

## PREMEDICATION BEFORE DAY SURGERY

### *A Double-Blind Comparison of Diazepam and Placebo*

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The benzodiazepines are used widely as premedication in patients before surgery (Kangas, Kanto and Mansikka, 1977; Korttila et al., 1978; Kanto, Kangas and Mansikka, 1979; Studd and Eltringham, 1980). The absorption of orally administered diazepam is rapid and its duration of action relatively long. Indeed, premedication with diazepam may have certain advantages over premedication with chlordiazepoxide, morphine, promethazine and placebo. In particular, its sedative effects, when weighed against the side-effects, were better than those of the other agents (Haslett and Dundee, 1968) and an anxiolytic effect, without concurrent troublesome drowsiness, has been documented (Dundee and Haslett, 1970).

At Frederiksborg County Hospital, Hørsholm, Denmark, approximately 40% of the elective surgery is performed on an outpatient basis. Thus, it is important that any drugs given to patients undergoing such surgery do not influence the patient's condition after surgery. The present investigation examined the need for premedication before outpatient surgery and its influence on the general condition of the patient after surgery.

#### PATIENTS AND METHODS

The study was conducted as a double-blind, randomized investigation in which diazepam (tablets: Apozepam, AL-pharma, Copenhagen) 0.25 mg kg<sup>-1</sup> was compared with placebo.

Patients admitted to the day-unit for minor surgical procedures such as hernia repair, treatment of

#### SUMMARY

*Premedication with diazepam 0.25 mg kg<sup>-1</sup> by mouth was compared with placebo in a double-blind trial in patients undergoing day-case surgery under general anaesthesia. Diazepam decreased significantly preoperative discomfort and apprehension. The patients were discharged on time regardless of the type of premedication, and complaints at the time of discharge and on the following day could be related only to the length of anaesthesia and not to the type of premedication. Premedication given early in the morning remained effective for up to 6 h.*

varicose veins, excision of benign breast tumours, dilatation and curettage (D and C), laparoscopic sterilization, endoscopy and minor orthopaedic operations were studied.

Before admission a physical examination was performed and informed consent obtained. Each patient fulfilled the following criteria for inclusion in the study:

- (1) Age 15–60 yr
- (2) Weight > 40 kg
- (3) No concurrent psychoactive drug therapy
- (4) No abuse of alcohol
- (5) Healthy apart from the condition requiring surgical intervention

Only patients receiving general anaesthesia were included. Premedication was given at 08.00 h on the day of the operation, regardless of the time of surgery. Operations were, as far as possible, completed during the morning so that the patient could be discharged the same evening.

One of three techniques of anaesthesia was used:

- (1) Induction: Thiopentone i.v.
- Maintenance: Oxygen–nitrous oxide inhalation,

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possibly supplemented by thiopentone i.v.  
(2) Induction: Thiopentone i.v.  
Maintenance: Oxygen–nitrous oxide–halothane by inhalation.

(3) Induction: Thiopentone i.v.  
Maintenance: Oxygen–nitrous oxide–halothane by inhalation plus myoneural blockade.

In some patients, atropine and fentanyl were given i.v. if deemed necessary.

Data were collated on two forms: one was filled in by the anaesthetist immediately before induction of anaesthesia and contained the following questions:

(a) "Does the patient present any of the following symptoms: Paleness, perspiration, cold extremities, dry mouth, slurred speech, emesis or vomiting?"

Each question to be answered with a "yes" or a "no".

(b) "Is the patient in a satisfactorily non-apprehensive state?"

On the basis of the answers to question (a), question (b) was answered. Only lack of all the first four symptoms mentioned, was recorded as a non-apprehensive state.

The same evening, an estimate of the patient's general condition was obtained. To be considered fit for discharge, the patient had to fulfil the following criteria:

- (1) Fully awake.
- (2) In the upright position without discomfort.
- (3) Willing to go home.
- (4) Under observation by a responsible adult during the night at home.
- (5) Transported home by a second person.

