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Original Research Article

Benzodiazepine hypnotics as oral preanaesthetic medication: a comparative clinical study

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ABSTRACT

Background: An ideal pre-medicant should allay fear and anxiety without producing its effect on vital functions of the body and body chemistry, with minimal depression of the respiratory and circulatory systems. The ideal pre-medicant with all good qualities and no side effects at all is yet to be found. The search for a drug which will be an appropriate pre-anesthetic medication is still going.
Methods: Four drugs of BZD group namely diazepam, nitrazepam, lorazepam, and oxazepam were chosen as oral pre-anesthetic medication. Total number of cases were 100, of which 25 patients belonging to each group of drug respectively. Standard doses of oxazepam (30 mg), nitrazepam (5 mg), diazepam (10 mg) and lorazepam (2 mg) by oral route were administered. All study participants were examined night before operation to observe the following clinical parameters like level of apprehension, excitement, blood pressure, heart rate, respiration (rate, rhythm and minute volume).
Results: Diazepam and nitrazepam produced fair degree of sedation whereas oxazepam appears to be lagging behind. So far as anxiolysis is concerned, all the drugs appear to be good anxiolytics. Nausea, vomiting and dizziness are some of the problems which may occasionally be faced by this group of drug. On reassessment of patients 60 minutes after premedication, it was revealed that the efficacy so as anxiolysis and sedative effect is concerned was in the following order, lorazepam headed the list; diazepam and nitrazepam followed closely and oxazepam was at the bottom. Toxicity in all the four drugs were minimal. The degree of sleepiness varied from drug to drug. Ninety minute after premedication patients were found to be in a better state of sedation than at 60 minute's level in all the four groups. The degree of sedation and anxiolysis was in the same order as that of 60 minutes level.
Conclusions: The overall impression was that four members of the benzodiazepines, serve as as a good premedication in the absence of pain. The sedation and anxioysis produced by them are of fair degree even when given orally. Side effects produced were minimal except in the lorazepam group when they are used as night time sedative. Given orally only lorazepam is capable of producing anterograde amnesia.

Keywords: Anxioysis, Anterograde amnesia, Benzodiazepines, Pre-anesthetic medication, Sedation

INTRODUCTION

Preanesthetic medicaments are administered for one or more of several reasons: to relieve apprehension, to supplement the anesthetic, to relieve pain and to control vomiting.[1] Effective premedication is an integral component of balanced anesthesia. As in adults, children also suffer from anxiety and separation from parents which may rise autonomic hyperactivity, dysrrythmias, hypersalivation, breath holding and laryngospasm

perioperatively. Additionally it can also add to surgical stress response. Establishment of adequate pre-anaesthetic sedation and amnesia for pre and intra-operative event has thus assumed an important role in the anesthetic management of pediatric patients.[2]

An ideal pre-medicant should allay fear and anxiety without producing its effect on vital functions of the body and body chemistry, with minimal depression of the respiratory and circulatory systems. It should be simple and pleasant to take and should act over a reasonably long period of time. It should facilitate quick induction and quick recovery from anesthesia. It should be safe and effective in all patients. A great variety of pre-anesthetic medications were used by anesthesiologists since long time but none of them could fulfill the criteria of an ideal one.[3,4]

All benzodiazepines in clinical use promote the binding of the major inhibitory neurotransmitter γ-aminobutyric acid (GABA) to the GABAA receptor, a multi-subunit, ligand-gated chloride channel. GABA binding induces the Cl–current through these channels. A number of distinct mechanisms of action are thought to contribute to the sedative-hypnotic, muscle-relaxant, anxiolytic, and anticonvulsant effects of the benzodiazepines, and specific subunits of the GABAA receptor are responsible for specific pharmacological properties of benzodiazepines. Virtually all effects of the benzodiazepines result from their actions on the CNS. The most prominent of these effects are sedation, hypnosis, decreased anxiety, muscle relaxation, anterograde amnesia, and anticonvulsant activity. The benzodiazepines are effective anxiolytics as both acute and chronic treatment.[5-7]

