PREOPERATIVE MEDICATION FOR DAY-CASE SURGERY
A Comparison Between Oxazepam and Temazepam

B. K. GREENWOOD AND E. G. BRADSHAW

SUMMARY
The effects of temazepam 20 mg, oxazepam 30 mg and placebo were compared when given as preoperative medication to patients undergoing day-case surgery. Temazepam caused a significant decrease in anxiety and produced sedation by 60 min, whereas those patients receiving oxazepam showed only minimal changes. Awakening time was prolonged with oxazepam but not with temazepam. Two hours after surgery, no significant sedation was recorded with either drug, and simple psychomotor testing showed unimpaired performance. Patient acceptability was high with both oxazepam and temazepam.

The majority of patients entering hospital for surgery are anxious or afraid (Norris and Baird, 1967; Ramsey, 1972; Leigh, Walker and Janaganathan, 1977) and benefit from preoperative medication. Rapid recovery and a swift return to street fitness are essential in the day-case surgery (DCS) unit (Ogg et al., 1979). However, there is often a reluctance to give preoperative medications in these units as the regimens used commonly for inpatients are long-acting and delay awakening (Adams, 1980).

This trial was designed to compare the usefulness of two short-acting derivatives of diazepam—temazepam and oxazepam. Both are rapidly metabolized, almost exclusively by conjugation (Alván, Siwers and Vessman, 1977; Fucella et at., 1977), and in contrast to diazepam, their metabolites have no pharmacological action.

PATIENTS AND METHODS
A double-blind, between-patient trial was designed to include 72 DCS patients between the ages of 16 and 65 yr. All patients were in ASA categories I or II and were not receiving concurrent psychotropic medication. The operations performed were mainly minor orthopaedic, ENT and general and genito-urinary surgery.

After giving informed consent, the patients were randomly allocated to one of three groups. All patients received a similar soft gelatin capsule 1 h before the estimated time of operation. Group A received temazepam 20 mg, group B oxazepam 30 mg and group C placebo.

Immediately before the ingestion of the capsule (time 0), and after careful explanation, patients were asked to complete three simple tests: The Weschler Digit Symbol Substitution Test (DSST) was used (Weschler, 1944) to quantify psychomotor performance. Patients were asked to complete, as far as possible, a standardized DSST and the total number of correct responses in 60 s was scored (the score at time 0 was taken as a control value, and improvement or impairment in ability was recorded). Self-assessed anxiety and sedation were scored separately using the 100-mm visual linear analogue scale (LAS), and the distance in mm from zero anxiety and zero sedation was noted.

These three tests were repeated 30 min and 60 min after the ingestion of the capsule, the only change being that the code of symbols corresponding to digits for the DSST was rearranged to avoid any effect of medium-term memory.

General anaesthesia was induced with Althesin 3.0–5.0 ml preceded by fentanyl 1 μg kg⁻¹ and maintained with 70% nitrous oxide and 1.5% halothane in oxygen via a Penlon Bain coaxial circuit.

Following the operation the time to the first correct response by the patient to a given command (time to correct response (TCR)) (Cormack, 1979) was recorded. At TCR + 1 h and TCR + 2 h, sedation level and psychomotor performance were assessed as before. Heart rate, arterial pressure and respiratory rate were recorded before the administration of the capsule, before the induction of anae-
thesia, and on arrival in the recovery room. Interval times for preoperative medication to operation, and cessation of anaesthesia to TCR were recorded, as was the duration of the operation.

Untoward events attributed to the induction of anaesthesia were noted, as were any side-effects observed in the period after operation. Immediately before discharge, patients were asked if the capsules taken had been of value and, if so, to what extent. Results were analysed using Students t test and Chi squared test with Yates' correction factor.

RESULTS

There were no significant differences between the three groups of patients in respect of sex, age and weight (table I).

The time from the administration of the preoperative medication to the induction of anaesthesia was similar in the three groups, as was the duration of operation, but the time from the end of anaesthesia to the time of the first correct response (TCR) was significantly longer with oxazepam (P<0.05) (table II).

