Title : INTRAVENOUS DEZOCINE (WY-16,225) FOR POSTOPERATIVE PAIN RELIEF

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INTRODUCTION. Dezocine (D), a bridged aminotetralin, chemically related to benzomorphan, is a new mixed agonist-antagonist analgesic. In animals D is reported to have minimal dependence liability, antagonist properties less than that of nalorphine and high therapeutic index (greater than 1000).[1] We studied 3 doses of intravenous D for moderate to severe postoperative pain and compared its effects with those of morphine and placebo under controlled double blind conditions.

METHOD. Following institutional approval, 198 consenting (ASA Class I or II) patients undergoing either general, orthopedic or gynecological operation under standard premedication and anesthesia were studied. In the recovery room after patients complained of moderate to severe pain for at least 15 min, one of the test medications was given IV in a random double blind fashion. Test medications were D 2.5, 5 or 10 mg; morphine 5 mg or placebo (0.9% NaCl). Observations were made at baseline, and then at 15, 30, 60, 120, 180, 240, 300 and 360 min following administration of test medication. Pain intensity (severe, moderate, mild, or none), pain relief scores (complete relief, 4; a lot of relief, 3; moderate relief, 2; little relief, 1; none, 0; and worse, -1) and visual analog scale (a 100 mm horizontal line with "no pain" at one end and "worst pain ever felt" on the other) were used to measure effectiveness of the medications. When adequate pain relief was not obtained within 30 min after test medication, a rescue analgesic (morphine in 2 mg IV increments) was given and study terminated. Degree of sedation (marked, moderate, mild, or nil) and frequency of side effects were noted. Blood pressure, pulse and respirations were recorded. At the end of the study physicians gave an overall satisfactory or unsatisfactory grade depending on degree and duration of pain relief and presence or absence of adverse reaction. The day after surgery patients gave their global assessment of pain medication as excellent, good, fair, or poor. Statistical analysis was performed by analysis of covariance with initial pain severity as the covariant and pairwise comparison done by Student's t test, $p < 0.05$ being considered significant.

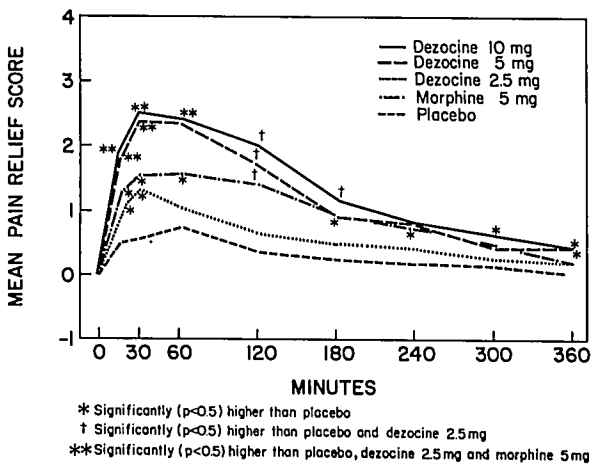
RESULTS. Demographic parameters (not shown) were comparable between the groups. Results from the 3 pain relief assessments were very similar; therefore, only results of pain relief scores are shown (Fig. 1). D, both 10 and 5 mg, produced significantly better pain relief than placebo up to 6 and 4 hours respectively and significantly better pain relief than morphine 5 mg at 15, 30, and 60 min. Morphine 5 mg was better than placebo throughout the study except at 5 hours and better than D 2.5 mg only at 120 min. D 2.5 mg was better than placebo only at 15 and 30 min. There was no difference in sedation grades between the active agents. Adverse effects were infrequent in all groups and differences were not significant. Physicians' overall evaluation favored D 5 and 10 mg over placebo and morphine (Fig. 2). Patients' evaluation favored D 10 mg over placebo, morphine 5 mg, and D 5 and 2.5 mg.

DISCUSSION. Partial agonists like D may have advantages over pure agonists i.e. lower incidence of respiratory depression (ceiling effect), lower dependence liability and lower frequency of other side effects. These advantages of the partial agonists may enable us to treat postoperative pain more efficiently without unneccessary fears. However, some agonist-antagonists e.g. pentazocine, butorphanol and possibly nalbuphine are reported to have agonist effects on kappa, delta, and possibly sigma receptors and thus may have undesirable psychotomimetic effects. D appears to act primarily on mu receptors and only partially on delta receptors, (personal communication, S. H. Snyder, Dept Neuroscience, Pharmacology and Experimental Therapeutics, Johns Hopkins Univ School of Med) and thus should have an advantage over the other three available agonist-antagonists and have less psychotomimetic and sedative effects. D with its quicker onset and more potent pain relieving properties than morphine should be an important addition to the existing analgesic drugs.

REFERENCE.

1. Malis JL, Rosenthale ME, Gluckman MI: Animal pharmacology of WY-16,225, a new analgesic agent. J Pharmacol Exp Ther 194:488-498, 1975

MEAN PAIN RELIEF VERSUS TIME



* Significantly ($p<0.5$) higher than placebo
† Significantly ($p<0.5$) higher than placebo and dezocine 2.5 mg
** Significantly ($p<0.5$) higher than placebo, dezocine 2.5 mg and morphine 5 mg