The pharmacological main effects of benzodiazepines are: reduction of anxiety and aggression, induction of sleep, reduction of muscle tone, anticonvulsant effect and anterograde amnesia.[6,7]

Benzodiazepines are well absorbed when given orally, usually giving a peak plasma concentration in about 1 h. Some (e.g. oxazepam, lorazepam) are absorbed more slowly. They bind strongly to plasma protein, and their high lipid solubility causes many of them to accumulate gradually in body fat. They are normally given by mouth but can be given intravenously (e.g. diazepam in status epilepticus, midazolam in anesthesia) or rectally. Intramuscular injection often results in slow absorption.[7]

The evidence suggests that the benzodiazepines are closer to the ideal of allaying apprehension without producing side effects that most other drugs available. In this study we intended to use the four commonly used members of BZDs family named oxazepam (30 mg), nitrazepam (5 mg), diazepam (10 mg) and lorazepam (2 mg) by oral route. BZDs may be considered as good pre-anesthetic medications in circumstances where pain is not an associated factor. The therapeutic effect is better and is achieved more quickly when it is given by mouth than intramuscularly. Indeed, when injected it is sufficiently painful to interfere with the tranquillizing effect.[8,9]

The drugs are used as night sedative and also is morning pre-anesthetic medications, to assess their relative potency as well as to detect any undesirable effects that may have been produced. The other purpose of the study was to compare and contrast the efficacy and toxicity of four members of this pharmacological group. The degree of sedation, anxiolysis, side effects and amnesic effects have been assessed by a method of scoring formulated by Dundee et al.[10]

METHODS

The present study was carried out in a tertiary a tertiary care teaching hospital in Patna. Study was approved by the local ethics committee and an informed parental consent was obtained from the parents of the patients. A pre-anaesthetic checkup which included taking a detailed history and a thorough general physical examination of the patients was carried out a day prior to surgery.

Four drugs of BZD group namely diazepam, nitrazepam, lorazepam, and oxazepam were chosen as oral pre-anesthetic medication. Total numbers of cases were 100, of which 25 patients belonging to each group of drug respectively. Standard doses of oxazepam (30 mg), nitrazepam (5 mg), diazepam (10 mg) and lorazepam (2 mg) by oral route were administered. Subjects were of ages between 25-35 years and of body weight between 35 - 55 kg. Subjects above 55 kg body weight excluded from the study. All study participants were examined night before operation to observe the following clinical parameters like level of apprehension, excitement, blood pressure, and heart rate, respiration (rate, rhythm and minute volume).

Night sedation was given with the same drug that was given as premedication with same doses. Patients were given again examined at 7 am of the next morning. All the previous parameters were assessed as also the following parameters like sedation, emetic effects, dizziness, or ant other side effects that have been produced by the drug.

Pre-anesthetic medication was given one and a half hour before operation by any of the drug like oxazepam (30 mg), nitrazepam (5 mg), diazepam (10 mg) and lorazepam (2 mg) which was given as night sedative. After premedication the patient was observed at 60 minute and 90 minute interval to note the cardiovascular and respiratory effects as well as apprehension, excitement, sedation or any other side effects. All the study participants were operated under same anesthetic technique. The patient was induced with sleep dose of thiopentone and intubation was carried out after relaxation with gallamine (2 mg/kg body weight) and anesthesia was maintained with N_2O: O_2 (70:30) with

controlled ventilation with brain co-axial circuit. Patients were reversed as usual with neostigmine and atropine. A method of scoring done according to Dundee and More.[11,12] The subjective and objective responses to the drug were recorded to the following schemes.

