect to happen. All subjects had had previous experience of the effects of a wide range of drugs of abuse, and they knew what effects opioid antagonist drugs produce in opioid-dependent individuals. The study protocol was approved by both the local Institutional Review Board and the Ministry of Health. The study design and procedures were carried out in accordance with the Declaration of Helsinki. Subjects signed an informed consent form and were paid for their participation. All subjects completed their participation in the study.

Setting. Subjects participated while residing in a clinical setting (internal medicine ward, Hospital del Mar) for a minimum period of 14 days. Experimental sessions were conducted in a quiet research area of the Department of Pharmacology and Toxicology especially designed for psychopharmacology studies. The testing room had two seats, electric light of constant intensity and equipment for physiological monitoring and cardiorespiratory resuscitation. Volunteers remained in a comfortable seat during the entire session.

Study procedures. Subjects were individually tested in nine experimental sessions separated by 24- or 48-hr periods. Sessions started between 8:00 and 9:00 A.M. for all subjects (with the exception of subject no. 3 who started at 11:00 A.M.) and lasted approximately 4.5 hr. The oral dose of 30 mg of methadone hydrochloride (Esteve, Barcelona, Spain) was given approximately 20 hr before the beginning of each experimental session. Consumption of other drugs was not allowed during the study with the exception of nonopioid analgesics prescribed by the investigators.

Urine samples were collected daily for screening of drugs of abuse using an EMIT system (Syva Co., San Jose, CA). The presence of a positive result could invalidate the experimental session, and repeated positive results could motivate the subject’s exclusion. No evidence of consumption of drugs of abuse was found. Tobacco smoking was permitted, except during the experimental sessions.

Two investigators familiar with the pharmacological effects of opioid drugs conducted the sessions. Investigators were not allowed to interact with subjects concerning the effects of drugs and the outcome of the experimental sessions, unless giving routine explanations about the methods that had to be followed.

A training session was carried out in which no drugs were administered but, otherwise, the methods followed were the same as those used in the test sessions. The purpose of this session was to familiarize the subjects with the methods and instruments used, and the results were not included in the analysis. After a 10-min resting period, baseline measures were collected. Approximately 30 min after the beginning of each session, subjects received an i.m. injection of placebo or active drug. The session continued in the testing room for 4 hr after the drug administration. Measures were always collected in the same order, i.e., physiological measures, subjects’ questionnaires, pupil diameter and psychomotor performance. At the end of the session, subjects returned to the hospital room where they received their dose of methadone.

Drugs. Eight experimental conditions were studied: placebo, morphine sulphate (20, 40 and 60 mg), naloxone hydrochloride (0.1 and 0.2 mg) and pentazocine lactate (equivalent to 45 and 60 mg of pentazocine base). Commercially available preparations of morphine (20 mg/mL; Serra Pamies, Taragona, Spain), naloxone (0.4 mg/mL; Abelló, Madrid, Spain) and pentazocine (38.5 mg/mL, equivalent to 30 mg/mL of pentazocine base; Fides, Barcelona, Spain) were used. Placebo consisted of sterile physiological saline solution. All drugs were diluted in saline to reach a constant volume of 3 ml and were administered by intramuscular route in one buttocck.

Study design. Experimental conditions were ordered using a randomized block order design, each block consisting of a 4 x 4 latin square structure. In the first block, subjects received placebo, morphine (20 mg), naloxone (0.1 mg) and pentazocine (45 mg). In the second block, subjects received morphine (40 and 60 mg), naloxone (0.2 mg) and pentazocine (60 mg). This design (with the lowest doses in the first block and the highest doses in the second) was adopted for safety reasons, so that the study could be stopped and medication codes opened if drug effects from the first block were so intense that it was judged ethically unacceptable to continue the study. All the drugs were administered under double-blind conditions.

