



Dr. Troutman

The efficacy of alphaprodine in pedodontics

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Abstract

The use of alphaprodine for sedating difficult to manage children is discussed. One hundred and three cases (ages 1-11 years) with a mean age of 3 years, 6 months, were treated and evaluated utilizing alphaprodine alone, with nitrous oxide/oxygen supplementation, and in combination with hydroxyzine or promethazine supplemented with nitrous oxide/oxygen as needed. Patient selection criteria consisted of the patient who presented with negative or definitely negative behavior, utilizing the Frankl scale, and required dental treatment that could be accomplished within 1½ hours. A wide dose range was used (.2 to 1.8 mg/kg). All patients were monitored with blood pressure and pulse and respiratory rates using a precordial stethoscope. Alphaprodine was shown to be 87% effective in this group of patients. Side effects, including nausea, swelling at the injection site, postoperative dizziness, prolonged sedation, and respiratory depression were observed in 13 of the 103 cases. All cases were minor and were successfully treated in the office without complications or were closely monitored until the condition subsided. There was no significant relationship between effectiveness and drug dosages based on mg/kg or between side effects and drug dosages. Subjective preoperative evaluation of the patient by the treating dentist leading to the selection of an effective dose or drug combinations seemed to play the greatest role in the successful treatment of the patients.

Every available and acceptable means should be used to provide optimum, comprehensive health care to child patients. When it comes to managing the child's behavior in a dental situation, that includes patience, understanding, behavior modification, restraint, preoperative sedation and general anesthesia; whatever is indicated.

In our experience, the most effective drugs for the control of unacceptable behavior in children in a dental situation have been the narcotics, alone or in combination with tranquilizers and/or antihistamines. It is important to understand that the reason for the

use of narcotics in pediatric dentistry is for its sedative effect and not for its analgesic effect.

Over the past 10 years, we have found alphaprodine to be an excellent adjunct to providing dental care for young, uncooperative children. Many pedodontists feel similarly. The removal of alphaprodine from the market has left many pedodontists bewildered because the drug had enabled them to provide care for many patients in their offices that heretofore would have been admitted to the hospital because general anesthesia would be required to provide the needed care.

The purpose of this retrospective study was to show that alphaprodine is a safe and effective drug for peri-procedural sedation in pediatric dentistry.

Literature Review

The use of alphaprodine for the management of dental patients has been reported utilizing many different techniques since 1960 when Robinson¹ reported using it subcutaneously for adult patients.

DeLapa² also reported using alphaprodine subcutaneously in combination with intravenous thiopental sodium. It was not until 1966, when Corbett³ reported on the use of alphaprodine for "Premedication for Children" that attention was called to its use for children.

In 1973, Wright and McAulay⁴ reported their survey "Current Premedicating Trends in Pedodontics." At that time, this drug was used by about 20% of the pedodontists surveyed. About 13% used it in combination and about 7% alone.

In 1975, Creedon⁵ stated that alphaprodine was generally administered submucosally in the mucobuccal fold in the retromolar area. Creedon also recommended its use in children 3 to 6 years of age and stated that it is generally not successful in controlling the behavior of schoolage children. The reported effective operating time for alphaprodine, at a dose of .5mg/lb (1 mg/kg) administered submucosally is 1½ to 2 hours.⁵

In 1979, King and Berlocher⁶ recommended using alphaprodine submucosally in combination with promethazine at a dosage of .2-.24 mg/lb of alphaprodine and 25-50 mg of promethazine orally given 30-45 minutes before the injection of the alphaprodine.

Reported side effects include itching of the nose and mucous membranes, respiratory depression, a wheal at the injection site, (Figure 1), nausea (usually upon sitting up at the completion of the procedure), decreased respiratory rate and decreased pulse rate.