- Sedation graded as "good", "fair", "slight", or "nil". Good sedation is said to be present when patient drops off to sleep when undisturbed, but is not so deeply sedated as to cause anxiety.
- Apprehension is the degree of apprehension was graded as "absent", "slight", "moderate" or "marked" according to a self-formulated questionnaire as suggested by Psychologist.
- Excitement indicates a restlessness or a delirious condition of the patient and is easily classified as "marked" or "nil" or "slight".
- Dizziness occurring on the morning or after pre-medication was graded as "marked", "slight" or "nil".
- Cardiovascular effects: the fall in systolic blood pressure attributable to the premedication was graded as: "Nil" (0-20 mgHg), "Moderate (21-40 mmHg) and "Severe' (41+ mmHg).
- Amnesic effects (anterograde amnesia) of the drug the patient was asked some specific questions and show three different picture cards between 60 to 90 minutes after premedication. The patient was visited 24 hours after operation and was asked whether the patient can remember the questions and cards. If not then the patient was shown a composite of nine different picture cards including three pictures which have already been shown. The anterograde amnesia was classified as follows: memory (nil, hazy, clear) and amnesia (complete, partial, nil).

Table 1: Dundee and more scoring system on efficacy and toxicity effects criteria[12]

Score	Desired effects criteria	Toxic effects criteria
5	Good sedation with no apprehension or excitement	Patient unmanageable, or other severe side effects
4	Good sedation with some decrease in apprehension or fair sedation with absence of apprehension	Severe nausea or dizziness or moderate cardiovascular effects
3	Either fair sedation or decrease in apprehension but not both	Slight cardiovascular effect or dizziness and nausea
2	Marked apprehension with slight sedation, or slight apprehension with no sedation.	Slight dizziness or nausea
1	No sedation with marked apprehension	Nil

To facilitate interpretation of the overall pre-operative effects of drugs a scoring scheme has been devised by Dundee and More to grade the "desired" and "toxic" effects on purely clinical basis.[11]

The net soring is obtained by subtracting the toxicity score from the efficacy score, thus giving nine categories ranging from +4 (good sedation, no apprehension, excitement or other side effects) to -4 (no sedation with marked apprehension and severe side effects).

Overall effect of the drug as assessed by statistical analysis and the significance of the incidence distribution of efficacy score was calculated by Ridit analysis method described by Bross.[13]

RESULTS

In present study total number of cases were 100, of which 25 patients belonging to each group of drug respectively. Standard doses of oxazepam (30 mg), nitrazepam (5 mg), diazepam (10 mg) and lorazepam (2 mg) by oral route were administered.

The difference in pulse rate/min in Group O (oxazepam series) between was statistically significant between at night and at morning of next day after tab oxazepam intake (Table 4) but after 60 mins and 90 mins of premedication was not significant.

Table 2: Distribution of age in years in all the drug groups.

	Group O (Oxazepam series)	Group N (Nitrazepam series)	Group D (Diazepam series)	Group L (Lorazepam series)
Range (Years)	23 - 20	24 - 34	25 - 35	26 - 35
Mean±SD	28.96±2.87	28.44±2.15	28.88±3.05	29.8±2.72

Table 3: Distribution of body weight in kg in all the drug groups.

	Group O (Oxazepam series)	Group N (Nitrazepam series)	Group D (Diazepam series)	Group L (Lorazepam series)
Range (Kg)	35 - 54	35 - 48	35 - 50	38 - 51
Mean±SD	43±4.62	43.36±3.79	43.36±3.77	43.84±3.57

Table 4: Changes in pulse rate/min in group O (Oxazepam series).

	At night	At morning	After pre-medication		P value
			At 60 mins	At 90 mins	
Range (rate/min)	76 - 124	72 - 100	78 - 100	76 - 100	
Mean ± SD	93.28±10.18	83.2±7.97*	91.52±8.82	87.04±7.13**	* p < 0.001 ** p < 0.02

Table 5: Changes in pulse rate/min in group N (Nitrazepam series).

	At night	At morning	After pre-medication		P value
			At 60 mins	At 90 mins	
Range (rate/min)	80 - 126	72 - 112	68 - 120	68 - 110	
Mean±SD	100.4±14.83	93.2±10.76*	94.2±13.49	91.2±11.78**	* p < 0.05 ** p < 0.025

Table 6: Changes in pulse rate/min in group D (Diazepam series).

