COMPARISON OF THE I.V. ADMINISTRATION OF MIDAZOLAM AND DIAZEPAM AS SEDATION DURING SPINAL ANAESTHESIA

J. H. MCCLURE, D. T. BROWN AND J. A. W. WILDSMITH

SUMMARY
Midazolam hydrochloride and diazepam in emulsion were compared as i.v. sedatives for spinal anaesthesia. Mean doses of midazolam 12 mg and diazepam 27 mg were required to induce sleep and provide good or adequate sedation throughout surgery of approximately 1 h duration. Neither drug caused loss of the airway or significant cardiorespiratory changes. The frequency of drowsiness after operation was greater following sedation with diazepam, but objective testing of recovery with the Trieger test showed no significant difference between the two drugs. The frequency of amnesia was greater following midazolam.

Although regional anaesthesia has many advantages, its use may be limited by the unwillingness of patients to remain awake during surgery. This may be overcome by the induction of light general anaesthesia or by the administration of sedative drugs. Diazepam i.v. is used frequently for this purpose, but it is not ideal. The original formulation, Valium (Roche), may cause pain on injection and late thrombophlebitis (Hegarty and Dundee, 1977). A newer product, Diazemuls (Kabivitrum), is virtually free from these complications (Schou Olesen and Huttel, 1980), but the problem of delayed recovery remains (Baird and Hailey, 1972).

The water-soluble benzodiazepine, midazolam, is shorter acting than diazepam (Brown et al., 1979) and has been proposed as an alternative sedative in the circumstances in which diazepam is used currently (Gamble et al., 1981). Thus, it seemed appropriate to compare the effects of the i.v. administration of midazolam hydrochloride and diazepam (Diazemuls) as sedation during spinal anaesthesia.

PATIENTS AND METHODS
Twenty healthy patients undergoing surgery to the legs or perineum under spinal anaesthesia gave informed consent for the study, and were allocated randomly to receive one of the study drugs as sedation during the procedure. Recovery from sedation was assessed using the Trieger test (Newman, Trieger and Miller, 1969) and a practice test was performed on the day before surgery.

The Trieger test was devised as a simple objective measurement of recovery from general anaesthesia. It consists of a series of dots arranged in a simple pattern which the patient connects by pencil as accurately as possible. The accuracy and timing are compared with a baseline test carried out before sedation. Any decrease in accuracy is measured by recording the number of dots missed and the cumulative distance of miss in mm, compared with the baseline. The patient must be in the same position for all tests and use reading spectacles if these are normally worn.

Patients were premedicated with temazepam 10 mg by mouth 1 h before the induction of anaesthesia. In the anaesthetic room an i.v. cannula (21-gauge Venflon-Viggo) was placed in a vein on the dorsum of a hand, heart rate and arterial pressure were measured and the baseline Trieger test performed. Lumbar puncture was performed in the lateral position at the 3rd interspace and 0.5% plain bupivacaine 4 ml was injected at 1 ml per 5 s. The patients were returned to the supine position and heart rate, arterial pressure and the upper level of blockade (analgesia to pinprick) recorded every 5 min until spread ceased. Respiratory rate was then recorded.

The concentrations of the midazolam solution and the diazepam emulsion were 5 mg ml⁻¹. An initial dose of midazolam 0.1 mg kg⁻¹ or diazepam 0.2 mg kg⁻¹ was injected at 1 ml min⁻¹ via the indwelling cannula, which was not used for any other substance. The nature of the drug used was not known to the observer. Increments of half the initial...
dose were given at the same rate, but with a pause of 1 min between each, until the end-point of sleep, undisturbed by speaking or the measurement of arterial pressure, was reached. Once this end-point was reached, any evidence of airway obstruction was noted and heart rate, arterial pressure and respiratory rate were recorded. Heart rate and arterial pressure were recorded at 10-min intervals during surgery.

Quality of sedation during surgery was graded as "good", "acceptable" or "poor". "Good" meant that the patient lay still throughout surgery; "acceptable" that the patient moved but settled with reassurance and "poor" that the patient required additional i.v. sedation. At the end of surgery the patient's conscious level was noted whilst undisturbed and each patient was then shown a simple picture to test recall later.