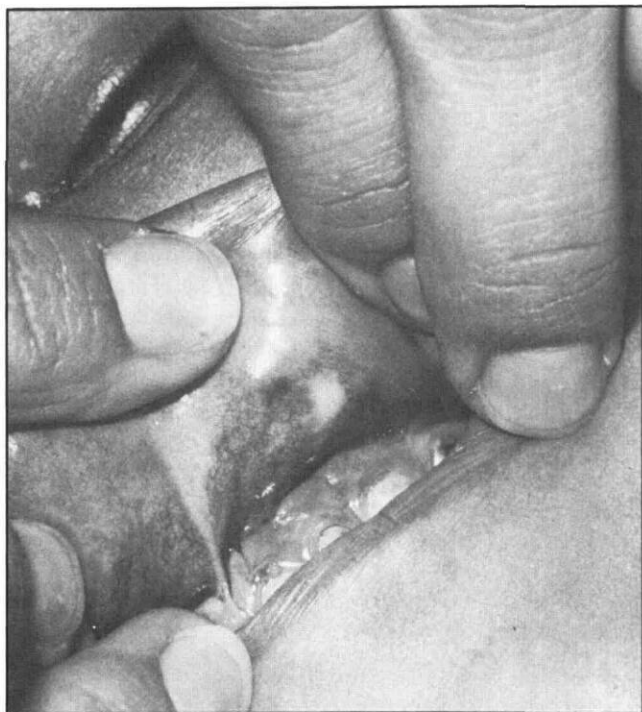


Figure 1. Wheal at the site of submucosal injection of alphaprodine and promethazine.

King and Berlocher⁶ state that a reversal agent (e.g. naloxone) should be readily available in case of emergency.

Although the original package insert did not recommend the use of alphaprodine in children, the dental literature has established that it can and has been used safely in children, especially in children from six months to six years of age.

A review of the literature, as well as a personal survey of postdoctoral pedodontic program directors, revealed that the dosage range being used in pedodontic programs was between 0.2 and 1.2 mg/kg, with a mean dose of .86 mg/kg and a median dose of 1.0 mg/kg.

Methods and Materials

A retrospective evaluation was accomplished for 103 patients, between the ages of 1 year and 11 years with a mean age of 3 years, 6 months, and a weight

range of 8-31 kg with a mean weight of 16.6 kg, who were selected for treatment with alphaprodine as the principal sedation agent. Seventy-five percent of the patients included in the study were between the ages of 2 years and 4 years, 11 months. Only 2 patients were over 7 years, 6 months; one was 10 years and another 11 years.

The principal criterion for deciding to sedate each patient was a prior treatment or examination experience where the patient was considered to be unmanageable via conventional behavior management techniques. The child's behavior fell into either the category of "negative" or "definitely negative" by the Frankl behavior rating scale.⁷

Frankl's Categories of Behavior

Rating 1: Definitely Negative

Refusal of treatment, crying forcefully, fearful, or any other overt evidence of extreme negativism.

Rating 2: Negative

Reluctant to accept treatment, uncooperative, some evidence of negative attitude but not pronounced, i.e., sullen, withdrawn.

Rating 3: Positive

Acceptance of treatment; at times cautious, willingness to comply with the dentist, at times with reservation but patient follows the dentist's directions cooperatively.

Rating 4: Definitely Positive

Good rapport with the dentist, interested in the dental procedures, laughing and enjoying the situation.

A second criterion was that the planned dental treatment procedures could be completed within 1½ hrs. All patients were restrained with the "Pedi-Wrap"^a prior to commencing treatment (Figure 2).

Vital signs were obtained on all patients prior to administration of the alphaprodine (e.g., temperature, blood pressure, pulse rate and respiratory rate) and recorded. Blood pressure, pulse rate, and respiratory rate were also taken prior to the start of dental treatment and upon the completion of treatment and recorded on the data base (Figure 3). All patients were NPO for a minimum of 4 hours and a maximum of 6 hours preoperatively.

Alphaprodine was administered utilizing a 1cc tuberculin syringe and a 26 gauge, 3/8 inch needle. All injections were given in the maxillary buccal

^aManufactured by Clark Associates, Worcester, MA.

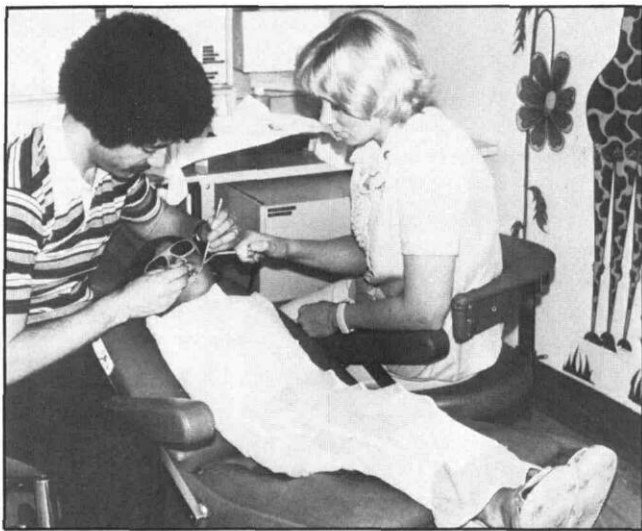


Figure 2. Patient restrained with Pedi-Wrap®.

