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Sedation liabilities in pedodontics

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Case reports of child morbidity and mortality resulting from sedatives administered during dental procedures have appeared in dental journals on the average of once every two to three years. These published reports in addition to several unreported cases have led to speculation as to the risks involved with various child sedative techniques. Therefore, research in sedation liabilities in children's dentistry was initiated.

The research goals were threefold:

1. to obtain case history reports of adverse reactions which occurred during child sedation procedures and to analyze these reports for common variables,
2. to obtain information on sedative procedures currently employed by children's dentists and to determine specific sedative techniques and trends,
3. to determine the incidence of adverse reactions with the various sedation procedures and to compare the relative liabilities between sedation techniques.

The research efforts were varied; several computer and manual searches of the medical and dental literature were conducted to establish background information for the project. A national survey was taken of the members of the American Society of Dentistry for Children (ASDC) to determine what sedation procedures were actually being used and to obtain case reports of any sedation-related adverse reactions. A second survey was made of all state dental societies and state board of dental examiners to determine if any drug-related adverse reactions occurred within their respective states. A third survey was conducted of the advanced education pedodontic programs to determine what child sedation procedures were currently being advocated. Under the freedom of information act, the Food and Drug Administration supplied information on pertinent drug-related adverse reactions. Finally, companies providing professional liability insurance were contacted in an effort to obtain additional information on adverse reactions.

The most productive effort was the information obtained from the ASDC survey which was conducted

in March and June of 1980. Society members were mailed 6,397 questionnaires. Each questionnaire consisted of questions relating to sedative drug usage and provided a form to gather information on adverse reactions which might have occurred. There was a response rate of 45.5%; 2,911 of the questionnaires were returned. Chart 1 shows the geographic distribution of the ASDC survey response.

The first alphaprodine data which is to be presented describes the method in which alphaprodine is used for child sedation in dentistry. Chart 2 demonstrates the geographic distribution of those responders who indicated they used alphaprodine. Alphaprodine has been termed a "West Coast" sedative in children's dentistry and this is reflected by this scattergram. This geographic distribution coincides with the earliest literature advocating the use of alphaprodine in children's dentistry which was published in local west coast dental journals. It was also found that a general correlation existed in the geographic use of alphaprodine and the geographic distribution of pedodontic programs advocating alphaprodine sedation.

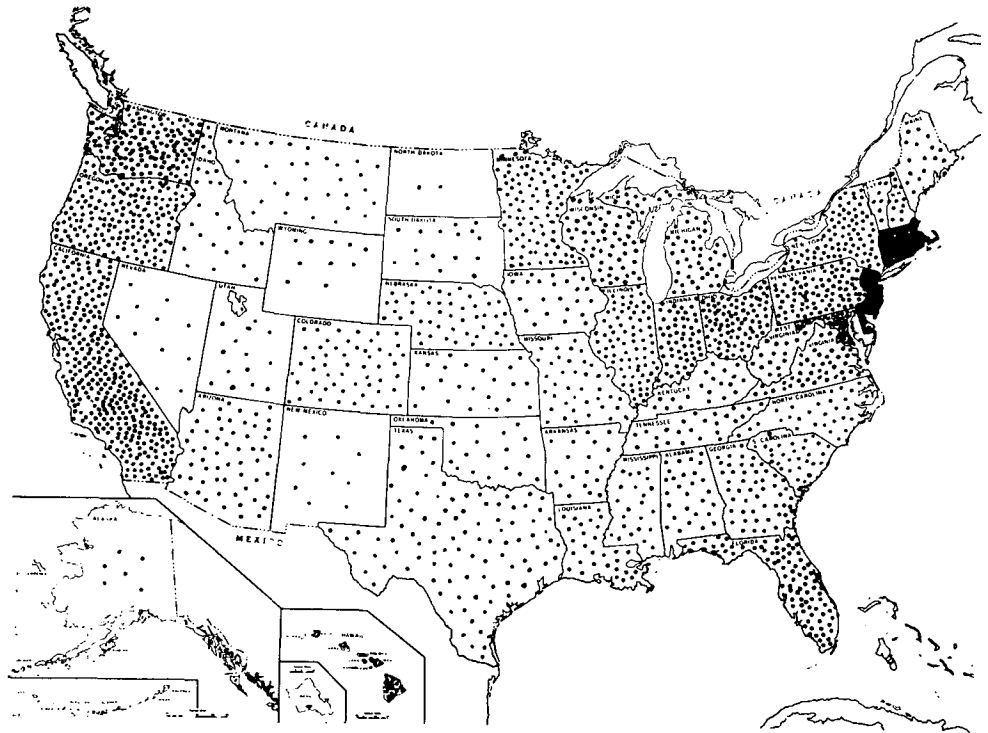
It was found that the most common method of sedating children in dentistry was the use of a narcotic sedative. Table 1 shows the breakdown of the types of narcotics being used by pedodontists. Alphaprodine and meperidine are the only two drugs of this category in widespread use.