The estimate of the patient's general condition was made as follows:

- (c) 1. Patient unaffected by anaesthesia, discharge recommended.  
2. Patient slightly affected by anaesthesia, discharge recommended.  
3. Patient very affected by anaesthesia, discharge not recommended.

At the time of discharge a second form (table I) was given to the patient, who was asked not to read the questions until the following day.

The chi-square test was used for the statistical evaluation; the level for a significant difference was taken as  $P = 0.05$ .

#### RESULTS

The study comprised 202 patients: 104 (85 women) were premedicated with diazepam and 98 (82

TABLE I. *Discharge questionnaire*

- (a) "Did you have any alcohol, wine or beer on the evening before the operation? If 'yes', please specify."
- (b) "Did you have any tranquilizer or hypnotic on the evening before the operation? If 'yes', please specify."
- (c) "Did you experience the stay in the ward, before the operation, but after you had your premedication as  
1. unpleasant?  
2. not unpleasant?  
3. do not remember?"
- (d) "Did you experience the stay in the operating room as  
1. unpleasant?  
2. not unpleasant?  
3. do not remember?"
- (e) "In case of any discomfort experienced, did this discomfort consist of  
1. nausea?  
2. vomiting?  
3. headache?  
4. dizziness?  
5. palpitations?  
6. tiredness?  
7. apprehension?  
8. excitement?"
- (f) "Did you experience any discomfort while waking up from the anaesthesia?"
- (g) "At the time of discharge, did you experience any discomfort like  
1. drowsiness?  
2. tiredness?  
3. headache?  
4. nausea?  
5. vomiting?  
6. dizziness?  
7. reduced power of concentration?"
- (h) "The day after the operation, did you experience any of the following symptoms:  
1. drowsiness?  
2. tiredness?  
3. headache?  
4. nausea?  
5. vomiting?  
6. dizziness?  
7. reduced power of concentration?"

women) received placebo.

The randomization was tested by means of the Mann–Whitney rank sum test and was found to be satisfactory. The two test groups were comparable with regard to age, sex, weight, length of anaesthesia, type of anaesthesia and type of surgical intervention.

#### Observations before surgery on the day of operation

Diazepam was superior to placebo in that it decreased preoperative fear and anxiety. No sig-

TABLE II. Numbers of patients experiencing preoperative discomfort

Type of discomfort	Diazepam (n=104)	Placebo (n=98)	P
Anxiety	10	31	<0.005
Fear	3	10	<0.05
Tiredness	9	5	ns
Headache	3	8	ns
Dizziness	5	2	ns
Nausea	1	3	ns
Vomiting	0	0	ns
Difficulty concentrating	1	0	ns
Chills	0	2	ns
Dyspnoea/feeling of oppression	1	0	ns
Total number of patients experiencing discomfort	20	41	<0.0005

nificant difference in symptoms such as tiredness, headache, dizziness, nausea and vomiting was seen between the two groups (table II). One patient premedicated with diazepam complained of dyspnoea and a feeling of oppression. She had experienced similar symptoms previously, after taking diazepam. This was the only patient experiencing unforeseen effects from the medication. The operation was performed as planned, and the patient was discharged in a satisfactory condition.

The surgical procedures performed and the number of patients with preoperative discomfort related to type of operation are shown in table III.

From the anaesthetist's evaluation of the degree of sedation before operation, those who had received diazepam were significantly less apprehensive. The combination "subjectively satisfied patient"/"objectively non-apprehensive patient" was found significantly more frequently in those who had received diazepam (table IV).

The preoperative waiting time was the same in both groups. Among those patients experiencing subjective discomfort and inadequate sedation, the number of patients who waited a short time, a medium period of time and a long time (maximum 6 h) did not deviate significantly from the expected.

