half-life ($t_{1/2}$) and clearance (Clp) of the drug. Difference was also observed in the AUC_0^∞, elimination $t_{1/2}$ and C_{max} of the derived metabolite, N.

Conclusion: It is likely that both Chinese and Nepalese patients did not eliminate P as effectively as the Caucasian patients after a single IM dose and that they produced more N-demethylated metabolite, N, which stayed longer in the Asian groups.

Table 1
Mean (±S.E.M.) Disposition Parameters of Pethidine and Norpethidine

Parameter	Caucasian (n = 8)		Chinese (n = 5)		Nepalese (n = 7)	
	P	N	P	N	P	N
AUC_0^∞ (ng ml^{-1}·h)	1160 ±158	1568 ±145	1740 ±162	1736 ±388	1284 ±121	3199 ±588
T_{max} (hr)	0.9± 0.04	4.8± 0.5	0.73± 0.16	6.0± 0.6	1.04± 0.17	4.9± 0.4
C_{max} (ng ml^{-1})	208.6± 24	30.5± 1.6	246.4 ± 29.4	28.8± 1.9	202.2 ± 29.9	27.9± 1.7
Clp (ml min^{-1} kg^{-1})	28.9± 3.7	–	18.6 ± 1.3	–	26.2 ± 1.8	–
Vd (L kg^{-1})	5.4± 1.0	–	7.0 ± 1.4	–	8.7 ± 1.3	–
Elimination $t_{1/2}$ (h)	4.3± 0.4	33.5± 2.0	7.9 ± 0.9	39.6± 8.6	6.3 ± 0.6	77.4± 13.5

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The influence of several contaminants of street narcotics on experimental morphine withdrawal syndrome

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It is known that street narcotics are often contaminated with several substances and impurities that could increase the prevalence and severity of toxic complications from opioids compared when they are used alone (U.N. Reports, 1987).

The pharmacological profile of these contaminant substances is different, and these differences could affecting on several forms the expression of morphine withdrawal syndrome. This may be an important factor for the therapeutic approach of this pathology.

Some of the products used as amphetamine, scopolamine, aspirin or amitriptyline have a mechanism of action based in the modification of several neurotransmitter that are altered in morphine withdrawal syndrome (dopamine, choline, prostaglandine, noradrenaline and serotonine) (Maynert and Klingman, 1962).

In this paper we have investigated the ability of these substances to alter salient signs of motor activity during morphine withdrawal syndrome. Opiate dependence was induced by two daily injections of morphine during a period of five days (Schaeffer and Michael, 1983). In the first experiment, the withdrawal syndrome was precipitated by naloxone two hours after amphetamine and aspirin injection. In second assay, amitriptyline, scopolamine, aspirin and amphetamine were injected 30 minutes before naloxone. Measured withdrawal jumping and wet-dog-shake were not affected by aspirin when administered two hours before naloxone. However, aspirin (100, 150 and 200 mg/kg) increased the number of jumps and reduced the number of wet-dog-shake ($U = 14$, $p < 0.01$; $U = 20$, $p < 0.05$; $U = 8$, $p < 0.01$, respectively) when was 30 minutes before naloxone. Amphetamine, injected two hours before naloxone, decreased the number of jumps at the doses of 1 mg/kg ($U = 10$, $p < 0.01$). This effect was also evident on

wet-dog-shake at the same dose ($U = 17$, $p < 0.05$) and at the dose of 2 mg/kg ($U = 3$, $p < 0.01$) when injected 30 minutes before naloxone. Jumping and wet-dog-shake were not modified by scopolamine. Amitriptyline produced a decrease of number of jumps at the dose of 20 mg/kg ($U = 11$, $p < 0.01$) but did not show any change on wet-dog-shake behaviour.

In conclussion, the results obtained clearly show that the different contaminants of street narcotics, almost the substances investigated in this study, may modify the severity and frequency of morphine withdrawal syndrome and it is possible that these modifications are important to the management of morphine withdrawal syndrome in man.

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Controlled-release oral morphine (MS contin tablets, MSC) in postoperative pain

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Controlled-release oral morphine is routinely used in the management of cancer-related pain. In studies in cancer pain, MSC has been shown to be both safe and effective in the prevention of breakthrough pain when administered every 12 hours (Kaiko 1989, Hanks 1989). Improved compliance, convenience and uninterrupted nighttime sleep can thus be provided. Previous post-operative studies have demonstrated comparable therapeutic effects of MSC and intramuscular morphine but these studies were not designed to fully elucidate the MSC dose-response relationship. This study was undertaken to assess its therapeutic profile in postoperative pain and to evaluate its efficacy and safety in doses of 30, 60, 90 and 120 mg relative to 10 mg IM morphine and placebo in 146 patients reporting moderate or severe pain after abdominal hyserectomy.

A trained nurse observed obtained patient's reports of pain relief (none, 0; a little, 1; moderate, 2; a lot, 3; complete, 4) and recorded side effects at 1, 2, 3, 4, 5, 6, 7, 8, 10 and 12 hours following drug administration or until pain returned to baseline in this randomized, double-blind, double-dummy, parallel-group study in patients with demonstrated gastrointestinal function. Mean (se) pain relief was calculated for each treatment in terms of: peak pain relief (PPR), the highest relief score reported, the individual pain relief score at the 6th-hour (6 hrPR) observation and total pain relief (TOTPAR), the area under the time-effect curve. The percentage of patients with one or more side effects (%ADR) was calculated for each treatment. These primary end points are tabulated below.

Drug	10 mgIM	Placebo	30 mgMSC	60 mgMSC	90 mgMSC	120 mgMS
N Pts	41	38	21	21	19	6
PPR	2.78(0.13)[a*]	1.50(0.18)	2.00(0.32)	2.67(0.31) [a]	2.64(0.33) [a]	3.17(0.48) [b]
6 hrPR	0.68(0.19)	0.18(0.12)	1.05(0.28)	1.48(0.37) [c]	2.00(0.40) [c]	2.83(0.60) [d]
TOTPAR	9.62(1.06)	3.65(1.19)	9.79(2.40)	15.52(3.24) [a]	18.71(3.40) [c]	25.17(5.44)
%ADR	61	45	48	71	64	100

Dose response was observed for all pain relief parameters. Except for the MSC 30 mg dose, all MSC doses provided significantly higher scores for all pain relief parameters when compared with placebo. Peak effects comparable to that