When this data is compared to earlier surveys of narcotic drug usage by pedodontists, it appears that alphaprodine has been increasing in popularity relative to meperidine.

Graph 1 demonstrates the manner in which narcotics are being used. Although this graph relates to narcotics in general, the same trends were found for alphaprodine users. Most clinicians used alphaprodine with a cosedative; the most common cosedative is promethazine, followed by hydroxyzine. The alphaprodine/promethazine technique is about three times more popular than the alphaprodine/hydroxyzine technique.

The fourth category comprises cases in which the

Chart 1. Geographic distribution of the ASDC survey response (N=2911).



child died. There have been at least 25 cases of death or severe morbidity in the past 20 years. In subsequent analyses, the adverse reactions will be divided into minor and severe reactions. The term "severe reactions" will refer to reports in which the child was hospitalized, had severe morbidity, or died.

Graph 2 demonstrates the mode of administration of alphaprodine: the subcutaneous or oral submucosal route is the most popular. The most common sites of the oral submucosal injection is in the buccal fold, the sublingual area, or the mandibular retromolar region.

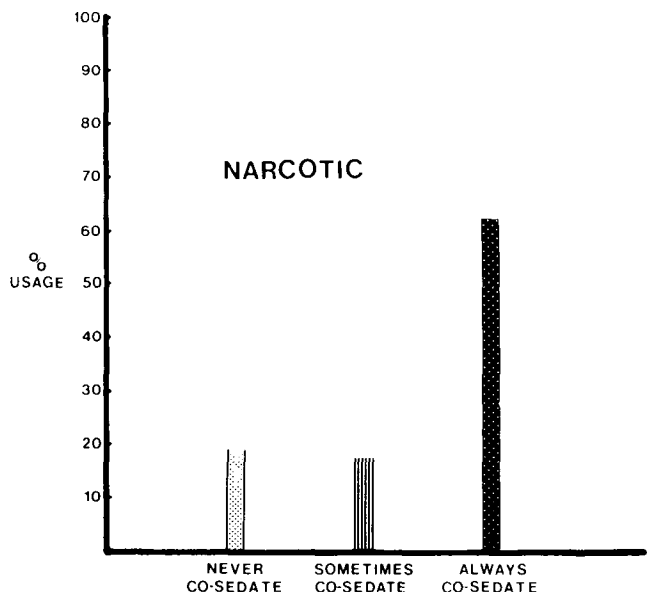
The next three graphs are representative of the dosages used in alphaprodine sedation techniques. Within the questionnaire there were two methods in which a clinician could indicate dosages for a specific sedation technique: one was by milligrams per pound and the other was a low and a high dosage range.

Graph 3 is a percent cumulative frequency graph of the responses given by clinicians administering

alphaprodine on a mg/lb basis. The specific technique was the use of alphaprodine submucosally without a cosedative. This graph is a convenient way of visualizing the percentage of clinicians using a given dosage. For example, at the 50% level (which is the median), the dose was 0.25 mg/lb. That is, one half of the clinicians were injecting alphaprodine submucosally without a cosedative at or below 0.25 mg/lb. If the low and high 25th-percentiles are considered extremes, then the middle half of these clinicians used a dosage range

<i>Pedodontic Narcotic Users (N=513)</i>		
Demerol	262	51.1%
Nisentil	173	33.7%
Fentanyl	0	0
Other	78	15.2%

Table 1. Breakdown of the types of narcotics used by pedodontists.



Graph 1. Manner in which narcotics are being used.