#### Observations after surgery on the day of operation

The number of patients who experienced discomfort while waking up from anaesthesia did not differ significantly between the two groups. In particular, no increase in amnesia was recorded after diazepam. The patients experiencing discomfort could not be characterized with regard to type of operation per-

TABLE III. The number of patients undergoing the various surgical procedures. (Number of patients claiming preoperative discomfort)

Type of operation	Diazepam (n=104(20))	Placebo (n=98(41))
Abortion	38(8)	39(17)
Laparoscopic sterilization	15(5)	10(5)
Dilatation and curettage	11(3)	12(4)
Operation for varicose veins	11(1)	11(4)
Operation for inguinal hernia	11(1)	7
Minor orthopaedic surgery	7(1)	10(3)
Operation for mammary tumour	8(1)	3(2)
Others	3	6(6)

formed, or the technique or duration of anaesthesia.

The number of patients discharged "objectively unaffected, on time" did not differ significantly when the two groups were compared and the duration of anaesthesia was taken into account. A significant increase in the number of patients who were discharged "slightly affected, on time" was found among those who had been anaesthetized for more than 45 min (fig. 1).

Only two patients were not discharged on time. One patient in the diazepam group who had undergone laparoscopic sterilization had to be transferred to the ward because of pain and vomiting. One patient in the placebo group could not be discharged because of pain after an operation for epicondylitis lateralis humeri.

At the time of discharge, the number of patients with complaints was not significantly different in the two groups. Based on the patient's own evaluation, no relationship between duration of anaesthesia and discomfort experienced could be shown (fig. 2).

#### The day after operation

There was no significant difference between the

TABLE IV. Evaluation of the degree of sedation before surgery

	Diazepam (n=104)	Placebo (n=98)	P
Anaesthetist's evaluation			
Number of non-apprehensive patients	83	55	<0.005
Combined evaluation by the patient and the anaesthetist			
Both satisfied	71	37	<0.0005
Both dissatisfied	8	23	<0.005
One satisfied, one dissatisfied	25	38	<0.05

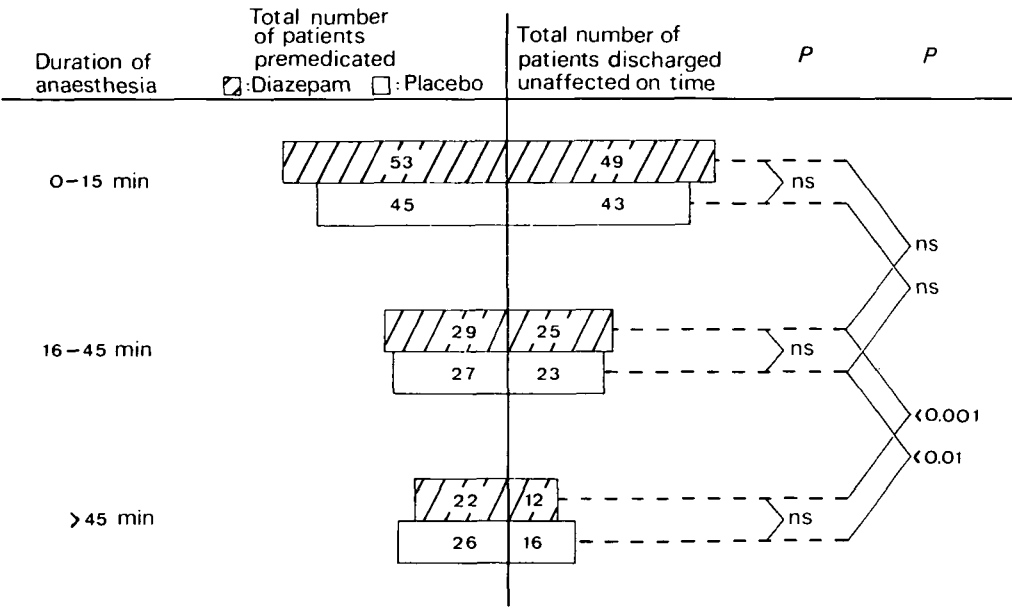


FIG. 1. Number of patients discharged *objectively* unaffected, on time.

patients treated with diazepam or placebo (fig. 3). All patients anaesthetized for less than 15 min received anaesthetic technique 1, while those anaesthetized for longer than 15 min received anaesthetic techniques 2 or 3.