	At night	At morning	After pre-medication		P value
			At 60 mins	At 90 mins	
Range (rate/min)	72 - 120	64 - 124	68 - 120	68 -126	
Mean±SD	94.56±13.4	91.12±13.23*	92±12.48	89.2±3.09**	* p < 0.3 ** p < 0.1

Table 7: Changes in pulse rate/min in group L (Lorazepam series).

	At night	At morning	After pre-medication		P value
			At 60 mins	At 90 mins	
Range (rate/min)	80 - 124	78 - 120	76 - 110	76 - 110	
Mean±SD	92.52±12.55	96.8±11.2*	91.52±9.14	89.28±9.15**	* p < 0.8 ** p < 0.02

Table 8: Changes in systolic BP in group O, group N, group D and group L.

Group O	At night	At morning	After pre-medication		P value
			At 60 mins	At 90 mins	
Range (mmHg)	100 - 140	96 - 130	100 - 134	90 - 130	
Mean±SD	122.72±8.92	112.88 ±8.33*	112±9.27	106.72±9.06**	* p < 0.001, ** p < 0.001
Group N					
Range (mmHg)	110 - 140	96 - 130	90 - 130	90 - 130	
Mean±SD	123.12±7.63	115.44±9.25*	107.12±10.21	104.8±10.35**	* p < 0.005, ** p < 0.001
Group D					
Range (mmHg)	106 - 140	100 - 130	96 - 130	96 - 130	
Mean±SD	119.12±9.60	113.68±10.33*	110±10.53	109.2±8.35**	* p < 0.05, ** p < 0.001
Group L					
Range (mmHg)	110 - 150	96 - 140	96 - 130	96 - 126	
Mean±SD	124. 08±14.63	120.56±19.25*	113.44±16.21	109.02±16.35**	* p < 0.25, ** p < 0.001

Table 9: Changes in respiratory rate in group O, group N, group D and group L

Group O	At night	At morning	After pre-medication		P value
			At 60 mins	At 90 mins	
Range (rate/min)	17 - 30	16 - 25	16 - 25	17 - 26	
Mean±SD	22.76±3.07	20.88±2.40*	21.12±2.33	20.48±2.40**	* p < 0.05, ** p < 0.01
Group N					
Range (rate/min)	17 - 30	14 - 27	11 - 30	12 - 27	
Mean±SD	22.2±2.97	20.44±3.17*	19.84±4.12	19±3.3**	* p < 0.05, ** p < 0.001
Group D					
Range (rate/min)	14 - 33	14 - 28	14 - 30	12 - 25	
Mean±SD	21.16±4.34	18.68±3.78*	19.16±4.26	18.84±3.96**	* p < 0.05, ** p < 0.05
Group L					
Range (rate/min)	13 - 30	12 - 28	13 - 25	13 - 23	
Mean±SD	19.96±4.56	18.88±4.35*	19.32±3.35	18.48±2.84**	* p < 0.4, ** p < 0.1

Table 10: Changes in tidal volume in group O, group N, group D and group L.

Group O	At night	At morning	After pre-medication		P value
			At 60 mins	At 90 mins	
Range (ml)	312 - 466	220 - 440	240 - 444	250 - 450	
Mean±SD	385±38	358.12±52.37*	342±53.59	348.04±52.19**	* p < 2.05, ** p <0.05
Group N					
Range (ml)	208 - 500	222 - 433	217 - 419	260 - 446	
Mean±SD	385.32±65.69	358.56±54.32*	342.16±62.82	338.12±64.23**	* p < 0.1, ** p <0.02
Group D					
Range (ml)	214 - 525	250 - 571	222 - 485	211 - 468	
Mean±SD	372.88±83.72	383.96±76.09*	348.48±75.37	345.12±71.37**	* p < 0.6, ** p < 0.4
Group L					
Range (ml)	227 - 615	221 - 583	250 - 411	250 - 433	
Mean±SD	404.4± 96.98	374.28±84.84*	329.44±50.26	366.68±50.26**	* p < 0.25, ** p < 0.05

Table 11: Distribution of efficacy score (number of patients) in group O, group N.