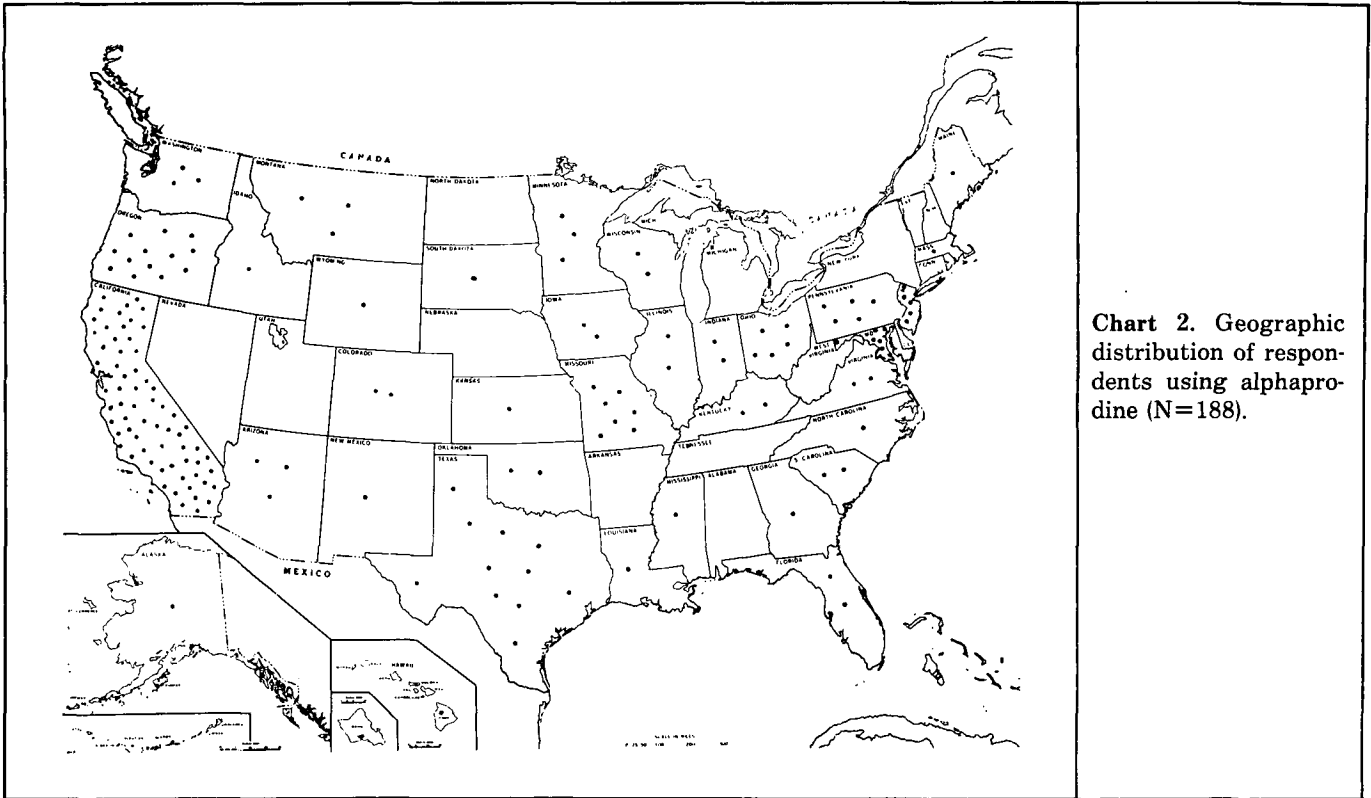


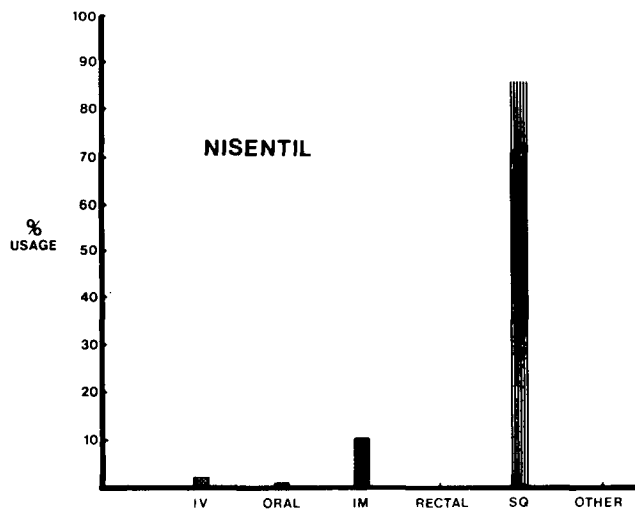
Chart 2. Geographic distribution of respondents using alphaprodine (N=188).

of about 0.2 to 0.4 mg/lb.