Two and three hours after injection of the sedative drug, conscious level was noted again in the undisturbed patient, before heart rate and arterial pressure was measured and a Trieger test performed. The cannula was removed 2 h after the injection of the sedative drug.

On the morning after surgery patients were asked how they felt, the injection site was inspected and recall of the previous day's events tested. One week later they were sent a postcard requesting information on any late venous sequelae.

RESULTS

The physical characteristics of the patients, the duration of surgery and the upper level of spinal blockade are detailed in table I. Mean doses of midazolam 12 mg (the initial dose plus an average of 2.0 increments) and of diazepam 27 mg (the initial dose plus an average of 2.4 increments) were required to induce sleep (table II). Sedation was judged to be good in nine of the 10 midazolam patients and in eight of the 10 patients receiving diazepam. Sedation was considered acceptable in the other patients. Operations lasted between 45 and 75 min and no patient required additional sedation after the initial doses.

At the end of surgery two midazolam patients were wide awake, seven were drowsy and one was asleep although rousable. In the diazepam group one patient was wide awake, five were drowsy and four were asleep, although rousable. Subsequently, more patients were awake sooner in the midazolam group (fig. 1). The results of the Trieger tests are shown in table III and are expressed as the change from the baseline reading. In both groups there were marked changes from baseline at 2 h and only small changes at 3 h after sedation. There were no statistically significant differences between the groups.

<table>
<thead>
<tr>
<th>TABLE I. Patient characteristics (mean ± SEM)</th>
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<tr>
<td>Age (yr)</td>
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<td>Weight (kg)</td>
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<td>Height (cm)</td>
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<tr>
<td>Duration of surgery (min)</td>
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<td>Level of blockade (dermatome)</td>
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<table>
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<tr>
<th>TABLE II. Dosage (mean ± SEM)</th>
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<tr>
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<tr>
<td>Initial dose (mg)</td>
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<td>Number of increments</td>
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<td>Total dose (mg)</td>
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FIG. 1. Observed condition after operation. Black columns = asleep but rousable; stippled columns = drowsy; open columns = wide awake.
The mean circulatory changes are shown in figure 2. There were small decreases in mean systolic arterial pressure and small increases in mean heart rate after both administration of the spinal anaesthetic and either sedative drug. Respiratory rate increased from 16.5±1.2 b.p.m. (mean±SEM) to 18.6±1.2 b.p.m. after midazolam and increased from 15.6±1.1 b.p.m. to 17.5±1.9 b.p.m. after diazepam. These differences were not significant. No patient showed evidence of airway obstruction after either drug.

On the morning after surgery all the patients felt normal, except for one in the diazepam group who felt "distinctly hungover". All patients remembered the lumbar puncture and the start of the sedative injection. More patients recalled events during and immediately following surgery in the diazepam group (table IV).

No patient had any pain at the time of, or subsequent to, the injection of the sedative drug. One midazolam patient had 3 cm of erythema along the course of the vein on the dorsum of the hand on the day after injection and another in the midazolam group noted a small painless swelling on day 7.
**TABLE IV. Number of patients recalling events after sedation.**

<table>
<thead>
<tr>
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<th>Midazolam</th>
<th>Diazepam</th>
<th>(P^*)</th>
</tr>
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<tbody>
<tr>
<td>During operation</td>
<td>1</td>
<td>5</td>
<td>0.14</td>
</tr>
<tr>
<td>Picture at end</td>
<td>0</td>
<td>5</td>
<td>0.03</td>
</tr>
<tr>
<td>Return to ward</td>
<td>2</td>
<td>7</td>
<td>0.07</td>
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</table>

All patients would be happy to have the same anaesthetic technique again.

**DISCUSSION**

The ideal sedative drug, suitable for use during regional anaesthesia, should produce reliable sedation or sleep with maintenance of the airway. There should be minimal effects on circulation and respiration and recovery should be rapid with no residual drowsiness.

This study has shown that both drugs produce effective sedation during spinal anaesthesia. Neither drug produced clinically significant effects on heart rate, arterial pressure or respiratory rate. In this study no patient showed evidence of airway obstruction.