In the diazepam and the placebo groups, 67 and 69 of the patients, respectively, received fentanyl 0.05-0.15 mg during anaesthesia. No difference in fentanyl dosage between subgroups (e.g. short or long anaesthesia) or relationship between fentanyl

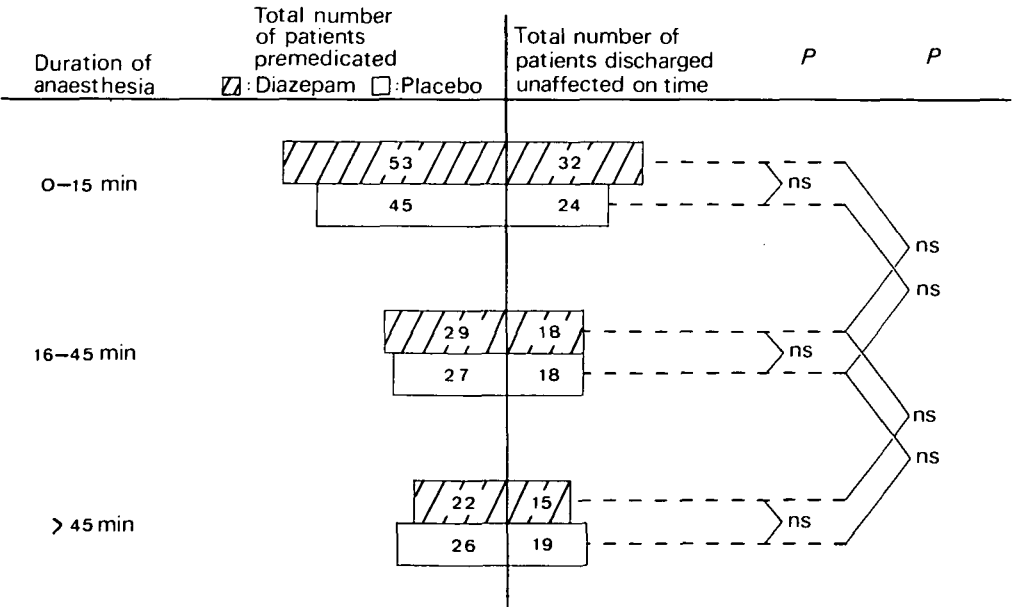


FIG. 2. Number of patients discharged *subjectively* unaffected, on time.