Using responses from clinicians who use a dosage range, graph 4 shows the low and high dose for the same alphaprodine technique. As can be seen, at the median, the dosage range is approximately 6 to 9 mg, and the middle half of these clinicians used a dosage of approximately 4-12 mg.

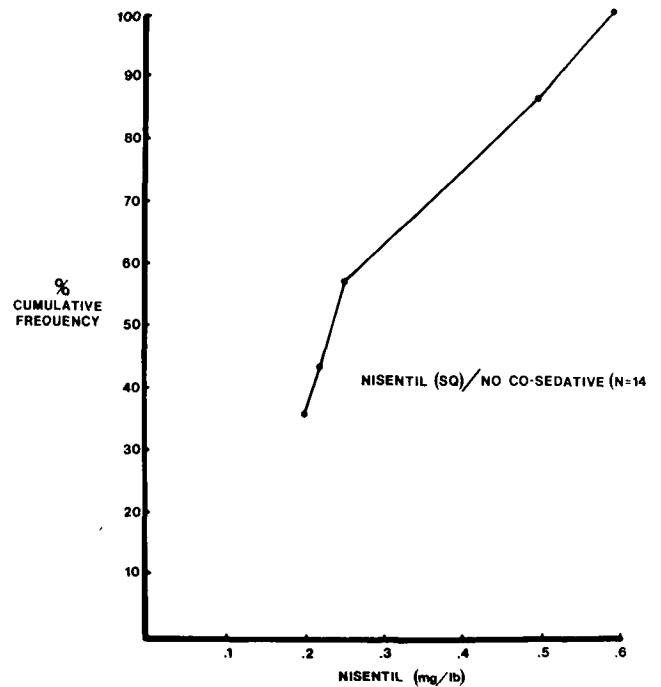
Graph 5 describes the same data shown in graph 4 by showing the frequency distribution of various dosage ranges. As can be seen, the majority of the clinicians using this technique used dosages below 12 mg.

Similar dosage results were demonstrated for the

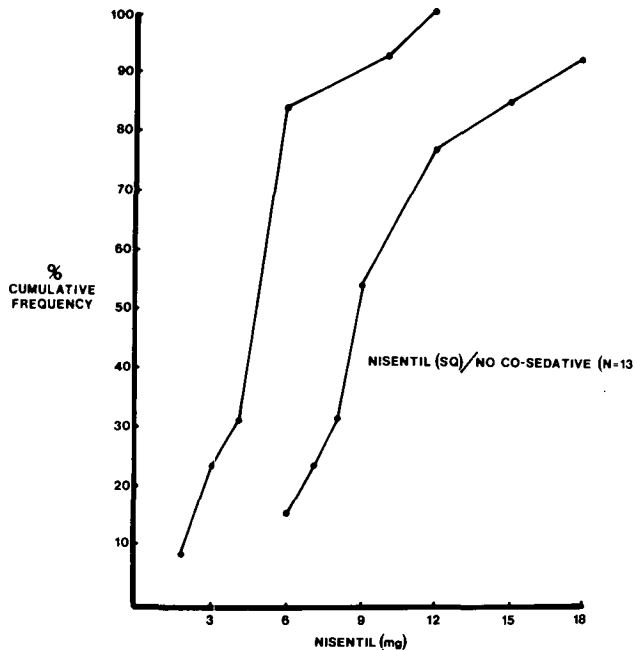


Graph 2. Mode of administration of alphaprodine.

alphaprodine/promethazine and the alphaprodine/hydroxyzine techniques even though lower dosages would be expected. In all three alphaprodine sedation procedures the clinicians tended to use the same doses. This observation compares favorably with publications suggesting the use of alphaprodine



Graph 3. Percent cumulative frequency of responses given by clinicians administering alphaprodine on a mg/lb basis.