More undisturbed patients were observed to be awake at the end of surgery and at both 2 and 3 h after receiving midazolam than after diazepam. However, amnesia was more frequent after midazolam, an effect that has been observed in dental practice (Kawar et al., 1982). Recovery, assessed by the Triegar test up to 3 h after sedation, was similar with both drugs. The Triegar test was chosen to assess recovery objectively as it is a practicable test of recovery which may be performed by the supine patient following spinal anaesthesia.

Although patients were observed to be more alert following midazolam, the Triegar test failed to show any significant difference in recovery between these two drugs. This may have been because of the small number of patients studied or the Triegar test may not be sensitive enough to detect small differences between the two drugs. Testing may not have been carried out for a sufficient length of time to detect possible remobilization of drug or appearance of active metabolites, both of which have been observed with diazepam (Baird and Hailey, 1972). Premedication with temazepam may also have affected recovery in each group. Premedication was considered necessary, as a pilot study using unpremedicated patients resulted in an unacceptable frequency of vasovagal attacks following lumbar puncture.

It is notable that the mean total dosage (0.19 mg kg\(^{-1}\)) of midazolam was greater than that used by Kawar and associates (1982) in dentistry (0.09 mg kg\(^{-1}\)) and by Al-Khudairi, Whitwam, and McClory (1982) in gastroscopy (0.1 mg kg\(^{-1}\)). However, our requirements were for more heavily sedated patients whose co-operation was not essential during the operation.

No patient in either group demonstrated clinically significant venous sequelae secondary to the i.v. injection.

Midazolam is a suitable alternative to diazepam as sedation during regional anaesthesia and the greater frequency of profound amnesia offers a distinct advantage.

**ACKNOWLEDGEMENTS**

We wish to acknowledge Roche Products Ltd for their advice and the supply of midazolam and Mr R. I. Harris who helped in the statistical analysis.

**REFERENCES**


COMPARAIION ENTRE L'ADMINISTRATION INTRA VENNEUSE DE MIDAZOLAM ET DE DIAZEPAM POUR LA SEDATION AU COURS DE L'ANESTHESIE RACHIDIENNE

RESUME
Le chlorhydrate de midazolam i.v. et le diazepam en émulsion i.v. ont été comparés pour leurs propriétés sédatives au cours de l'anesthésie rachidienne. Des doses moyennes de 12 mg de midazolam et de 27 mg de diazepam ont été nécessaires pour entraîner la perte de connaissance et fournir une sédation bonne ou très bonne pendant un acte chirurgical durant environ 1 heure. Aucun des deux produits n’a provoqué une obstruction des voies aériennes ou des modifications cardio-respiratoires importantes. La fréquence de la somnolence post-opératoire était plus grande lors de l'utilisation du diazépam mais une étude objective du réveil par le test de Trieger ne montrait pas de différences significatives entre les deux agents. La fréquence de l’amnésie était plus grande avec le midazolam.

VERGLEICH ZWISCHEN INTRAVENÖSER GABE VON MIDAZOLAM UND DIAZEPAM ALS SEDATIVUM WÄHREND SPINALANÄSTHESIE

ZUSAMMENFASSUNG

COMPARACION DE LA ADMINISTRACION INTRAVENOSA DE MIDAZOLAM Y DE DIAZEPAM COMO SEDANTES DURANTE LA ANESTESIA DE LA ESPINA DORSAL

SUMARIO
Se compararon el hidrocloruro de midazolam y una emulsión de diazepam como sedantes de administración intravenosa para fines de anestesia de la espina dorsal. Fueron necesarias dosis medias de 12 mg de midazolam y 27 mg de diazepam para la inducción del sueño y para producir una sedación adecuada o conveniente durante la intervención quirúrgica de 1 h de duración aproximadamente. Ninguna de las drogas causó pérdida alguna en el conducto de aire ni cambio cardiorespiratorio significativo. La frecuencia de la somnolencia después de la operación fue superior a raíz del uso de diazepam, pero la comprobación objetiva de la recuperación siguiendo la prueba Trieger no mostró diferencia significativa alguna entre las dos drogas. La frecuencia de la amnésia fue superior a raíz del midazolam.