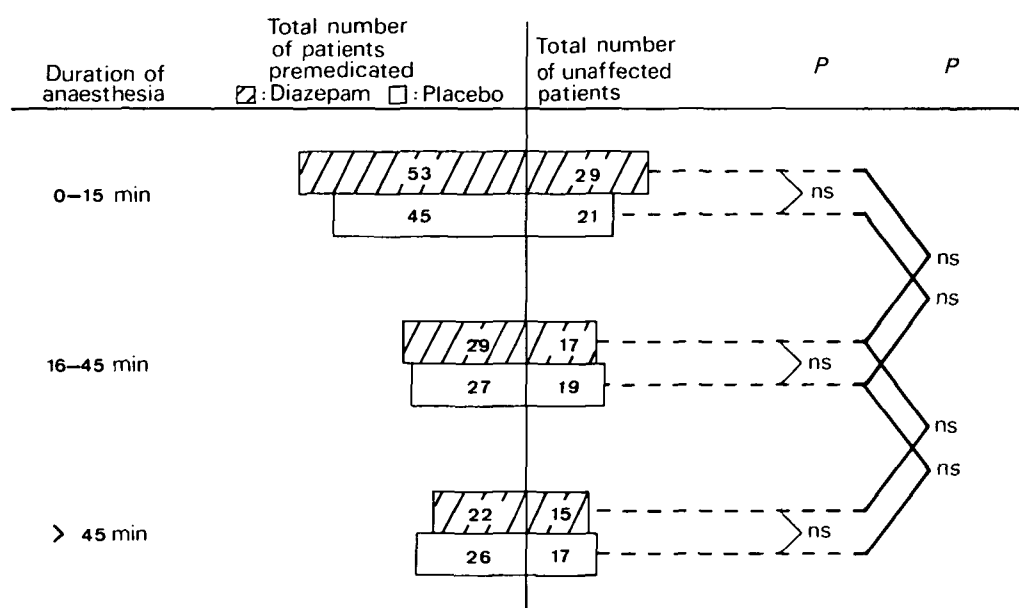


FIG. 3. Number of unaffected patients the day after operation.

administration and the condition of the patients at the time of discharge was found.

In the diazepam group, 33.7% of the patients took some alcohol the night before the operation; the corresponding percentage in the placebo group was 34.7. None had so much that it would affect the results. A barbiturate or a minor tranquillizer was taken by 3.8% and 7.1%, respectively, the night before the operation. Some of these patients may have had residual effects on the day of operation, but the difference between the groups was not significant and it is unlikely that this medication affected the results.

#### DISCUSSION

An increasing proportion of minor surgical procedures are performed on an outpatient basis. Traditionally, all patients undergoing general anaesthesia are premedicated and for this purpose a benzodiazepine is often preferred. Since the patients are discharged on the day of the operation it is important to know if this premedication is needed and if it has any influence on the patient's general condition at the time of discharge.

The results of the present investigation show that orally administered diazepam can be used as premedication in patients who are to undergo surgery on an outpatient basis.

It is interesting that 57 (58.2%) of the patients

given a placebo were satisfied with this "premedication" (table II), and that the anaesthetists found 55 (56.1%) of those given placebo to be without objective signs of apprehension (table IV). This is in agreement with the findings of Male and colleagues (1960) who found a placebo to work satisfactorily in 57% of the patients in a double-blind controlled investigation.

Kangas, Kanto and Sylvälähti (1976) showed that benzodiazepines with a long half-life could be used as premedication and could be given early in the morning without loss of sedative effect even if the waiting time before operation was long. In our study, the preoperative waiting time did not exceed 6 h and this observation was confirmed.

Diazepam reduced fear and anxiety in a significant proportion of the patients while other registered "discomfort-parameters" were not reduced significantly. Whether the need for premedication is greater among patients undergoing certain outpatient operations is unknown, and cannot be documented statistically from this study. However, a significant proportion of patients undergoing abortion had a need for preoperative sedation. The numbers of patients in the other subgroups were, unfortunately, too small for any clear conclusions to be drawn.

From the observers' and the patients' points of view, the duration of anaesthesia determined the patients' general condition on discharge and during

the following day. Prescott and co-workers (1976) found a poor relationship between the duration of anaesthesia and the patients' general condition in those undergoing operations for hernia and varicose veins. Only patients who had been under anaesthesia for an average of more than 89 min were drowsier than those who had been anaesthetized for a shorter time. The present investigation showed that patients who were anaesthetized for more than 45 min were objectively more affected than patients who had been anaesthetized for a shorter period. This difference in the condition after surgery could not be reproduced when the patients' subjective estimate was evaluated.

In volunteer studies, diazepam was found in the plasma 24 h after oral administration (Moolenaar et al., 1980). High plasma diazepam concentrations resulted in a marked deterioration of several mental functions and of co-ordination (Hillestad et al., 1974). Thus, diazepam and other benzodiazepines with a long half-life would seem less suitable as premedication for outpatient surgery since they decrease postoperative street-fitness, and personal responsibility.

In this study, however, no significant differences could be found between placebo- and diazepam-treated patients. Some of the properties and effects of diazepam may have been masked by general anaesthesia, but in conclusion, we found that premedication in outpatient surgery is advantageous because of the decrease in apprehension before operation. Orally administered diazepam can be given early in the morning without loss of effect if the operation is performed within 6 h. The general

condition at the time of the discharge and on the following day was not influenced by the premedication.

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