Graph 4. Low and high dose for the same alphaprodine technique.

in doses of 6, 9, and 12 mg depending on age and degree of combativeness of the child. These doses are also probably related to the convenience of drawing these amounts from 60 mg/cc multidose vials. However, the data seems contradictory to the accepted concept of using smaller narcotic doses when a cosedative is employed.

The next part of the discussion will describe the analysis of the case reports and the analysis of alphaprodine adverse reactions. Diagram 1 shows the analysis strategy which was used. The ASDC survey yielded 145 valid case reports of adverse reactions. Those were combined with 32 additional case reports obtained from the other sources mentioned earlier. This yielded 177 case reports for analysis. A general data pool was developed and general statistics were then computed as a function of key parameters such as the drugs involved; the sex, age, weight of the child; the type of adverse reaction; and severity of the reaction.

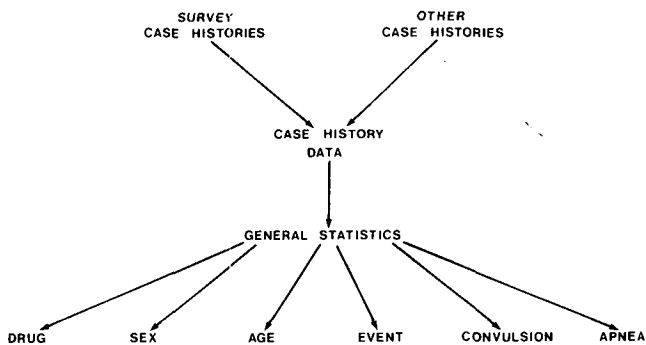
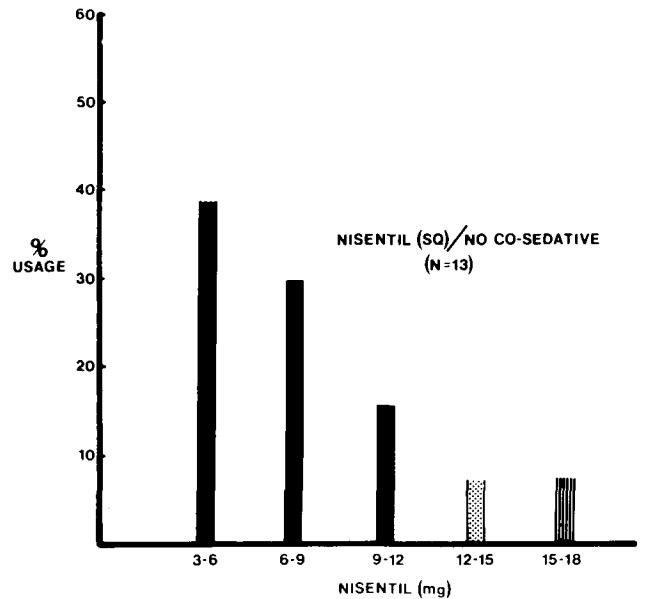


Diagram 1. Data and statistics flow chart.



Graph 5. Frequency distribution of various dosage ranges.

Case reports were considered valid if they met the following criteria: (1) the report indicated that the adverse reaction was a significant complication, that is, respiratory depression with cyanosis, convulsion, hospitalization as a result of sedation, cardiac arrest, or death; and (2) the report indicated that the incident occurred during a child sedation procedure in which drugs were being employed to calm the child. Excluded were case reports in which adverse reactions occurred only with nitrous oxide, local anesthetic, drugs which are not considered sedatives, or in which the adverse reaction occurred during a general anesthetic in a hospital setting.

Eleven percent of those clinicians using drugs to sedate children felt that they had had a significant adverse reaction.

The geographic distribution of the alphaprodine reactions are shown in chart 3. Again there seemed to be a general correlation between areas of high alphaprodine usage and areas where alphaprodine was advocated in teaching programs.

The prevalence of the adverse reactions is shown in graph 6, which shows an exponential increase in the number of adverse reactions as a function of time. There are probably several explanations for this prevalence curve. First, the use of sedatives in pediatric dentistry has greatly increased over this time period; secondly, both the number of pediatric dentists and the number of children being treated increased. Perhaps most significantly, most of the data came from a retrospective study in which the responder's memory was better at the time the data was gathered.

