SUMMARY

Midazolam was used for anaesthesia in 20 patients undergoing cardioversion; 10 received flumazenil, which caused immediate rapid reversal of anaesthesia, and these patients maintained $\text{SpO}_2$ greater than 95%, breathing air, within 5–10 min. In contrast, patients in the placebo group were still partially sedated and required oxygen therapy for up to 2 h to maintain a normal $\text{SpO}_2$. Arterial pressure, but not heart rate, also was greater in the flumazenil group in the recovery period.

KEY WORDS


Barbiturates, etomidate and propofol are used for anaesthesia during cardioversion where the use of benzodiazepines could be advantageous in terms of haemodynamic stability [1] and their effect on the myocardium [2, 3]. The relatively prolonged recovery after benzodiazepines, including midazolam, can now be terminated with flumazenil and this technique has been investigated in this study.

METHODS AND RESULTS

We studied 20 patients with atrial tachyarrhythmia. Exclusion criteria included chronic benzodiazepine medication, epilepsy, digoxin toxicity or electrolyte imbalance. No premedication was given. An 18-gauge cannula was inserted into a forearm vein; mean arterial pressure (MAP), $\text{SpO}_2$ and ECG (including Holter analysis) were recorded. After preoxygenation, anaesthesia was induced with incremental doses of midazolam (0.1 mg $\text{kg}^{-1}$ followed by doses of 0.05 mg $\text{kg}^{-1}$) i.v. and cardioversion performed. Using random numbers, patients were allocated to two groups in a double blind design: group I received flumazenil 1 mg (diluted to 10 ml with 0.9% saline) i.v. and cardioversion performed. Using random numbers, patients were allocated to two groups in a double blind design: group I received flumazenil 1 mg (diluted to 10 ml with 0.9% saline) i.v. over 2 min after cardioversion and group II received 10 ml 0.9% saline i.v. over 2 min.

During recovery, sedation was assessed as follows: 1 = roused only by pain; 2 = not roused by voice but roused by mild physical stimulation; 3 = mild drowsiness, sleeping intermittently, easily roused by voice; 4 = slight drowsiness, awake and fully orientated; 5 = fully alert, orientated, no evidence of drowsiness.

Patients recovered in the left lateral position until awake, and additional airway support was provided as necessary with a Guedel airway and jaw support. Oxygen 4 litre $\text{min}^{-1}$ was administered via a Hudson mask until $\text{SpO}_2$ > 95% was maintained breathing air; this was assessed at 5-min intervals by withdrawal of oxygen therapy; if $\text{SpO}_2$ decreased to less than 95%, therapy was restarted.

The results are expressed as mean (SD) or median (range) in the text, and as mean (SE) in figure 1. Significance was assessed by unpaired Student's $t$ or Mann–Whitney $U$ tests.

Five patients in each group had atrial fibrillation and five had atrial flutter.

There was no significant difference between groups I and II, respectively, in age (61.6 (51–76) yr and 63.9 (42–79) yr), weight (71.3 (13.2) kg and 71.2 (9.7) kg), mean dose of midazolam (11.9 (3.2) mg and 13.9 (3.8) mg), duration of procedure (8.8 (3.1) min and 9.1 (2.5) min), MAP before induction (105 (16.3) mm Hg and 98.1 (11.8) mm Hg), heart rate before induction (109 (34) beat min$^{-1}$ and 105 (24) beat min$^{-1}$), number of shocks (2.0 (0.9) and 2.3 (0.9)) or current drug therapy. Cardioversion was successful in all patients in the flumazenil group and in nine of those receiving placebo.

Flumazenil caused immediate reversal of the sedative effects of midazolam and, compared with placebo, sedation scores were significantly greater up to 90 min. By 2 h there was no significant difference between the groups (fig. 1).

Median $\text{SpO}_2$ before induction in groups I and II breathing air was 92 (88–96)% and 93 (87–97)% respectively. The median times to removal of oxygen therapy (i.e. to $\text{SpO}_2 > 95\%$ breathing air) after the procedure were 8 min and 100 min in the flumazenil and placebo groups, respectively ($P < 0.005$).

There were significant reductions in heart rate and MAP after cardioversion (fig. 1). There was no
significant difference in heart rate between the groups during recovery, but the MAP was significantly less in the placebo group for up to 1 h. After cardioversion, the incidence of ventricular or supraventricular ectopic beats was very low and distributed randomly in time without relationship to d.c. shock or administration of flumazenil (ns between groups).

**COMMENT**

This study is the first specific report of the use of midazolam, reversed with flumazenil, for anaesthesia for cardioversion. It confirms the suitability of midazolam, reversed with flumazenil, for sedation in patients with heart disease undergoing diagnostic and therapeutic procedures on the cardiovascular system [2] and suggests that it is a suitable anaesthetic technique for cardioversion.

Gamma-aminobutyric acid(A) and benzodiazepine receptors have been demonstrated in myocardial muscle fibres of experimental animals; stimulation causes changes in action potential duration and contractility [3] which would support the hypothesis that benzodiazepines have potentially beneficial antiarrhythmic effects. Diazepam has been used in the management of arrhythmias associated with chloroquine poisoning [4]. However, although flumazenil has precipitated arrhythmias in benzodiazepine overdose when combined with cardiotoxic drugs such as tricyclic antidepressant drugs and phenytoin, this has not been reported during reversal of acute benzodiazepine administration alone, as was the case in the present study. Arguably, benzodiazepines may be indicated for sedating patients with ischaemic heart disease and co-arrhythmias.

All patients had relatively greater mean arterial pressures before and immediately after cardioversion, which may have been caused not only by anxiety, but also by the nociceptive effects of the electrical stimulus. During recovery, the flumazenil group had a greater MAP compared with placebo, and this may be attributable to the higher state of arousal.

Benzodiazepines cause depression of ventilatory responses to carbon dioxide and hypoxia [5] and, while some authors state that these may not be reversed by flumazenil [5], others have shown an
increase in $\text{Sp}_\text{o}_2$ in patients anaesthetized with benzodiazepines after flumazenil [2].

In the present study, the time to maintenance of a baseline arterial oxygen saturation without oxygen therapy was much shorter in the group who received flumazenil, but the study design did not allow any conclusions regarding the immediate reversal or otherwise of the depressed hypoxic ventilatory drive induced by midazolam.

After midazolam anaesthesia there is either no resedation or the patients return to a drowsy state 30–60 min after the initial arousal by flumazenil; thereafter they recover normally, with the advantage of having been in a safer state during the early part of recovery [2]. This study confirmed that the flumazenil group required less active care during recovery.

Recent work suggests that flumazenil is unlikely to cause an acute abstinence response [6]; however, the response to flumazenil of a myocardium chronically adapted to benzodiazepines is unknown.

REFERENCES