Subject-rated measures. Subjects completed questionnaires for the evaluation of subjective effects of opioid drugs at base line and at 20, 40, 60, 80, 120, 180 and 240 min after drug administration. Questionnaires were administered in paper-and-pencil format. Subjects were instructed to give responses according to the scale they felt while completing the questionnaires. Subject-rated measures consisted of: 1) visual analog scales; 2) drug classification questionnaire; 3) adjective rating scales and 4) a shortened 49-item form of the ARCI. On the visual analog scales, subjects rated their current degree of “any effect,” “high,” “good effects,” “bad effects,” “liking” and “sick” by placing a mark along a horizontal 100-mm straight line marked at either end with the words “none” and “maximum.” The score in these scales was the distance in millimeters from the left extreme of the line. In the pharmacological class questionnaire, subjects had to classify the effects as most similar to those of 11 drug classes of psychoactive drugs (with examples of names of common compounds used in Spain) including placebo, opioid agonists, opioid antagonists, neuroleptics, barbiturates, benzodiaz-
pines, hallucinogens, amphetamine-like stimulants, cocaine, alcohol, cannabinoids and other. The adjective rating scales consisted of a list of adjectives that the subject rated on a 5-point scale from 0 ("not at all") to 4 ("strongly"). The items on the list were divided into three scales as follows: an agonist scale [items derived from the Single Dose Questionnaire (Fraser et al., 1961) plus symptoms associated with morphine-like drugs effects], an antagonist scale [items derived from the Himmelbach opioid abstinence scale (Kolb and Himmelbach, 1938)] and an agonist-antagonist scale [which reflects symptoms usually associated with the administration of mixed agonist-antagonist opioid analgesics (Preston et al., 1987a)]. The rating for individual items were summed for a total score for each scale. The shortened form of the ARC consisted of 49 true/false items. The visual analog scales was measured using a Maddox-wing device (Clem-}

Subject-rated measures. The statistical results of the subject-rated measures are shown in table 2. The comparisons between the peak effect values of the eight experimental conditions (one-factor repeated measures ANOVA) and the comparisons of the peak effect values of placebo with each of the study drugs (Dunnett's test), for those variables found to be statistically significant in the ANOVA are shown in table 2. Arrows indicate direction of significant changes relative to placebo.

The time course of effects of the "any effect" visual analog scale is shown in figure 1. Morphine-related increases did not reach statistical significance, whereas naltrexone and pentazocine produced significant increases. Although morphine tended to increase the scores in the "high" and "good effects" scales, significant changes were observed only in the total scores of "liking" after the administration of 80 mg (data not shown). Naloxone (0.2 mg) and both doses of pentazocine produced significant increases in the peak of "bad effects" ratings (table 2).

The effects of pentazocine, naltrexone and morphine on two scales of the ARC are shown in figure 2. Morphine produced significant dose-related increases in the MBG scale, and the 60 mg dose also increased scores of the BG scale. Naloxone (0.2 mg) and pentazocine (45 and 60 mg) increased the scores of the LSD scale, indicating the emergence of dysphoric changes. Pentazocine 45 mg was, at least, as effective as the 60 mg dose in increasing LSD scale scores (fig. 2). In addition, there was a tendency for pentazocine to increase the scores of the PCAG scale, but these changes did not reach the significance level (data not shown).

The effects of pentazocine, naltrexone and morphine on the adjective rating scales are shown in figure 3. No significant changes in any scale were observed after morphine administration, although it produced a trend toward increases in the agonist scale. Naloxone and pentazocine produced no morphine-like changes, but they both precipitated withdrawal symptoms as shown by significant increases in the antagonist scale (fig. 3). Again, the changes produced by naloxone appeared to be dose related, whereas this trend was not observed for the doses of pentazocine. In addition to withdrawal symptoms, pentazocine (45 mg) produced significant increases in the peak and total effect values on the agonist-antagonist scale that were not observed with the other drugs and doses (table 2; fig. 3).

A more detailed analysis of the responses on individual items in the agonist and agonist-antagonist scales comparing the effects of placebo, naloxone and pentazocine is presented in figure 4. Because morphine produced no effects on these scales,
TABLE 2
Statistical results of subject-rated measures (peak effects)