Graph 7 shows the total number of adverse reactions associated with various sedatives. This graph

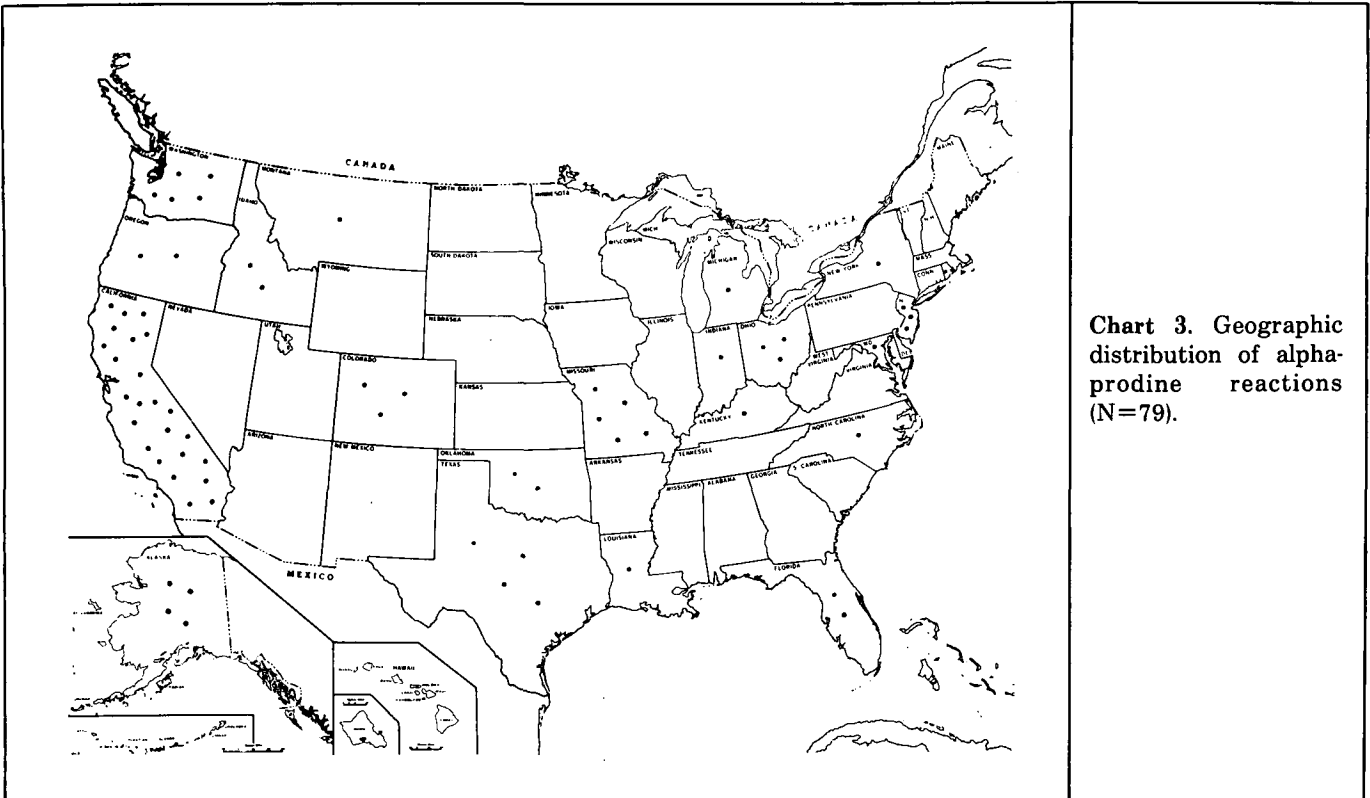
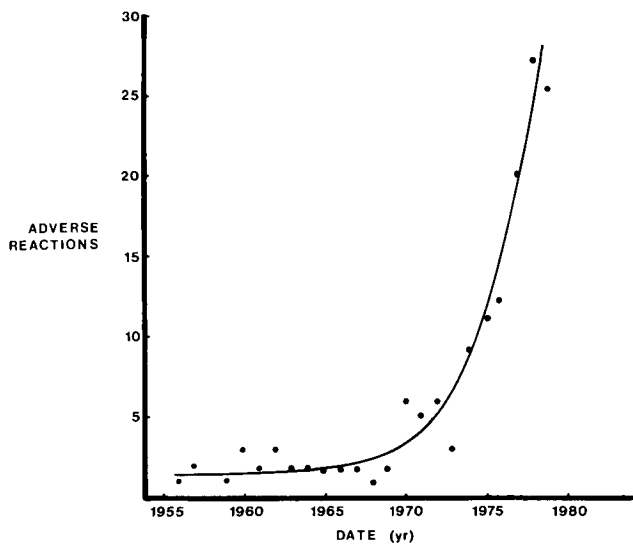


