THE USE OF DIAZEPAM IN PAEDIATRIC PREMEDICATION

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THERE is probably no other preoperative sedation more critical and necessary than that for children, yet in this field relatively few efforts have been made to find suitable agents. Diazepam, which has recently been made available (trade name "Valium Injectable," Roche), belongs to the tranquillizer family with a formula of 7-chloro-1, 3-dihydro-1-methyl-5-phenyl-2H, 4 benzo-diazepin-2-one.

This compound is colorless, with a crystalline base which is soluble in water. The molecular weight is 284.74. It has been found in animal studies to have muscle relaxant activity¹ and anti-strychnine activity.^{2,3} Clinical studies⁴ have shown that it decreases the mean arterial blood pressure, the pulse rate, and the respiration. The onset of action is rapid when administered intramuscularly and clinical sedative effects should be noted from twenty minutes to half an hour after administration. No liver toxicity has ever been detected.

Tornetta⁵ found that diazepam was very effective in reducing preoperative tension and in establishing a good state of mind without excessive sedation. Brandt and Oakes⁶ in 1965 confirmed these results and found that there were no side effects when Diazepam was used as a premedicant under controlled conditions. However, Cormier *et al.*⁷ could not detect any difference in preoperative sedation between diazepam and meperidine. Because of these discrepancies, and in order to further elucidate the effects of diazepam in preoperative paediatric medication, we undertook comparative studies using this drug in various combinations with other drugs.

Our criteria for this study were established to test and to statistically evaluate the drug effects of diazepam in comparison with meperidine, pentobarbital, atropine, and scopolamine in various combinations. Ideally, premedication should achieve preoperative sedation and co-operation without depression of the vital functions. It should facilitate induction and maintenance of anaesthesia, and a continuation of effects during the early postoperative period, manifesting itself in anti-emetic properties and analgesia, is desirable. Viewed in this light the parameters under evaluation were preoperative sedation, consciousness, and

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co-operation, as well as postoperative analgesia and anti-emetic properties. So as not to influence the effects of the different premedicants, the anaesthetic administered in *all* cases was nitrous oxide, halothane and methoxyflurane through an endotracheal tube.

METHOD

A total of 250 patients with a mean age of 5.1 years and a mean weight of 51.2 pounds were tested using a double-blind technique. These patients were assessed immediately before induction, on the termination of anaesthesia, and again during their stay in the recovery room. The dose of diazepam was 1 mg./kg. up to 25 kg. body weight. The dose of meperidine was 0.5 mg./kg. body weight. These two drugs were used in various combinations during our study with scopolamine 0.3 to 0.4 mg. total dosage intramuscularly, atropine 0.3 to 0.4 mg. total dosage i.m., and pentobarbital 5 mg./kg. body weight, rectally as the case required. The results were tabulated (see Tables I-V), the chi-square was calculated, and $p \leq 0.05$ was accepted as statistically significant.

RESULTS

In all groups, the recovery time was under thirty minutes and no side-effects were noted. In the diazepam-atropine group, the maximum recovery time was 20 minutes, the minimum 5 minutes, and the mean 9.6 minutes. The mean arterial blood pressure was 110/78, the mean respiration 20 per minute, and the mean pulse was 98.2 per minute. In the meperidine-scopolamine group, the maximum recovery time was 20 minutes, the minimum 5 minutes, and the mean 10.2 minutes. The mean arterial blood pressure, respiration, and pulse were 110/80, 20 per minute and 98.8 per minute respectively. In the pentobarbital-meperidine-atropine group, the maximum recovery time was 25 minutes, the minimum 5 minutes, and the mean 13.6 minutes. The mean arterial blood pressure was 106/75, the mean respiration 20 per minute, and the mean pulse 111.7 per minute. This group, it may be noted, exhibited an average pulse rate increase of thirteen beats per minute, from 98.7 to 111.7 per minute. In the diazepam-scopolamine group, the maximum recovery time was 20 minutes, the minimum 5 minutes and the mean 9.2 minutes. The mean arterial blood pressure was 108/76, the mean respiration, 20 per minute, and the mean pulse was 97.7 per minute.

In analysing the results of the first two groups to be compared (see Table I), we note that sedation was significantly greater in patients premedicated with diazepam-atropine than in those given a meperidine-atropine combination ($p < 0.05$). Other comparisons between these two groups did not reveal any significant differences. In the next set of comparisons (see Table II) we find no statistical significance favouring either the diazepam-scopolamine combination or the pentobarbital-meperidine-scopolamine combination either preoperatively or post-operatively, evidenced by the fact that the chi-square gave $p > 0.50$ for this series. In Table III it is noted that diazepam combined with scopolamine demonstrates significantly greater preoperative co-operation than does a pre-

TABLE I

	Diazepam/Atropine	Meperidine/Scopolamine
Section 1: Preoperative evaluation of sedation		
Tranquil	40	28
Tense	2	6
Excited	10	14
Total	52	48
Section 2: Preoperative evaluation of consciousness		
Sleepy	18	22
Awake	34	26
Total	52	48
Section 3: Preoperative evaluation of co-operation		
Co-operative	24	18
Unco-operative	28	30
Total	52	48
Section 4: Postoperative evaluation of sedation and analgesia		
Crying	34	32
Quiet	18	16
Total	52	48
Section 5: Postoperative evaluation of anti-emetic properties		
Vomiting	14	15
No vomiting	38	33
Total	52	48

medicant of diazepam-atropine ($p < 0.02$). In the next two groups to be compared (see Table IV), it is observed that a meperidine-atropine-pentobarbital union produced significantly more favourable results in the preoperative evaluation of sedation, consciousness, and co-operation than the meperidine scopolamine group ($p < 0.01$). In the final comparison (see Table V), we found that the effects on sedation, consciousness, and co-operation were significantly better in the diazepam-scopolamine group than in the group given meperidine with scopolamine. (Section 1, $p < 0.01$; section 2, $p < 0.05$; and section 3, $p < 0.01$.)