<table>
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<tr>
<th></th>
<th>F (7, 35)</th>
<th>P</th>
<th>Pentazocine (mg)</th>
<th>Naloxone (mg)</th>
<th>Morphine (mg)</th>
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</thead>
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<tr>
<td></td>
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<td>45</td>
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<td>.0015</td>
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<td>t**</td>
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<td>Good effects</td>
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<tr>
<td>Bad effects</td>
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<td>.0010</td>
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<td>Sick</td>
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<td>.0791</td>
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<td>Adjective rating scales</td>
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<tr>
<td>Antagonist</td>
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<td>.0015</td>
<td>t**</td>
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<td>.1249</td>
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</table>

only the highest dose is shown for reference. Multiple comparisons (Duncan's multiple range test) are indicated by letters "a," "b" and "c." When significant differences were not detected, points are labeled with the same letter. As can be seen from figure 4A, no qualitative differences between naloxone and pentazocine in the antagonist scale items were found. Naloxone produced no or minimal increases in the agonist-antagonist scale items (fig. 4B). However, the ratings on the items "confused" and "lightheaded" were significantly higher after pentazocine administration than after placebo or naloxone.

Characterization of effects. The responses given by subjects in the drug classification questionnaire at 240 min after drug administration are presented in table 3. The maximum possible number of classifications was six for each experimental condition (equivalent to the total number of exposures to each condition). Subjects classified the effects of placebo appropriately on at least 50% of occasions. Subjects consistently classified morphine as an opioid agonist, and a dose-response relation was observed. Simultaneously, placebo classifications decreased as a function of the morphine dose. Naloxone was classified as an opioid antagonist by at least four subjects, but there was no apparent dose-response relation. Pentazocine was classified as antagonist by some individuals, and as hallucinogen or alcohol by others. By combining the results from both doses of pentazocine, subjects characterized the effects as most similar to hallucinogens on four occasions, opioid antagonists on three and alcohol on three (maximum possible number of classifications was 12).

Physiological measures. The time course of effects on the pupil diameter values is shown in figure 5. The highest dose of morphine produced a significant decrease in the total 240-min values (Dunnett's test, P < .01), whereas significant increases in peak and total effect were produced by the highest doses of naloxone (Dunnett's test, P < .05) and pentazocine (Dunnett's test, P < .01). In addition to these effects, the only physiological effect observed was an increase in systolic blood pressure values (which increased by approximately 10 mm Hg) after the administration of both doses of pentazocine (Dunnett's test, P < .05).

Psychomotor performance. There was a trend for morphine to produce exophoria (relaxation of the extracocular musculature), whereas naloxone tended to increase esophoria scores. Although the ANOVA showed significant differences between experimental conditions (F = 4.14; P = .0021), these effects were not different from placebo. Heterophoria values for pentazocine did not differ from those for placebo.

Time course of precipitated withdrawal. Additional analyses were performed comparing the effects of naloxone and pentazocine in some measures indicating opioid withdrawal ("any effect" and "bad effect" visual analog scales, ARCI-LSD scale, agonist scale and pupil diameter) to determine whether there were differences in the time course of naloxone and pentazocine withdrawal. No interactions between drug doses and time were observed in the three-factor ANOVA for the variables studied, indicating that the time course of withdrawal was probably similar for naloxone and pentazocine.

Nonstandardized observations. After the administration of pentazocine (60 mg), subject 6 experienced psychotomimetic changes, with depersonalization, derealization and difficulties in concentration. These effects were reported by the subject at the end of the session and peaked at 7 hr after drug administration. The subject indicated that the effects of the methadone dose (240 min after pentazocine administration) were the same as usual and he was not experiencing withdrawal symptoms. These effects were described by the volunteer as LSD-like, but otherwise they were not perceived to be particularly disturbing; thus, the investigators considered it was not necessary to open the medication codes or to administer any additional medication. The effects disappeared 30 to 35 hr after pentazocine administration. The volunteer was not experiencing any effect next morning (48 hr postadministration), and the experimental sessions were therefore continued.

Discussion

The effects of the standard drugs morphine and naloxone in this study were similar to those reported in previous studies carried out in opioid-dependent human subjects. As expected, the mu agonist morphine produced a pattern of effects char-
The effects of i.m. doses of morphine (40 and 60 mg) were as expected for a mu agonist. In previous studies using a similar design, the mu agonist hydromorphone has been administered to volunteers dependent upon the same dose of methadone as in the present study (30 mg/24 hr p.o.). Based on their analgesic equivalence, hydromorphone is assumed to be 7 to 8 times more potent than morphine (Jaffe and Martin, 1990), whereas it appears to be 9 times more potent than morphine in producing euphorigenic effects (Jasinski et al., 1978). The effects of acute doses of hydromorphone, 4 and 8 mg (Preston et al., 1988, 1989b), and 5 and 10 mg (Strain et al., 1992) were similar to those of morphine in the present study, although some differences in the sensitivity of several measures may be found, probably related to cross-cultural differences in the subjects and evaluation instruments used.