space (Figure 4). Throughout the treatment period, the patient was monitored with a precordial stethoscope located in the area of the suprasternal notch, and a custom ear piece worn by the operator (Figure 4). This enabled the operator to constantly monitor the breathing and the pulse rate of the patients. In all cases, oxygen was administered via a nasal hood throughout the treatment period (Figure 4). Naloxone in a dose of 0.2 mg was drawn up and ready prior to the administration of the alphaprodine. Local anesthesia was always used for ac-

complishing dental treatment. The anesthetic, in the form of 2% xylocaine with 1:100,000 epinephrine, was administered after the sedative effect of the drugs had become apparent.

The dose of alphaprodine was determined by utilizing several criteria:

1. behavior at the evaluation appointment and at the treatment appointment,
2. weight of patient in kilograms,
3. amount of body fatty tissue,
4. extent of planned treatment,
5. whether the patient was premedicated with a tranquilizer — hydroxyzine, promethazine, diazepam, (Valium®).

The choice of whether to use preprocedural sedation medication in the form of a tranquilizer or nitrous oxide/oxygen was purely subjective and at the discretion of the operator based upon his/her preoperative evaluation of the patient's behavior.

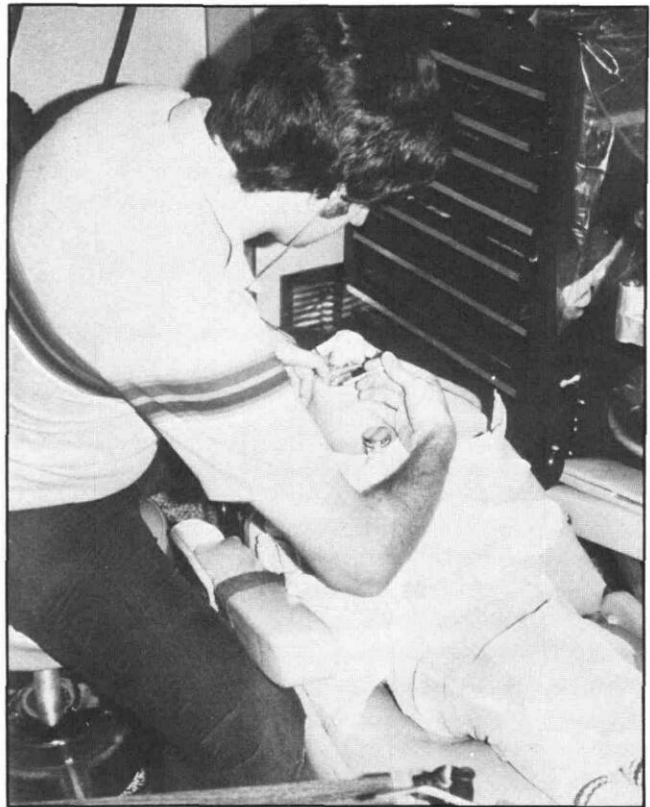


Figure 4. Use of nasal hood for administering nitrous oxide and oxygen. Position of precordial stethoscope attached to earpiece worn by operator to monitor respiration and pulse.

