

Title : Adrenergic Response to Morphine and Valium Anesthesia

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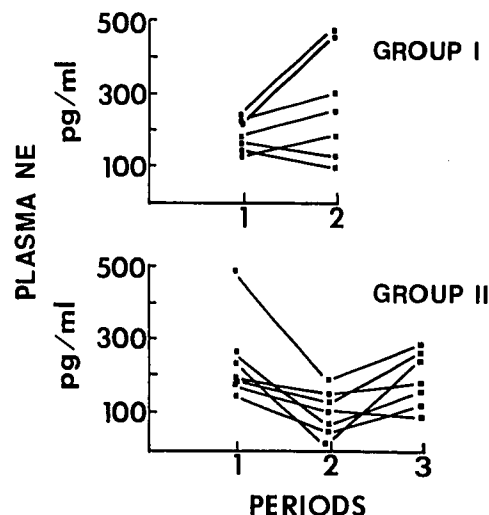
Introduction. Large doses of intravenous morphine sulfate (MS) with oxygen (O₂) alone is a popular anesthetic method in high risk patients as this technique produces minimal cardiovascular depression. It has been proposed that the observed circulatory stability with this anesthetic is due to stimulation of the sympathetic nervous system. As MS does not consistently produce loss of consciousness even in large doses, the sedative diazepam (V) is often combined with MS to anesthetize patients. There is concern that this approach may depress sympathetic nervous system activity. Recent advances in methodology allow accurate analysis of plasma catecholamine concentrations, so that adrenergic activity can be more precisely evaluated. This study was performed to assess the integrity of the sympathetic nervous system following MS, and MS + V anesthesia. In the latter state, the degree of adrenergic inhibition was tested by surgical stimulation.

Methods. Fourteen patients scheduled for cardiovascular surgery were studied with the approval of the Human Research Committee, University of California, San Francisco. All patients had documented ischemic heart disease and had been treated with nitrates and propranolol. Premedication consisted of MS 10 mg and scopolamine 0.4-0.6 mg (IM). Operating room monitoring included an ECG, and radial and pulmonary artery catheters. Awake control measurements consisted of standard hemodynamic variables and blood withdrawn for analysis of plasma norepinephrine (NE) and epinephrine (E) by radio enzymatic assay (Period 1). Anesthesia was induced with either intravenous MS, 2 mg/kg infused at rates of 5-7 mg/min (Group 1, N=7) or MS 2 mg/kg plus intravenous V, 20-30 mg. Ventilation with 100% O₂ was assisted throughout the induction periods, and arterial blood gases periodically sampled, PaCO₂ maintained at awake values (PaCO₂ = 46 torr). With diminution of spontaneous inspiratory efforts, endotracheal intubation was performed facilitated by succinylcholine and ventilation controlled. Repeat measurements of hemodynamic variables and plasma catecholamines were made at the completion of both induction periods (Period 2) and in Group 2 patients following skin incision (Period 3).

Results. Awake control measurements in both Groups were similar. Hemodynamic variables were within normal range, and plasma NE and E were not significantly different. Group 1 patients demonstrated small but significant reductions in heart

rate (HR) and mean systemic arterial pressure (MAP) but cardiac (CI) and stroke volume (SVI) indices were unchanged following induction. MS anesthesia resulted in stable or increased levels of plasma NE with marked variability noted in the response of individual patients (Fig. 1). Plasma E mirrored this response. Group 2 patients manifested similar reductions in HR and MAP after induction. However, depression of CI and SVI was frequently observed in this group. Plasma NE decreased in every patient following V + MS anesthesia. Plasma E also fell from awake values (123±35 to 23±4 pg/ml, p<0.05). These patients responded to skin incision by increases in MAP and vascular resistance (SVR) but little improvement in CI and SVI. Plasma NE rose to awake levels as did plasma E (89±22 pg/ml).

Conclusions. Large dose intravenous MS produces little cardiovascular depression and may enhance adrenergic activity although there is wide variation in any individuals' sympathetic response. This unpredictability may well be related to varying awareness levels in different patients. Addition of V attenuates the beneficial circulatory effects of MS and produces a consistent significant obtundation of sympathetic activity. Surgical stimuli evokes an adrenergic response in the face of V + MS anesthesia, the combination of which can result in some hemodynamic deterioration, suggesting that this technique is not without circulatory consequence during surgery.



Supported by the Veterans Administration