Recent research has shown that low acute doses of naloxone (0.05–0.2 mg i.v.) can precipitate withdrawal in subjects receiving 24 mg of oral methadone daily (Kanof et al., 1992). In two studies by Preston et al. (1988, 1989b), the same doses of i.m. naloxone as those used in the present study precipitated a dose-related withdrawal syndrome, which was observed in a number of physiological and subjective measures, with the 0.1-mg dose producing no or limited effects. Beside increases in pupil diameter, no physiological changes after naloxone administration were found probably due to a lower sensitivity in the methods of measurement used in this study in comparison to previous works (repeated determinations vs. continuous monitoring).

However, the presence of significant increases in the antagonist effects scale, along with increases in the LSD scale and in visual analog scales reflecting aversive changes, strongly indicates a naloxone-precipitated withdrawal syndrome.
The assessment of the degree of heterophoria showed a trend of morphine toward a relaxation of the extraocular musculature, whereas naloxone produced the opposite effect. Heterophoria has not been previously studied in opioid-dependent humans, but the mu agonist fentanyl produced exophoria in nondependent healthy volunteers (Manner et al., 1987; Zacny et al., 1992). Although in the present study the effects of morphine and naloxone did not reach statistical significance when compared to placebo, differences between both drugs suggest that measurement of heterophoria may be a simple and useful method for the assessment of agonist and antagonist properties.

Pentazocine, like naloxone, precipitated a withdrawal syndrome, which was evidenced in a number of subjective effects measures as well as by increases in the pupil diameter. The pentazocine-precipitated withdrawal was not dose related. Whether or not this finding corresponds to a ceiling effect as has been reported in nondependent opioid abusers (Jasinski et al., 1970; Preston et al., 1987b) cannot be drawn from our data. The precipitation of withdrawal by pentazocine in opioid-dependent subjects has been previously shown in animal species (e.g., Gilbert and Martin, 1976) as well as in humans dependent...
Categorized by letters subjects. Multiple comparisons (Duncan’s multiple range)
240 mIII responses six methadone-dependent Nne values of the total
dose
Because morphine produced no effects on these scales, only the highest
In antagonist (A) and agonist-antagonist (B) adjective rating scales.
Fig.
Other abbreviations are as figure
-detected, pouts are labeled with the same letter. M60, morphine 60 mg.
been described
phenomenon has not
240 mg/24 hr of morphine s.c. receiving doses of 60 and
120 mg of pentazocine (Jasinski et al., 1970). However, this
phenomenon has not been described in methadone-dependent
subjects nor have direct comparisons with the pure antagonist
naltrexone been conducted. It should be noted that subjects in
the study of Jasinski et al. (1970), presented a comparatively
higher level of opioid physical dependence than those in
the present study.
In contrast, the effects of pentazocine in nondependent hu-
mans have been described as predominantly morphine-like
(Jasinski et al., 1970; Preston et al., 1987b; 1992; Preston and
Bigelow, 1993). Thus, the overall profile of pentazocine effects
in nondependent and opioid-dependent human subjects is con-
sistent with pentazocine acting as an intermediate efficacy mu
opioid. Indeed, pentazocine produces agonist effects in situations
in which low efficacy is required (nondependent subjects),
whereas it produces antagonist effects in situations in which
high efficacy is required (opioid-dependent subjects). Recent
preclinical behavioral data support the notion that the opioid
isomer (−)-pentazocine acts as an intermediate efficacy mu
opioid (Picker et al., 1992). This is in accordance with observ-
ations made with other mixed agonist-antagonist opioids, such as
butorphanol and nalbuphine, which also preferentially pro-
duced morphine-like effects in nondependent humans (Jasinski
et al., 1975; Jasinski and Mansky, 1972), whereas they precip-
itated withdrawal in methadone-dependent humans (Preston
et al., 1988, 1989b). In contrast, buprenorphine produced mor-
phine-like effects in nondependent subjects (Jasinski et al.,
1976) but caused neither agonist- nor antagonist-like effects in
volunteers dependent upon methadone (Strain et al., 1992).
Some of the effects of pentazocine observed in the present
study were different from those of naltrexone. However, they are
consistent with the effects of pentazocine reported in previous
studies in nondependent humans. Increases in blood pressure
have been described in either patients with acute myocardial
infarction (Lee et al., 1975; Jasinski and Mansky, 1972), whereas they precip-
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1976) but caused neither agonist- nor antagonist-like effects in
volunteers dependent upon methadone (Strain et al., 1992).