DATA BASE: PEDODONTIC PREMEDICATION EXPERIENCE			
1) Patient name:	TAYLOR, Tony		H.H.# 92-30-98
2) Patient age:	2-1/2	weight: 27 lbs	sex: (M) F
3) Reason for Premedication (circle one or more)			
<input checked="" type="checkbox"/> Anxious	hyperactive		
<input checked="" type="checkbox"/> Fearful	language problem		
<input checked="" type="checkbox"/> Hysterical	medical problem (specify)		
<input checked="" type="checkbox"/> Uncooperative	other: required physical restraint		
4) Medication administered (circle)	Dose (mg)	Route (I.M., P.O.)	
Chloral Hydrate (Noctec)			
Hydroxyzine (Vistaril)	50 X 2	PO 15 min 1 hr Preop	
Meperidine (Demerol)			
Alphaprodine (Nisentil)	9:47 10	S.M.	
Promethazine (Phenergan)			
Diazepam (Valium)			
Scopolamine Hcl.			
Ketamine (Ketalar)			
Naloxone (Narcan)	12:10 0.2	S.M.	
Succinylcholine			
Other N ₂ O/O ₂	50/50	INHALATION	
5) Level of consciousness during procedure (circle one)			
<input type="checkbox"/> Somnolent (not responsive to commands)			
<input checked="" type="checkbox"/> (Heavily Sedated)			
<input type="checkbox"/> Lightly Sedated			
<input type="checkbox"/> Conscious/Alert			
<input type="checkbox"/> Other			
6) Treatment Rendered (ex. 3 ssc's, 2 extractions)	2 SSC, 2 CII AMAL.		
7) Vital Signs:	Pulse	Resp.	Blood Pressure
Before premed.	104	24	100/60 98.4
Before tx.	100	24	100/60
Before dismissal	112	24	100/60
8) Side effects (ex. nausea, dizziness)	none		
9) Efficacy of Premedication used (circle one)			
<input checked="" type="checkbox"/> Very effective			
<input type="checkbox"/> Effective			
<input type="checkbox"/> Ineffective			
10) Resident's name:	J. K. [Signature]		Date: Sept 1, 1980

Figure 3. Pedodontic premedication experience — data base.

The effectiveness of the sedation-treatment experience with alphaprodine in this study was based on the operator's evaluation of whether he/she was able to accomplish the planned treatment. The rating scale used was: (1) ineffective, (2) effective, and (3) very effective. The results were considered very ef-

fective when the planned treatment was accomplished with ease; effective when the planned treatment was accomplished, although with some difficulty; and ineffective when planned treatment was not able to be accomplished. In evaluating effectiveness, patients were divided into six groups (Figure 5):

1. alphaprodine alone (15 cases),
2. alphaprodine with nitrous oxide only (11 cases),
3. alphaprodine with promethazine combination (30 cases),
4. alphaprodine with hydroxyzine (21 cases),
5. alphaprodine with hydroxyzine and diazepam (11 cases),
6. alphaprodine with hydroxyzine and chloral hydrate (15 cases).

In the hydroxyzine, promethazine and hydroxyzine, diazepam or chloral hydrate combinations, nitrous oxide/oxygen was used as deemed necessary to supplement the sedative drugs. In 11 cases diazepam was given orally (.2-.35 mg/kg) with hydroxyzine, and in 15 cases chloral hydrate was given orally with hydroxyzine. The preferred method of administration for these preprocedural medications is to accomplish it in the office about ½ hour preoperatively. In this way the patient can be monitored and the proper administration and dose can be ascertained.

Naloxone was administered postoperatively to patients on the basis of how reactive they were at the completion of the treatment session. Patients were monitored postoperatively for a minimum of one hour prior to discharge.

Results

Of a total of 103 patients treated with alphaprodine: 54 (52%) were considered very effective (score 3), 33 (32%) were considered effective (score 2), and 16 (16%) were considered ineffective (score 1). The dosage range used was a minimum of 0.2 mg/kg and a maximum dose of 1.8 mg/kg (Figure 6). In only one case was the dose of 1.8 mg/kg used, the next lowest dose being 1.3 mg/kg. The median

dose was 0.9 mg/kg (32%) and the second most frequent dose was 0.8 mg/kg (21%). Ninety-two percent of the cases were treated utilizing a dosage range from 0.4 mg/kg to 1.1 mg/kg. The average effectiveness of this alphaprodine sedation technique was also compared to dosage (Figure 7).

The ineffective cases (16) were treated utilizing the higher end of the dosage range (0.8 mg/kg to 1.3 mg/kg). Of these 16 cases, 5 were sedated with alphaprodine alone and 11 were treated using various drugs in combination with the alphaprodine. The effectiveness of the alphaprodine sedation technique described also seems to decrease significantly above the dose of 0.9 mg/kg (Figure 7). Side effects were reported in 13 of the 103 cases. Reported side effects included: nausea (2), unreactive for a prolonged period postoperatively (1), postoperative dizziness (1), swelling at the injection site (8), and respiratory depression (1) (Figure 8). In all cases the side effects were minor and were easily treated or were closely monitored until they subsided. The single case of respiratory depression was treated with 0.2 mg of naloxone administered submucosally at the first sign of depression.

