Title: INTRAVENOUS NICARDIPINE FOR TREATMENT OF POSTOPERATIVE HYPERTENSION

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Introduction: Because of their preferential peripheral vasodilator properties, dihydropyridine calcium channel blockers represent an interesting group of drugs for treatment of postoperative hypertension. However, their use in this indication has been limited by the lack of intravenous forms due to their light instability and poor aqueous solubility. Nicardipine, a new dihydropyridine calcium channel blocker, is light-stable and water-soluble, therefore suitable for intravenous administration.[1] This study was designed to assess the efficacy of intravenous (IV) nicardipine in treatment of postoperative hypertension.

Methods: 11 postsurgical patients--7 male and 4 female--(signed Informed Consent), aged 63.5 ± 4 years, weight 78.9 ± 2 kg, who underwent cardiac (7), vascular (2), hiatal hernia surgery (1), and renal transplant (1). They were divided into 2 groups of 5 patients each, according to the dose of IV nicardipine used for titration; 10 and 15 mg/hr, respectively (one patient who underwent cardiac surgery did not receive IV nicardipine because of a complete heart block which appeared immediately prior to the start of IV nicardipine). Hypertension was defined as systolic blood pressure > 120 mmHg or diastolic blood pressure > 80 mmHg (cardiac surgery) and systolic blood pressure > 140 mmHg or diastolic blood pressure > 95 mmHg (non-cardiac surgery). After inclusion, patients received nicardipine for up to 40 min (titration period) with a therapeutic end point defined as a decrease in systolic or diastolic blood pressure of ≥ 15%. After achieving therapeutic response, patients received IV nicardipine for up to 24 hours (maintenance period). Arterial blood pressure was recorded via a catheter inserted in the radial artery. In addition, in 4 patients a 7F Swan-Ganz pulmonary catheter allowed measurements of cardiac output by thermodilution method. At the end of baseline, titration, and maintenance, arterial blood samples (10 ml each) were collected for determination of nicardipine plasma concentration by gas chromatography with electron capture.[2] Data were analyzed using Student's t-tests and presented as mean ± SEM.

Results: Baseline systolic and diastolic blood pressure and heart rate were 168 ± 6 mmHg and 86 ± 4 mmHg and 85 ± 4 beats/min, respectively. In Group I and II, IV nicardipine produced a rapid decrease in both systolic (32 ± 2 mmHg and 25 ± 3 mmHg, respectively) and diastolic (17 ± 2 mmHg and 13 ± 3 mmHg, respectively) blood pressure during the titration period while heart rate remained unchanged (89 ± 4 bts/min). The time for reaching therapeutic end point was similar in Groups I and II (for systolic arterial blood pressure 6.3 ± 2.4 min vs 7.0 ± 1.5 min and for diastolic blood pressure 3.8 ± 0.9 min vs 5.3 ± 0.8 min). After titration, patients (except for one due to administative reasons) were included in the maintenance period. They received IV nicardipine for 0.5 - 4.5 hours in 7 cases, 4.5 - 12 hours in 1 case, and for 24 hours in 1 case. Except for one, the reason for discontinuing IV nicardipine was either systolic (88 mmHg; n = 1) or diastolic hypotension (57 ± 3 mmHg; n = 7). During maintenance, IV nicardipine was infused at a rate of 2.7 ± 0.2 mg/hr. At the end of maintenance, heart rate increased by 15% from baseline. Infusion of IV nicardipine was associated with an increase in cardiac output (from a baseline of 3.8 ± 0.5 l/min to 4.5 ± 0.8 l/min at the end of titration) and a decrease in systemic vascular resistance from a baseline of 2063 ± 605 dynes.sec/cm$^5$ to 1656 ± 85 dynes.sec/cm$^5$. In addition, IV nicardipine produced a decrease in double product (systolic blood pressure x heart rate x $10^{-3}$ from a baseline of 14.5 ± 0.9 mmHg.bts/min to 11.9 ± 1 mmHg.bts/min. Nicardipine plasma concentration was 60 ± ng/ml at the end of titration and 52 ± 6 ng/ml at the end of maintenance.

Discussion: IV nicardipine represents the first dihydropyridine derivative developed for intravenous use. Our preliminary study indicates that IV nicardipine is a potent peripheral vasodilator for treatment of postoperative hypertension. Although at the end of titration no tachycardia was recorded, at the end of maintenance heart rate was higher than baseline. Because of the induced increase in myocardial oxygen demand, reflex tachycardia associated with vasodilator therapy is considered deleterious, especially in patients with coronary artery disease. During IV nicardipine the increase in heart rate was associated with a concomitant decrease in double product, an index of myocardial oxygen consumption. This then suggests an overall beneficial effect of IV nicardipine on myocardial oxygen balance. Hence, nicardipine is a potent coronary vasodilator and has anti-anginal properties despite an acute reflex tachycardia.[3]

References:

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