Fig. 4. Effects of pentazocine, naltrexone and placebo on individual items
in antagonist (A) and agonist-antagonist (B) adjective rating scales.
Because morphine produced no effects on these scales, only the highest
dose is shown for reference. Each point is the mean change from base-
line values of the total 240 min responses in six methadone-dependent
subjects. Multiple comparisons (Duncan’s multiple range test) are indi-
cated by letters “a,” “b” and “c.” When significant differences were not
detected, points are labeled with the same letter. M60, morphine 60 mg.
Other abbreviations are as in figure 2.

Fig. 5. Time course of effects of pentazocine, naltrexone and morphine
on the pupil diameter measures in methadone-dependent humans. See
figure 1 for other details.

effect has also been described in naltrexone-precipitated with-
drawal conditions (e.g., Preston et al., 1989b; Strain et al., 1992)
two observations indicate that, in the present study, this was a
specific effect of pentazocine rather than a withdrawal effect:
1) the increases corresponded only to systolic blood pressure
and 2) the naltrexone-precipitated withdrawal was not parallel
with changes in blood pressure. The lack of cross tolerance to
the pressor effect of pentazocine in opioid-dependent subjects
supports that, as previously shown in nondependent humans
(Preston and Bigelow, 1993), a mechanism of action other than
through mu receptors may be involved.
Pentazocine also produced a series of subjective effects that
were not observed after naltrexone administration. Pentazocine
increased the scores on the agonist-antagonist scale, which
reflects effects related to confusion and changes in perception,
as well as increases in the ratings of two individual items
(“confused” and “lightheaded”). Sedation, as measured by the
PCAG scale, was increased, although not significantly, by pen-
tazocine. In addition, the effects of pentazocine were classified
by the subjects as being similar to hallucinogens or alcohol
more frequently than to an antagonist. Moreover, one subject
presented psychotomimetic changes after the administration of
pentazocine (60 mg). Although it could not be demonstrated
that the effects experienced by this subject were causally related
to pentazocine administration, Jasinski et al. (1970) observed a similar pattern of psychotomimetic effects, which lasted more than 12 hr, after the administration of large doses of pentazocine (120 mg/70 kg) to morphine-dependent subjects. Overall, these effects of pentazocine, which cannot be classified either as morphine-like or as antagonist-like, are consistent with previous reports in nondependent subjects (Fraser and Rosenberg, 1964; Jasinski et al., 1970; Preston et al., 1978b). Therefore, their presence in this study may be interpreted as a lack of cross tolerance to some effects that are probably not µ mediated. Whether they are mediated through kappa or sigma/phenylcyclidine sites cannot be drawn from the results of the present study.

The methods developed in the Addiction Research Center for the human laboratory evaluation of opioid compounds have been fully used in a non-American context. The overall profile of effects after the administration of standard drugs was similar to that obtained in equivalent American populations. The validity of results is also supported by the following observations: 1) there was good agreement between physiological measures of opioid effect (e.g., pupil diameter) and subjective effects measures (e.g., ARCI scales, visual analog scales) and 2) different measures of similar phenomena yielded similar patterns of response (e.g., “liking” and MBG).

In summary, the present study shows the feasibility and applicability of methods traditionally used for the clinical evaluation of abuse liability of opioid analgesics in a non-English-speaking sociocultural context. Our data support that, in humans, pentazocine acts as a partial µ agonist with a non-µ component of activity. Finally, these results indicate that the abuse liability of pentazocine in opioid-dependent individuals is low.

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