Discussion

Analysis of the data reveals that in 84% of the patients determined to be untreatable utilizing routine management techniques and who were sedated with alphaprodine, treatment was accomplished. In 16% of the cases treatment was unable to be accomplished. The dose range used was wide and there was no significant relationship between the alphaprodine dose in mg/kg and its effectiveness in controlling unacceptable behavior. There was a higher percentage of effectiveness when alphaprodine was used in combination with other drugs (Figure 5): alphaprodine alone; 27% ineffective, 73% effective, and Combinations; 15% ineffective, 85% effective.

There does appear to be some significance to the fact that the failures (ineffective cases) were at the higher dose levels (.8 to 1.3 mg/kg). There could be two explanations for this phenomenon:

	Drug(s)	Cases	*Effectiveness			% Effectiveness
			1	2	3	
Figure 5. Effectiveness of alphaprodine and drug combinations in controlling undesirable behavior.	Alphaprodine alone	15	4	5	6	73%
	Alphaprodine & N ₂ O	11	1	6	4	90%
	Alphaprodine & Hydroxyzine	21	1	4	16	95%
	Alphaprodine, Hydroxyzine & Diazepam	11	3	3	5	73%
	Alphaprodine, Hydroxyzine & Chloral Hydrate	15	1	7	7	93%
	Alphaprodine & Promethazine	30	6	8	16	80%

*1. ineffective, 2. effective, 3. very effective

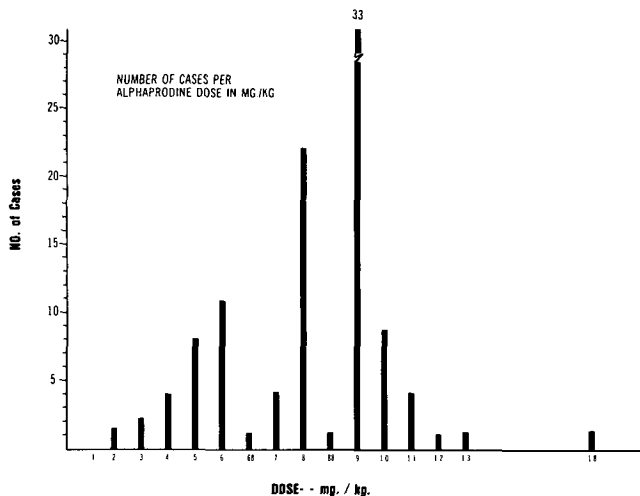


Figure 6. Number of cases per alphaprodine dose in mg/kg.

- (1) In considering all the criteria, a judgement error was made in setting the alphaprodine dose levels too low or in selecting the inappropriate drug combination, or
- (2) The patient was not appropriate for sedation and general anesthesia would have been more appropriate to provide adequate treatment.

There was also no relationship between alphaprodine dose in mg/kg and side effects (Figure 9). The most prevalent side effect (8 out of 13) was swelling at the injection site. In 7 of 8 such cases, promethazine was used as the tranquilizer, and it was administered submucosally along with the alphaprodine. In only one case was there swelling at the injection site when alphaprodine was injected alone submucosally. In three cases where postoperative dizziness, a prolonged unreactive period postoperatively, and respiratory depression were reported, the children were on the heavier and older side of the weight and age range: (1) unreactive — 31 kg 7 yr, (2) dizziness — 23 kg 5 yr, and (3) respiratory depression — 29 kg 11 yr. In each of the above three cases alphaprodine was combined with oral hydroxyzine and chloral hydrate.

The prolonged action of the chloral hydrate can explain the first two, and respiratory depression has been reported with chloral hydrate.¹² The combination of alphaprodine, hydroxyzine, and chloral hydrate in these cases may possibly be attributed to the additive effects of the sedative drugs in combination with the alphaprodine. The use of alphaprodine in combination with one or more tranquilizer or sedative drugs has been cautioned by several authors.^{2,3,5,6,8,9,10}

When the effectiveness of the drug was related to age, there was no significant difference in effectiveness in the age group ranging from 1 year to 7 years, 6 months. Only two cases were over the age of 7 years, 6 months and although they were con-