Score Group O	At morning	At 60 minutes after pre-medication	At 90 minutes after pre-medication
1	6	6	6
2	12	6	6
3	7	13	9
4	0	0	3
5	0	0	1
Total	**25**	**25**	**25**
Group N			
1	3	3	2
2	5	6	5
3	17	6	7
4	0	10	11
5	0	0	0
Total	**25**	**25**	**25**

Since all patients were usually anxious and apprehensive about the next day's concern, the pulse rate was higher than normal in all groups (Table 4, 5, 6, 7).

Table 12: Distribution of efficacy score (number of patients) in group D, group L.

Score Group O	At morning	At 60 mins after pre-medication	At 90 mins after pre-medication
1	1	2	3
2	7	3	3
3	17	11	9
4	0	8	8
5	0	1	2
Total	**25**	**25**	**25**
Group N			
1	0	1	1
2	11	5	4
3	11	4	3
4	3	3	5
5	0	12	12
Total	**25**	**25**	**25**

In the morning, there was a slight rise in pulse rate in 4 patients in Group O, 8 patients in group L and 7 patients in group D series. In those apprehension was unchanged or slightly decreased and sedation was slight.

Table 13: Distribution of toxic score (number of patients) in group O, group N.

Score Group O	At morning	At 60 mins after pre-medication	At 90 mins after pre-medication
1	16	21	22
2	9	4	3
3	0	0	0
4	0	0	0
5	0	0	0
Total	**25**	**25**	**25**
Group N			
1	22	24	22
2	3	0	2
3	0	1	1
4	0	0	0
5	0	0	0
Total	**25**	**25**	**25**

Table 14: Distribution of toxic score (number of patients) in group D, group L.

Score Group O	At morning	At 60 mins after pre-medication	At 90 mins after pre-medication
1	14	21	22
2	10	4	3
3	1	0	0
4	0	0	0
5	0	0	0
Total	**25**	**25**	**25**
Group N			
1	7	16	19
2	10	8	5
3	0	0	0
4	8	1	1
5	0	0	0
Total	**25**	**25**	**25**

Table 15: Distribution of net score in group O, group N, group D and group L.

	Group O	Group N	Group D	Group L
At morning	0.72±0.72	1.52 ±0.805	1.2±0.8	0.36±1.59
At 60 mins after pre-medication	1.2±0.938	1.92±1.16	1.96±1.038	2.4±1.76
At 90 mins after pre-medication	1.52±0.135	1.96±1.148	2.2±0.978	2.56±1.57

In the morning the meal fall in systolic blood pressure compared to night (Table 8). Because patients were mostly less anxious and well sedated in all groups. Maximum fall was in group O i.e. 9.84 mmHg (Table 8). In group-N and group-D both tranquility and sedation were of fair degree and the patients were found to be quiet and just sleepy where as in Group-O most of the patients were tranquil, quiet, and awake.

Some of them though not frankly frightened did show some degree of apprehension. It may be compared that at 60 minutes, group-L produced more tranquil and sleepy patients than its competitors.In net scoring, Group-O received at morning 0.72±0.72, but received 1.2±0.938 at 60 minutes and 1.52± 0.135 at 90 minutes, after pre-medication. Group-N received at morning 1.52±0.805, but received 1.92±1.16 minutes and 1.96±1.148 at 90 minutes, after pre-medication. Group-L received at morning 0.36±1.59, but received 2.4±1.76 minutes and 2.56±1.57 at 90 minutes, after pre-medication (Table 15). In all groups, there was increase in net scoring from morning to 90 minutes after pre-medication.

DISCUSSION

An anesthesiologist has a vital role to play by prescribing an adequate and appropriate premedication to make the patient quiet, restful and calm mentally prepared for an uneventful surgery. The value of pre-operative visit by the anesthetist hardly needs monitoring. Benzodiazepines are now used mainly for treating acute anxiety states, behavioural emergencies and during procedures such as endoscopy. They are also used as premedication before surgery (both medical and dental). Under these circumstances their anxiolytic, sedative and amnesic properties may be beneficial. Intravenous midazolam can be used to induce anaesthesia. The main reasons for using sedative-hypnotic premedication were allaying anxiety and providing sedation.[14]

