TITLE : CLONIDINE FOR POSTOPERATIVE ANALGESIA : EPIDURAL VERSUS IM STUDY

AUTHORS : F. BONNET, M.D.*, O. BOICO, M.D.*, S. ROSTAING, M.D.*, J.F. LORIFERNE, M.D.*, L. QUINTIN, M.D.*, M. GHIGNONE, M.D.**

AFFILIATION : * Department of Anesthesiology, Hôpital Henri MONDOR, 94010 CRETEIL - FRANCE
** Department of Anesthesiology, University of Pittsburgh - U.S.A.

INTRODUCTION

Postoperative patients often require potent analgesic techniques with minimal side effects. Since it has been documented that clonidine (C), an alpha 2 adrenergic agonist, has analgesic properties when administered epidurally, this could be the appropriate route for administration in postoperative patients (1). Nevertheless an analgesic effect has been demonstrated after C systemic administration (2). The aim of this study was therefore to compare the features of C induced analgesia after IM or epidural administration in order to evaluate the mechanism of C action and to determine which route is more suitable for relief of postoperative pain when C is given as the sole analgesic agent.

MATERIAL AND METHODS

Twenty ASA I-II patients scheduled for peripheral orthopedic or perineal surgery were included in this study after informed consent and ethics committee approval. Patients were operated on epidural anesthesia using local anesthetic agents. Postoperatively, after recovery from sensory and motor blockade, patients were allocated randomly in 2 groups. In the first group (8 women, 2 men, age 45.5 ± 20.8 years, weight 67.4±11.9 kg, height 166.7 ± 7.6 cm) patients received 2 mg/kg epidural clonidine (EC) in a 15 ml isotonic saline solution injected through a previously inserted epidural catheter. In the second group (7 women, 3 men, age 52.3 ± 17.9 years, weight : 66.6 ± 9.0 kg, height 165.1 ± 7.8 cm), 2 mcg/kg C in a 5 ml isotonic saline solution were IM administered (IMC group). In both groups, pain score was assessed on a visual analog scale (VAS) graded from 0 (no pain) to 10 (maximum pain) first before C administration, then after, every 15 min for the first 2 hours and then every 30 min for the next 4 hours. Whenever, patients complained of pain after C injection, they received 500 mg IV paracetamol. Duration of C action was the time elapsed between C injection and paracetamol requirement. Pain relief was calculated as the percent reduction of pain. Blood pressure and heart rate were monitored throughout the study. C plasma concentrations were measured at 15,30,45, 60,90,120,180,240,300,360 min and 24 hours after C injection, by radio-immunoassay (3).
Statistical analysis used a 2-way ANOVA, appropriate Student t-test or Mann-Whitney test.
Results are expressed as mean ± SD.

RESULTS

The onset of pain relief was observed within 15 min following C injection in the 2 groups. C had equivalent analgesic properties when administered epidurally or IM as asserted by comparable maximum pain relief and duration of action in both groups (table 1). Drowsiness was noticed in all the patients within 15-20 min after C administration, lasting 141±37 min in the EC group and 118±43 min in the IMC group (NS). A moderate fall in mean arterial pressure was observed in the 2 groups (EC group : 29.5±11.5%, IMC group : 24.2±11.0%). 2 patients in the EC group and one in the IMC group experienced bradycardia <50/min. Pharmacokinetic parameters are reported in table 2.

TABLE 1 : FEATURES OF CLONIDINE ANALGESIA

	Pain assessment (VAS score)	Max.pain relief(%)	Duration of action(min)
EC group	7.8 ± 1.5	78.5±20.6	208 ± 87 (extr:45-360)
IMC group	7.0 ± 1.0	68.1±31.5	168 ± 99 (extr:60-300)

TABLE 2 : CLONIDINE PHARMACOKINETICS

	C max (ng/ml)	T max (min)	T 1/2 (h)	Vd (l/ng/ml)
EC group	0.91±0.36	70.0±82.2	24.9±7.4	2.87±0.47
IMC group	0.82±0.29	128.6±143.4	42.5±20.3	3.32±0.76

(Cmax: observed peak value. T max: time to reach Cmax T 1/2: elimination half life, Vd: volume of distribution)

DISCUSSION

C induces an efficient postoperative analgesia but of short duration. The features of pain relief after C administration are similar whatever the route of administration suggesting that the main site of C analgesic action is supraspinal. Supraspinal sites could be reach by means of vascular resorption after IM as well as epidural clonidine injection.

REFERENCES

1. EISENACH JC, DEWAN DM, ROSE JC et al
Anesthesiology 66, 496-501, 1987
2. SPAULDING TC, FIEDRIEG S, VENAFARO JJ et al
Eur. J. Pharmacol. 58, 19-25, 1979
3. ARNDTS SD, STAHLE H, FORSTER HJ
J. Pharmacol. Methods 6, 295-307, 1981.