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Effect of a low dose of midazolam on high blood pressure in dental patients: a randomised, double-blind, placebo-controlled, two-centre study☆

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Abstract

Some patients have transient hypertension before dental treatment as a result of anxiety and stress. Midazolam is an anxiolytic, and thought to be effective for the management of this sort of transient hypertension. We have evaluated in a randomised, controlled trial whether a low dose of midazolam can lower blood pressure in dental patients to an acceptable level without excessive sedation. Suitable patients were randomised to be given midazolam (trial group) or physiological saline (control group) intravenously. Blood pressure, heart rate, degree of anxiety, and amount of sedation were measured before and after injection. After injection, blood pressure in the trial group significantly decreased to clinically acceptable levels compared with controls. The degree of anxiety in the trial group was also significantly less than that in the control group, but there were no significant differences in sedation. These results suggest that injection of a low dose of midazolam stabilises the blood pressure of dental patients with transient hypertension.

Keywords: Hypertension; Anxiety; Midazolam; Sedation

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Introduction

Some people regard a dental clinic as a stressful environment, which will cause their blood pressure (BP) to rise, and dental procedures that cause stress are likely to result in further rises. It has therefore been postulated that dental patients may develop transient and unacceptably high BP during dental treatment despite having normal BP at home. In some cases, the rise may lead to harmful or even fatal consequences, such as a cerebrovascular accident or myocardial infarction.[1] Reduction in stress and anxiety that may be associated with dental treatment is therefore important in the management of patients with high BP.[2]

Midazolam is a benzodiazepine with a relatively rapid effect and short half-life, and is commonly used for sedation. It has an anxiolytic effect, which should be useful for management of BP in dental patients by decreasing stress and anxiety, but we know of no reliable data to support this. Only a few studies have assessed the clinical impact of midazolam given intravenously on anxiety and BP.[3] However, too large a dose will cause deep sedation,[4] and may induce adverse events such as obstruction of the airway and direct inhibition of the cardiovascular system.

We hypothesised that a relatively low dose of midazolam would induce only an anxiolytic effect and so effectively control high BP during dental treatment. According to previous reports,[3,5] an anxiolytic effect can be induced at a dose of 0.02-0.04 mg/kg. We have therefore evaluated the effect of a low dose of midazolam (0.02 mg/kg) on high BP, level of sedation, and anxiety in dental patients.

Methods

The study was designed as a randomised, parallel-group trial and was done at two centres (Okayama University Hospital and a private dental clinic) after approval by the Ethics Committee of Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences.

Eligibility of patients

Dental patients 18-64 years old who were listed for oral surgery or dental treatment and agreed to participate in this study were enrolled. Before enrollment, baseline cardiovascular and respiratory variables were measured. After the patient entered the outpatient operating theatre and had rested in a sitting position for at least five minutes, systolic and diastolic BP, mean arterial blood pressure (MAP), heart rate (HR), and arterial oxygen saturation (SpO_2) were measured with automated monitoring equipment (BSM-2301, Nihon Kohden, Tokyo, Japan). BP was measured at one-minute intervals according to the recommendation of the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure.[6] If the difference in systolic pressure was more than 5 mmHg on two occasions, additional measurements were taken until the difference was reduced to ≤5 mmHg, and the mean of the two lowest measurements was defined as the baseline BP. After baseline BP had been evaluated, subjects whose baseline BP was ≥140/ ≥90 mmHg, were defined as "patients with high BP".

Exclusion criteria were: uncontrolled or unstable hypertension, secondary hypertension caused by hyperthyroidism or pheochromocytoma, the use of sympathomimetic drugs, any contraindication to midazolam, pregnant or lactating women, and a psychiatric disorder (such as schizophrenia). The details of the protocol were explained, and written consent was obtained from each patient.

Protocol of the study

The protocol of the present study is shown in Fig. 1. After the patient had rested quietly for at least 10 minutes on a dental chair, baseline vital signs (BP, HR, and SpO_2) were recorded and anxiety assessed. They were then randomly allocated to have an injection of either low-dose midazolam (trial group) or physiological saline (control group). A venous line was placed in the upper arm with a 22-gauge intravenous catheter. Patients in the trial group were given midazolam (Dormicum®, Astellas Pharma, Tokyo, Japan) 0.02 mg/kg intravenously over 30 seconds. Patients in the control group were given an equal volume of physiological saline. Patients stayed in a sitting position and awake throughout the study. BP, HR, and SpO_2 were measured every two minutes until 10 minutes after the injection. Ten minutes later, anxiety was reassessed by self-reporting, and sedation assessed by the attending anaesthetist.

Outcome measures

The primary outcome measures were BP and category of BP 10 minutes after the injection of midazolam or physiological saline. The categories of BP were: clinically acceptable BP (<140 /<90 mmHg} or unacceptable BP (≥140/ ≥90 mmHg). HR and SpO_2 were also monitored. Secondary outcome measures were: visual analogue scale (VAS) for anxiety related to dental treatment, Japanese version of the Spielberger's State-Trait Anxiety Inventory (STAI), and Ramsay Sedation Score.[7] There were no changes to the outcomes after the trial began.

Size of sample

Based on a preliminary study, there was a mean (SD) reduction in systolic BP of 10 (7.5) % from baseline to 10 minutes after the injection of midazolam or physiological saline. Considering a β error of 5%, an α error of 5%, and 20% of patients lost to follow-up, the optimal sample to detect a 10 (7.5)% difference in drop in BP between the groups was 20 in each group.