The mean anxiety scores are shown in figure 1. Temazepam produced a significant degree of anxiolysis at 60 min after the administration of the capsule (P<0.01), but oxazepam had little effect.

Significant sedation was produced by temazepam at 30 min (P<0.01) and more so at 60 min (P<0.001), whereas oxazepam produced minimal changes (fig. 2). At TCR+120 min neither drug produced significant sedation when compared with placebo.

Patients given temazepam demonstrated an unchanged (+0.05±0.9) score in the DSST at 30 min and a decreased score (−1.81±0.82) at 60 min. This represents impaired ability (P<0.05) to do this test as the corresponding placebo group scores were +3.26±0.82 and +2.87±0.78, respectively. Oxazepam produced no changes significantly different from placebo in this test.

Systolic arterial pressure, heart rate and respiratory rate measured on admission, at induction and on recovery (TCR) showed no significant differences between the groups.

The frequency of untoward events, such as hiccups, cough, bronchospasm and muscle movement associated with the induction of anaesthesia did not vary significantly between the groups. The commonest side-effect in the postoperative period (table III) was headache, particularly in the placebo group (50%). The frequency was decreased in the temazepam group (25%) and decreased significantly in the oxazepam group (17%) (P<0.05). There were no differences in the frequencies of nausea or dizziness between the three groups.

Significantly more patients in the oxazepam group (18 of 24) and temazepam group (22 of 24) compared with placebo group (nine of 24) felt that the preoperative medication had been of help (P<0.05 and P<0.005, respectively).

<table>
<thead>
<tr>
<th>Group</th>
<th>Pre-med. to op.</th>
<th>Duration of operation</th>
<th>End of anaesthesia to TCR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxazepam 30 mg</td>
<td>86.3±5.5</td>
<td>20.1±2.1</td>
<td>5.9±1.3**</td>
</tr>
<tr>
<td>Temazepam 20 mg</td>
<td>89.1±3.4</td>
<td>18.7±2.1</td>
<td>3.2±0.7</td>
</tr>
<tr>
<td>Placebo</td>
<td>89.4±5.3</td>
<td>17.7±1.7</td>
<td>2.6±0.5</td>
</tr>
</tbody>
</table>

**Significantly prolonged recovery (P<0.05) compared with placebo.

TABLE I. Patient distribution, sex, age and weight

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>M</th>
<th>F</th>
<th>Mean age (yr)</th>
<th>Mean weight (kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxazepam 30 mg</td>
<td>24</td>
<td>14</td>
<td>10</td>
<td>39.8±3.2</td>
<td>65.9±2.3</td>
</tr>
<tr>
<td>Temazepam 20 mg</td>
<td>24</td>
<td>12</td>
<td>12</td>
<td>39.5±2.7</td>
<td>66.5±2.4</td>
</tr>
<tr>
<td>Placebo</td>
<td>24</td>
<td>11</td>
<td>13</td>
<td>37.4±2.7</td>
<td>67.5±2.0</td>
</tr>
</tbody>
</table>

FIG. 1. Mean anxiety score.
DISCUSSION

Although there are difficulties associated with the measurement of anxiety and sedation before operation (Dundee, Moore and Nicholl, 1962; Norris, 1969), Maxwell (1978) suggested that the linear analogue scale (LAS) can provide a relatively sensitive assessment of these subjective phenomena.

The results of our temazepam series were comparable to those of Beechey, Eltringham and Studd, (1981) who showed significant anxiolysis and sedation before surgery without prolonged recovery. Amarasekera (1980) demonstrated that temazepam provided more anxiolysis and sedation than diazepam, with a high degree of patient acceptability. This latter finding was in agreement with our results.

Patients taking oxazepam experienced little sedation or anxiolysis at 60 min. As the time to mean peak serum concentration is 114 min (Wretlind et al., 1977), this result might seem predictable. However, Bellantuono and colleagues (1980) state that there is no existing evidence correlating plasma concentrations of benzodiazepines and their clinical response and this was reaffirmed by Tansella and colleagues (1978) in a carefully controlled multiple-dose study.

