Prolonged Depression of Respiratory Rate Following Methadone Analgesia

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Recent evidence suggests that patients undergoing mitral valve replacement with morphine analgesia may have respiratory depression for at least 24 hours after operation.\(^1\) Cardiovascular and respiratory effects have also been demonstrated as long as six days after intravenous administration of morphine to patients who have impaired renal function.\(^2\) We present the case of a patient with normal renal function who had depression of respiratory rate for eight days following the use of intravenous methadone analgesia during anesthesia for replacement of the aortic valve.

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REPORT OF A CASE

An 81-year-old (43.7 kg) woman who had aortic stenosis was scheduled for aortic-valve replacement. Past medical history included two uncomplicated surgical procedures. Physical examination was remarkable only for the murmurs of aortic stenosis and mitral insufficiency. Preoperative laboratory data were within normal limits.

The patient was premedicated with morphine 3 mg, and scopolamine, 0.3 mg, im. Muscle relaxation was achieved with \(d\)-tubocurarine and succinylcholine and the trachea intubated. Intraoperative analgesia was provided with methadone, 30 mg, in 240 ml 5 per cent dextrose given over 30 minutes. Anesthesia was maintained with 50 per cent nitrous oxide in oxygen.

On the first postoperative day the patient was lethargic, with constricted pupils. Respiratory rate was 8/min, and the patient was moving only the right side of her body. The trachea was extubated after administration of 1.0 mg naloxone (Narcan), but the respiratory rate slowly declined to 9/min 4 hours later. On subsequent days, naloxone was administered to document the amount.

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![Graph](image_url)

**Fig. 1.** Respiratory rates before (●) and after (○) intravenous administration of naloxone. On postoperative days 9 and 10 no change in respiratory rate (○) was found after naloxone administration. Arterial blood samples were drawn before the daily dose of naloxone. The inspired oxygen fraction (\(F_{1O_2}\)) was delivered through an aerosol face mask after postoperative day 1.
of respiratory rate depression, the effect lasting 2 to 4 hours after the dose given. No narcotic or respiratory depressant was given postoperatively. The depression of respiratory rate, miosis, and lethargy gradually resolved over the next nine days (fig. 1). There was no evidence of hepatic or renal dysfunction postoperatively. The patient was discharged two weeks after her operation, alert, with normal respirations, and with residual left hemiparesis.

**DISCUSSION**

Only narcotic-induced depression of respiratory rate will be reversed with naloxone. As naloxone does not stimulate respiration in the absence of previously administered narcotic, we believe this case represents a prolonged effect of methadone.

Narcotic-induced respiratory depression may be prolonged with: 1) hepatic insufficiency leading to decreased drug metabolism; 2) renal insufficiency leading to decreased excretion of active drug or its metabolites; 3) interactions with phenothiazines, monoamine oxidase inhibitors, and imipramine-like drugs; 4) drug overdose resulting in prolonged effective blood levels; 5) continued metabolism, release of the drug and metabolites from tissues, or enterohepatic recirculation; 6) abnormal plasma protein-binding kinetics.

There was no history or clinical finding to support any of these causes in our patient.

**REFERENCES**


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**Diagonal Ear-lobe Crease as an Indicator of Operative Risk**

**David H. Sprague, M.D.**

Preliminary data reported by Frank suggested that the presence of a prominent crease in the lobule portion of the auricle was associated with premature cardiovascular disease. This presumptive relationship has been tested by others, and a positive association has been found between the diagonal ear-lobe crease and coronary-artery disease. In view of this finding, it would appear reasonable to assume that the crease could be used as an indicator of operative risk. This hypothesis was tested.

**METHODS**

Two hundred and twenty-two consecutive patients scheduled for elective surgery were followed from the day of operation to the day of discharge. The following information was recorded for each patient: presence or absence of the diagonal ear-lobe crease, clinical evidence of coronary heart disease, intraoperative cardiovascular complications, and postoperative cardiovascular complications. For the purposes of this study, the ear-lobe crease was