

TITLE: HEMODYNAMIC EFFECTS OF VARIABLE DOSE I.V. MILRINONE FOLLOWING CARDIAC SURGERY.
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We studied the effects of I.V. Milrinone, a new PDE III inhibitor, in 99 adults following elective cardiac surgery in five centres. Informed consent was obtained and ethical approval was given both locally and by the European Ethical Review Committee.

The aims of the study were; to assess the safety and efficacy of three infusion regimes of Milrinone. Patients were treated provided that cardiac index (CI) < 2.5l/m² and wedge pressure (PCWP) > 8 mmHg. After a bolus infusion of 50 mcg/kg over 10 mins, patients received maintenance infusions of either 0.375 (34 pts), 0.5 (34 pts) or 0.75 (31 pts) mcg/Kg/min. CI, PCWP, heart rate (HR), and systemic (MAP) and pulmonary (PAP) artery pressures were measured throughout. This data as well as systemic vascular resistance (SVR) and stroke index (SI) are shown as mean values in the Table at baseline, after 1 and 12 hours of therapy.

	CI (*)	PCWP mmHg	HR	SI ml	MAP mmHg	SVR (**)	PAP mmHg
LOW DOSE GROUP							
baseline	1.9	12	81	23	86	1876	20
+1 hr	2.6	9	91	28	81	1313	18
+12 hr	2.8	10	88	31	77	1113	17
MEDIUM DOSE GROUP							
baseline	1.9	12	81	24	85	1840	21
+1 hr	2.6	9	93	29	76	1206	19
+12 hr	2.8	10	91	32	73	1085	18
HIGH DOSE GROUP							
baseline	1.9	11	83	25	81	1698	19
+1 hr	2.8	9	94	31	72	1099	18
+12 hr	3.2	9	93	35	72	918	17

(*)=l/min/m2. (**)=dynes/sec/cm-5

Statistical analysis (analysis of variance, Students t Test) showed no differences between groups. There were increases in CI, HR and SI (p<0.01) in all dose groups during treatment. Falls in PCWP and SVR were seen in all groups during treatment (p<0.01); MAP also fell slightly (p<0.05).

Adverse effects were minimal; 5 pts showed non-significant arrhythmias, 2 pts developed rapid atrial fibrillation.

In conclusion, i.v. milrinone improved cardiac performance at each dosage studied and may be of benefit in patients following cardiac surgery.

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TITLE: EFFECT OF FLUMAZENIL ON ANESTHESIA INDUCED BY FLUNITRAZEPAM, KETAMINE, ETOMIDATE OR THIOPIENTAL
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Flumazenil has been shown to reverse the anesthetic effect of benzodiazepines. The present study was undertaken to evaluate whether flumazenil would reverse the anesthetic effect of flunitrazepam (F), ketamine (K), etomidate (E) or thiopental (T).

Eighty unpremedicated adult patients (ASA 1-2) scheduled for outpatient surgery were enrolled after obtaining institutional approval and informed consent. The patients were randomly allocated into 4 equal groups and were given iv the following induction agent: 4 mg F, 100 mg K, 20 mg E and 300 mg T. After induction, anesthesia was maintained with fentanyl 50 ug iv and 70% nitrous oxide in oxygen. At the completion of surgery, patients were allowed to breath 100% oxygen and at 3 min (time 0), patients' wakefulness were assessed with a score system of 5 (alert), 4 (lethargic), 3

(responsive to loud noise), 2 (responsive to painful stimulus, and 1 (not arousable). In a double-blind manner, half of the patients (N=10) in each group were then given 2 ml i.v. of a coded solution of either 0.2 mg flumazenil (f) or N-saline. Alertness, recall, motor coordination and adverse effects were assessed at 5, 15, 30, 60 and 120 min post-drug.

Flumazenil showed no effect on groups K and E, an immediate reversal effect on all patients of group F and reversed 6 patients in group T at 30 min - with an increased incidence of side effects (Table). This suggested some cross-reactivity between these two drugs. Consideration should also be given when using f in the differential diagnosis of drug overdosage to avoid potential adverse effects.

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SIDE EFFECTS

Re	VOMITING + ** ***	NAUSEA + ** ***	HEADACHE + ** ***	HALLUCINATION + ** ***
K + 1	- 6 3	1 3 1	- 1 -	- 1 -
K - 1	3 2 1	1 1 1	1 - -	- 1 -
E + 1	- 2 3	- - -	- - -	- - -
E - 1	1 2 -	- - -	- - -	- - -
T + 1	2 2 -	- - -	1 - -	- - -
T - 1	1 - -	- - -	1 - -	- - -
F + 1	- - -	- - -	- - -	- - -
F - 1	- - -	- - -	- - -	- - -