One of the most sensitive tests of psychomotor performance is the DSST (Wittenborn, 1979). Hart and co-workers (1976) concluded that the complex mental functions involved in DSST appear to be particularly sensitive to the effects of benzodiazepines. The test is useful in the clinical situation in that it does not require any specialized equipment other than the appropriate test sheets. It is easily understood and takes little time to perform. In addition it reflects an element of visuo-motor performance.

Nicholson (1979), in a volunteer study without the stress of operation, compared visuo-motor performance after temazepam and oxazepam. He found impaired performance at 30 min and 60 min with temazepam, but not with oxazepam. At 4.5 h performance was impaired with oxazepam, but not with temazepam. This is in broad agreement with our study except that we did not find the depression of performance produced by oxazepam following surgery, to be significant. In common with other

<table>
<thead>
<tr>
<th>Group</th>
<th>Headache</th>
<th>Nausea</th>
<th>Dizziness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxazepam 30 mg</td>
<td>4** (17%)</td>
<td>2 (8%)</td>
<td>2 (8%)</td>
</tr>
<tr>
<td>Temazepam 20 mg</td>
<td>6 (25%)</td>
<td>2 (8%)</td>
<td>3 (12%)</td>
</tr>
<tr>
<td>Placebo</td>
<td>12 (50%)</td>
<td>4 (17%)</td>
<td>4 (17%)</td>
</tr>
<tr>
<td>Total</td>
<td>22 (31%)</td>
<td>8 (11%)</td>
<td>9 (12%)</td>
</tr>
</tbody>
</table>
investigators (Beechey, Eltringham and Studd, 1981) the frequency of postoperative sequelae was decreased in the temazepam group. This decrease was even greater in the oxazepam group, particularly where headache was considered.

The patient acceptability of temazepam was highly significant, reaffirming the results of Amarasekera (1980). The acceptability of oxazepam was also significant, but this is surprising since there was little anxiolysis measured before operation. A possible explanation for this might be that, although testing was done at 60 min, the mean time to operation was 86 min. In consideration of the mean time to peak plasma concentration (114 min), the patients may well have been experiencing anxiolysis after the test time but before operation. It may be that administration of oxazepam 1.5–2 h before the operation would produce better effects, but this is usually impractical for day-case surgery.

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REFERENCES


PREMEDICATION EN CHIRURGIE AMBULATOIRE

Comparaison Entre Oxazepam et Temazepam

Nous avons comparé les effets du temazepam 20 mg, de l'oxazepam 30 mg, et d'un placebo administrés comme agents de prémédication à des patients subissant des actes de chirurgie ambulatoire. Le temazepam entraînait une diminution significative de l'anxiété et produisait une sédation en 60 min alors que les patients recevant de l'oxazepam n'étaient que peu touchés. Le temps de réveil était prolongé avec l'oxazepam mais pas avec le temazepam. Deux heures après la chirurgie, on ne retrouvait de somnolence décelable avec aucun des agents et des tests psychomoteurs simples objectivaient des performances normales. Le degré de coopération des patients était bon avec l'un ou l'autre agent.
PRÄOPERATIVE MEDIKATION FÜR AMBULANTE CHIRURGIE

Vergleich zwischen oxazepam und temazepam

ZUSAMMENFASSUNG


MEDICACION PREOPERATIVA PARA LA INTERVENCIÓN QUIRURJICA DE PACIENTES EXTERNOS:

un estudio comparativo entre el oxazepam el temazepam

SUMARIO

Se compararon los efectos de 20 mg de temazepam, 30 mg de oxazepam y de placebos al administrarse como medicación preoperatoria a pacientes externos sometidos a intervención quirúrgica. Temazepam causó una disminución significativa de la ansiedad y produjo sedación durante 60 minutos, mientras que aquellos pacientes que recibieron oxazepam mostraron tan sólo cambios mínimos. El periodo de tiempo hasta el despertar se prolongó con el oxazepam pero no con el temazepam. Dos horas después de la intervención quirúrgica no se registró sedación significativa alguna con ninguna de las drogas y una sencilla prueba sicomotora mostró que el rendimiento no se había visto afectado. La aceptabilidad del paciente fue alta tanto para el oxazepam como para el temazepam.