High levels of preoperative fear and anxiety correlate with various unfavorable outcomes, including increases in postoperative analgesic requirements, prolonged post-anesthesia care unit or hospital stays, and delayed negative psychological effects.[15]

In view of the high incidence and associated adverse outcomes in some patients groups, pharmacological (i.e., premedication) or psychological steps may be considered.15 Benzodiazepines are extensively used as oral premedication as they present the advantage of avoiding painful intravenous or intramuscular injections. They differ in their ability to relieve primary or secondary (e.g., situational) anxiety, act as anticonvulsants, provide muscle relaxation, and induce sedation.[15]

The present workers choose four drugs for a comparative study of their different properties. Both subjective and objective methods have been used as a guide to this study. The practical difficulties in estimating the degree of anxiety and apprehension are great, and no method as yet been devised with that much satisfaction. In common with other subjective states such as fear, anxiety and intoxication, sedation is associated with certain physiological changes and can be considered as a part of spectrum, the extreme of which are anxiety and sleep. At this extremes, there are certain physical signs which are easily recognized and measured. According to the predominance of the science of anxiety or sleep, it is possible to place the patients at point on the spectrum and thus to assess the degree of sedation. Thus the method, used clinically to assess premedication drugs, should be capable of measuring the degree of sedation produced. Subjective assessment alone is liable to errors and difficult to appreciate. Beechar et al in his classical work has shown that such subjective states are usually associated with objective changes, and can be quantified. In these work both subjective and objective methods have been used, like some specific questions, and heart rate, blood pressure and respiration etc.[16]

In all groups except group L (lorazepam series) was a rise in pulse rate. The probable cause of this rise was that during this time patients were transferred from the ward to the lobby outside the operation theatre.[17-19] In group-L there was fall in pulse rate inspite of all disturbances. This may be attributed to better sedative effect of the drug.

Interaction between the patient and the anesthesiologist often occurs during a unique visit on the day before the surgery. The anesthesiologist may follow a short check-up guide, perform a specific physical examination, and prescribe sedatives. Usually, this is the first or even the only opportunity for the anesthesiologist to contact the patient.

In order to avoid unnecessary anxiety, it is advisable that the patient who is to undergo surgery does not fear the upcoming procedure. The anesthesiologist's attention can greatly reduce anxiety even without using medicines.20 It is important to also consider that there might be some consideration as to how detailed the information should be that is given to the patient. In a British study, 82% of patients who underwent surgery had expressed their desire to know more about the surgical procedure prior to surgery. In addition, the most desired piece of information was the estimated length of stay in the hospital.[21] In a Danish study, patients asked more about pain, anesthesia duration, and risk of impairment of daily activities and less about sedatives or complications.[22]

The fall in BP possibly attributable to the good sedation and anxiolysis. Clinically it was not harmful as they were below 20 mmHg which was graded “nil” by Dundee et al.[12] So in our study there was no adverse effect on cardiovascular system by any drug group, which correlates with the finding of Norris et al, Dundee et al, Suri Y, Agelink et al and Jakobsen H who found no adverse cardiovascular responses with BZDs.[23-27] Benzodiazepines can influence autonomic neurocardiac regulation in man, probably through their interaction with the gamma-aminobutyric acid A-receptor chloride ion channel complex. The pattern of findings suggests that intravenous midazolam, diazepam and lorazepam influence human autonomic neuro-cardiac regulation in a biphasic way. First, they cause a reduction of central vagal tone, and second, they may decrease the cardiac pacemaker directly.

In order to find any change in respiratory patterns of the patients, the respiratory rate and tidal volume were studied at different times. It was found that there was gradually fall in respiratory rate in the morning and 90 mins after pre-medication. The fall was directly proportional to degree of sedation and anxiolysis but in none of the groups it was a cause for alarm. The finding of changes in tidal volume were mostly parallel to those of respiratory rates and showed a gradually decline, except Group-L at 90 minutes which were not remarkable and statistically and clinically insignificant. The finding was similar to those of Kangley et al and Burtes et al who found no cardio-pulmonary depression.[28,29] When we considerd the efficacy score we found that in the morning none of the patients in any of the groups received a score of 5.3 patients in group-L received a score of 4, i.e. patients had good sedation with some decrease in apprehension or fair sedation with absence of apprehension. It was found that the patients in Group-L had the maximum benefit from premedication received and inspite of being disturbed by the various preparations for operation, did not lose their tranquility or the effect of sedation.

