

Title: HEMODYNAMIC AND ENDOCRINE EFFECTS OF REVERSAL OF FENTANYL-INDUCED RESPIRATORY DEPRESSION BY NALBUPHINE

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The antagonist effect of agonist-antagonist, nalbuphine (NA) has been utilized for the reversal of the respiratory depressant effect of the agonists. Since pain causes increased secretion of norepinephrine (NE) and increased rate-pressure product (RPP), we determined (NE), epinephrine (E) and dopamine (DA) concentration and hemodynamic changes associated with reversal in addition to analogue pain scores.

Materials and Methods: Ten patients with a mean age \pm S.D. of 36.0 ± 14.9 yrs and mean weight \pm S.D. of 69 ± 11.5 kg. All patients gave a valid written consent as required by the Institutional Ethical Review Board. After 1.5 mg/kg i.m. hydroxyzine and 3.0 μ g/kg i.m. glycopyrrolate premedication, anesthesia has been maintained with fentanyl, $N_2O:O_2$, diazepam and pancuronium. Arterial $PaO_2 > 100$ Torr, $PaCO_2 = 28-38$ Torr were maintained. Alveolar PCO_2 , ventilation, blood gases, direct arterial pressure (AP), ECG were monitored. At the end of the procedure, 0.25 mg/kg i.v. pyridostigmine and 4.0 μ g/kg glycopyrrolate were given i.v. for reversal of neuromuscular block. Severe ventilatory depression and/or apnea lasting for 30 seconds was substantiated, before 0.1 mg/kg NA was given i.v. If adequate ventilation was not restored, an additional 0.1 mg/kg NA was given q 3 min. until full recovery.

Results: Apnea was reversed and normal ventilation restored in all 10 patients by NA with mean dose \pm S.D. of 0.227 ± 0.08 mg/kg. Only 1 patient required a single dose, 7 patients received two doses and 1 patient each 3 and 4 doses. Minute ventilation before reversal was 1.5 ± 1.2 L/min and at 15', 30', 45' and 60' following reversal were 10.5 ± 3.7 , 10.9 ± 3.1 , 11.5 ± 2.8 and 10.5 ± 2.5 L/min as shown in Table 1. Arterial $PaCO_2$ before reversal was 56.0 ± 5.0 Torr and after reversal 44.3 ± 4.3 , 49.4 ± 2.4 , 41.5 ± 2.7 and 42.1 ± 2.6 Torr resp. Arterial

PaO_2 and pH remained at normal level. A significant ($p \leq 0.05$) increase in AP occurred at 15 min following reversal from 135.0 ± 21.9 Torr to 147.1 ± 28.4 Torr, while a decrease ($p \leq 0.01$) was observed 1 hour after reversal to 121.6 ± 20.3 Torr. The changes in diastolic pressure, heart rate, norepinephrine, and dopamine levels were not significant. Epinephrine levels were significantly elevated after reversal $p \leq 0.01$. The mean pain score remained below 1.5 on a 0 to 10 analogue scale throughout the first hour.

Conclusions: Nalbuphine promptly and effectively reversed the respiratory depression. The lack of increase in norepinephrine and pain scores indicate that either the analgesic effect of fentanyl remained unaffected or nalbuphine itself provided analgesia for the postoperative pain.

TABLE 1

	Before Reversal	After Reversal			
		15'	30'	45'	60'
Min. Vent. L/min	1.5 ± 1.2	10.5*** ± 3.7	10.9*** ± 3.1	11.5*** ± 2.8	10.5*** ± 2.5
Resp. Rate RR/min	5.1 ± 3.9	18.8*** ± 5.0	20.4*** ± 6.5	19.3*** ± 6.4	17.8*** ± 4.4
SBP mmHg	135.0 ± 21.9	147.1* ± 28.4	133.4 ± 24.5	125.4 ± 17.1	121.6** ± 20.3
HR/min	74.9 ± 15.5	85.3 ± 21.4	78.2 ± 14.8	75.2 ± 12.4	76.4 ± 11.9
$PaCO_2$ mmHg	56.0 ± 5.0	44.3** ± 4.3	42.3* ± 3.3	41.5** ± 2.7	42.1** ± 2.6
NE pg/ml	391.3 ± 162.3	532.9 ± 308.1	509.0 ± 223.9	510.8 ± 251.8	427.1 ± 202.2
E pg/ml	182.3 ± 103.0	650.8** ± 436.9	677.9** ± 433.9	605.1** ± 343.5	517.3** ± 258.2
D pg/ml	44.0 ± 25.3	44.3 ± 24.4	41.6 ± 15.4	44.1 ± 23.1	46.2 ± 25.8
Analogue Pain Scores (1-10)	NA	1.2	0.95	0.95	0.7

* $p \leq 0.05$ ** $p \leq 0.01$ *** $p \leq 0.001$