CONCLUSIONS

These results demonstrate the safety of diazepam, since although our doses were double the recommended amount, no side-effects were encountered in our investigation. In view of the large volume to be injected, it was not feasible to further increase the quantity of diazepam. Postoperatively, no combination of drugs brought about sedation, analgesia or anti-emesis. However, in the preoperative evaluation, there was always a striking effect in favour of a diazepam-scopolamine combination as well as a meperidine-atropine-pentobarbital combination. In the final analysis, a diazepam-scopolamine combination seems to exhibit better clinical effects, although these results are not statistically significant.

Several authors⁸⁻¹⁰ had previously tested diazepam for preoperative medication

TABLE II

	Diazepam/Scopolamine	Pentobarbital/Meperidine/Atropine
Section 1: Preoperative evaluation of sedation		
Tranquil	60	60
Tense	5	7
Excited	10	8
Total	75	75
Section 2: Preoperative evaluation of consciousness		
Sleepy	50	53
Awake	25	22
Total	75	75
Section 3: Preoperative evaluation of co-operation		
Co-operative	54	48
Unco-operative	21	27
Total	75	75
Section 4: Postoperative evaluation of sedation and analgesia		
Crying	42	54
Quiet	33	21
Total	75	75
Section 5: Postoperative evaluation of anti-emetic properties		
Vomiting	14	20
No vomiting	61	55
Total	75	75

TABLE III

	Diazepam/Scopolamine	Diazepam/Atropine
Section 1: Preoperative evaluation of sedation		
Tranquil	60	40
Tense	5	2
Excited	10	10
Total	75	52
Section 2: Preoperative evaluation of consciousness		
Sleepy	50	18
Awake	25	34
Total	75	52
Section 3: Preoperative evaluation of co-operation		
Co-operative	54	24
Unco-operative	21	28
Total	75	52
Section 4: Postoperative evaluation of sedation and analgesia		
Crying	42	34
Quiet	33	18
Total	75	52
Section 5: Postoperative evaluation of anti-emetic properties		
Vomiting	14	14
No vomiting	61	38
Total	75	52

TABLE IV

	Meperidine/Scopolamine	Meperidine/Atropine/Pentobarbital
Section 1: Preoperative evaluation of sedation		
Tranquil	28	60
Tense	6	7
Excited	14	8
Total	48	75
Section 2: Preoperative evaluation of consciousness		
Sleepy	22	53
Awake	26	22
Total	48	75
Section 3: Preoperative evaluation of co-operation		
Co-operative	18	48
Unco-operative	30	27
Total	48	75
Section 4: Postoperative evaluation of sedation and analgesia		
Crying	32	54
Quiet	16	21
Total	48	75
Section 5: Postoperative evaluation of anti-emetic properties		
Vomiting	15	20
No Vomiting	33	55
Total	48	75

TABLE V

	Diazepam/Scopolamine	Meperidine/Scopolamine
Section 1: Preoperative evaluation of sedation		
Tranquil	60	28
Tense	5	6
Excited	10	14
Total	75	48
Section 2: Preoperative evaluation of consciousness		
Sleepy	50	22
Awake	25	26
Total	75	48
Section 3: Preoperative evaluation of co-operation		
Co-operative	54	18
Unco-operative	21	30
Total	75	48
Section 4: Postoperative evaluation of sedation and analgesia		
Crying	42	32
Quiet	33	16
Total	75	48
Section 5: Postoperative evaluation of anti-emetic properties		
Vomiting	14	15
No vomiting	61	33
Total	75	48

in adults. They were almost unanimously in favour of it, although their doses were smaller than those used in our study. It may be possible that the tranquillizing effect exerted by this drug increases in potency with the age of the patient, perhaps suggesting that the sensitivity of the central nervous system to diazepam is related in some way to its development. In this investigation, we did not clinically detect any amnesic, anti-emetic, or muscle relaxant effects. Further, diazepam seems to be definitely contraindicated in cases of myasthenia gravis where its spinal reflex blocking activity may suddenly become dangerous. If diazepam and atropine are used together, it would be wise to add the atropine to the diazepam, instead of vice versa, shortly before administration, in order to avoid a precipitate of benzoate and diazepam crystals.¹¹

SUMMARY

Diazepam and meperidine were compared in a double-blind study for preoperative medication in 250 children undergoing tonsillectomies and adenoidectomies. Preoperatively, diazepam could produce sedation, co-operation, and sleep, but none of these effects was evident postoperatively. No side-effects of this drug were encountered. A meperidine-atropine-pentobarbital combination was also found effective. The over-all comparison favoured diazepam clinically but not statistically.

RÉSUMÉ

Chez 250 enfants qui devaient subir une amygdalectomie et adénoïdectomie, nous avons fait une étude à double-inconnu pour comparer les effets du diazepam et de la mépéridine en prémédication. En préopératoire, le diazepam peut produire une sédation, de la coopération et même le sommeil, mais en postopératoire, il a été impossible d'observer ces effets. Nous n'avons pas observé d'effets secondaires. Une association mépéridine-atropine-pentobarbital s'est avérée également efficace. En définitive, cliniquement, la comparaison favorise le diazepam mais les statistiques ne le favorisent pas.

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