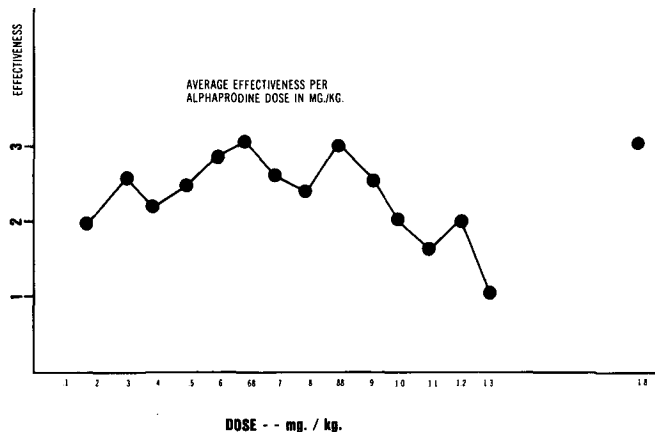


Figure 7. Average effectiveness of alphaprodine dosage in mg/kg.

Nausea	Unreactive	Dizziness	Swelling	Resp. Dep.
2	1	1	8	1

Side Effects / Drug Combination

Drugs	Cases	Side Effects
Alphaprodine alone	15	1 — Swelling
Alphaprodine & N ₂ O	11	2 — nausea
Alphaprodine & Hydroxyzine	21	0
Alphaprodine, Hydroxyzine & Diazepam	11	0
Alphaprodine, Hydroxyzine & Chloral Hydrate	15	1 — unreactive 31 kg, 7 yr 1 — resp. dep. 29 kg, 11 yr 1 — dizziness post op. 23 kg, 5 yr
Alphaprodine & Promethazine	30	7 — Swelling

Figure 8. Number and types of side effects and their incidence with various drugs and combinations.

sidered effective, no conclusion can be drawn from this data.

Conclusions

It is extremely difficult to draw concrete conclusions from this study due to the small number of cases evaluated in each category, and because of the wide variety of drug combinations involved. The high degree of operator subjective evaluation involved in determining dosage and drug combinations also

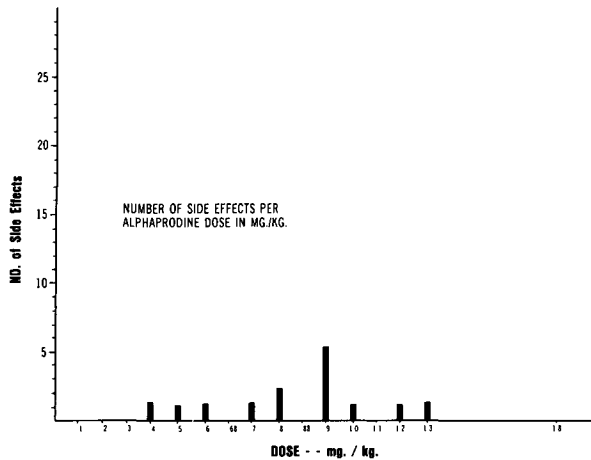


Figure 9. Number of side effects per alphaprodine dose in mg/kg.

makes it difficult to draw conclusions concerning efficacy relative to dose levels in mg/kg.

One significant conclusion which can be made is that one cannot assign a specific dose level, e.g., 0.5 mg/lb, that will be appropriate or effective all of the time for sedating child dental patients who are difficult to manage in the usual manner. A wide dose range can and should be utilized and additional drugs may be indicated depending upon the operator's evaluation of the patient. This is in agreement with the statement of Tobias, Lipschultz, and Album¹¹ that, "in premedication (sedation) in dentistry for children, we are dealing with a complex multifaceted situation, which includes all the environmental factors and the nature of the dental procedures required."

The use of sedation as a treatment modality in pediatric dentistry is a complicated endeavor and involves a great deal of subjective evaluation on the part of the treating doctor, which is in large part based upon a knowledge of the effects of different sedative drugs and upon operator expertise in evaluating patient behavior. The data presented should leave no doubt that alphaprodine is a safe and effective sedative drug for use with young,

1- to 7-year-old children for short (max. 1½ hrs.) dental procedures. This study also shows that the drug, when properly used and the patient properly monitored, has a wide, safe dose range.

The side effects experienced also indicate that alphaprodine should be used with great caution in combination with promethazine given submucosally, and when combined with multiple tranquilizing drugs.

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