In this study we could not elicit a definite relationship between changes in the clinical parameters (pulse rate, BP) and the efficacy score received by the different patients. In some cases they were directly proportional while in others they were found to be paradoxical.

So far the toxic score is concerned; group-L received the maximum score. One patient in this group received a toxic score of 4 even at 60 minutes and 90 minutes due to moderate fall in BP and marked dizziness. So fat toxicity is concerned, Group D appears to have minimal effects.

It appears that when net scoring is taken into account, Group-L at 90 minutes received the highest score. Second highest net score was obtained by the same group at 60 minute. The good sedation and anxiolysis that was produced by group-L resulting in its obtaining very high efficiency score but nausea and dizziness that it produced in the morning was the cause of its downfall resulting in a very low net score in the morning.

So as a premedicant, BZDs are good anxiolytic and sedative. Lorazepam was better than diazepam, and nitrazepam. Oxazepam having least of the property. This finding corroborates with the findings of Dundee et al, Norris et al, Kapp et al, Dundee et al, Kangley and Sharma et al.[23,24,28,30,31] Amnesia for unpleasant aspects of preoperative period, is a very useful property of premedication.

In the present study patients of group-L had complete anterograde amnesia except 3 who had partial anterograde amnesia. Other groups showed no anterograde amnesia. This finding corroborates with the finding of Dundee et al, Gallon et al, Burtles et al, Astley et al, Mac DS et al, and O'Boyle CA who found greater incidence of anterograde amnesia by lorazepam than other BZDs.[29.32-35] In the immediate postoperative period patients were awake in all groups but in lorazepam group patients were somewhat drowsy and needed postoperative sedation after a longer interval than the other groups. There was no emetic effect or other side effects noted in immediate post-operative period.

Diazepam and nitrazepam produced fair degree of sedation whereas oxazepam appears to be lagging behind. So far as anxiolysis is concerned, all the drugs appear to be good anxiolytics. Nausea, vomiting and dizziness are some of the problems which may occasionally be faced by this group of drug. In the following morning in the lorazepam group, fair number of patients showed nausea and dizziness on ambulation. Probably this could have been avoided by keeping the patient in bed rest. In the case of other drugs, these effects were minimal.

On reassessment of patients 60 minutes after premedication, it was revealed that the efficacy so as anxiolysis and sedative effect is concerned was in the following order, lorazepam headed the list; diazepam and nitrazepam followed closely and oxazepam was at the bottom. Toxicity in all the four drugs were minimal. Apart from few cases who showed some degree of apprehension attributable to the process of transport of patient to the operation theatre most of the patients in all groups were calm and sleepy. The degree of sleepiness varied from drug to drug.

Ninety minute after premedication patients was found to be in a better state of sedation than at 60 minute’s level in all the four groups. The degree of sedation and anxiolysis was in the same order as that of 60 minutes level.

CONCLUSION

The overall impression was that four members of the benzodiazepines serve as a good premedication in the absence of pain. The sedation and anxioysis produced by them are of fair degree even when given orally. Side effects produced were minimal except in the lorazepam group when they are used as night time sedative. Given orally only lorazepam is capable of producing antergrade amnesia.

Drugs to be used as premedicants before general or local anesthesia is induced must be selected with due regard to the patient's physical and mental state, the major anesthetic to be used, and the technique of administration. They should be prescribed by the person assigned to administer the anesthetic. Their purpose is to relieve the patient's anxiety, to reduce the amount of troublesome mucous secretions, to intensify the desired effect or reduce the required amount of the major anesthetic, and to decrease the incidence of complications of anesthesia, such as cardiac arrest, laryngospasm, and bronchial spasm.

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