Chart 3. Geographic distribution of alphaprodine reactions (N=79).

reflects a subjective evaluation of each case report to determine the drug which could be considered the major sedative used. For example, if alphaprodine and promethazine were used in combination, alphaprodine would be assigned the major sedative and promethazine the cosedative. Similar evaluations were made for all drug combinations. Graph 7 plots the major sedative as a function of adverse reaction; alphaprodine had the highest number of adverse reactions.

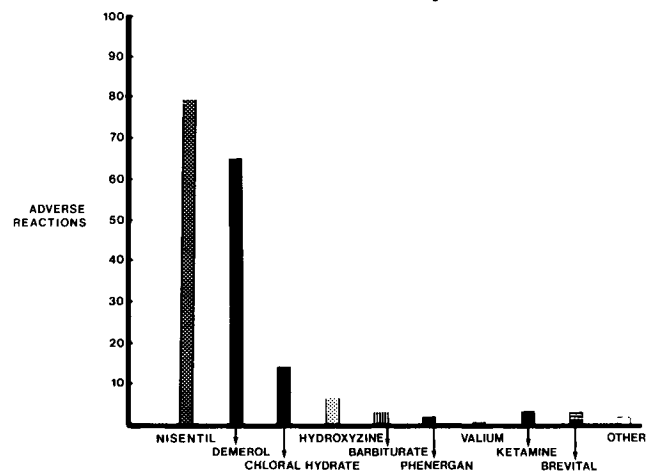
Each of the case reports were evaluated for degree



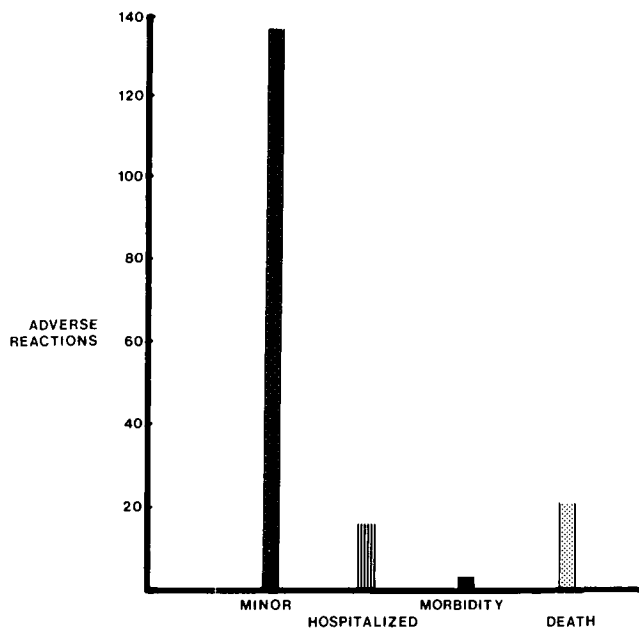
Graph 6. Prevalence of adverse reactions.

of severity. Graph 8 shows all of the adverse reactions divided into four categories. The case report was considered minor if the incident involved only the dental office staff, the advanced life support of a hospital was unnecessary, and the child fully recovered.

The vast majority of the adverse reactions reported fell into this category. The second category were those cases in which advanced life support was necessary and the child was transported to the hospital. Many of the children in this category were intubated and spent the night in an intensive care unit. However, these children fully recovered from



Graph 7. Total number of adverse reactions associated with various sedatives.



Graph 8. Adverse reactions divided into categories.

the episode. The third category was cases in which the child did not fully recover and had severe morbidity.

The fourth category comprises cases in which the child died. There have been at least 25 cases of death or severe morbidity in the past 20 years. In subsequent analyses, the adverse reactions will be divided into minor and severe reactions. The term "severe reactions" will refer to reports in which the child was hospitalized, had severe morbidity, or died.

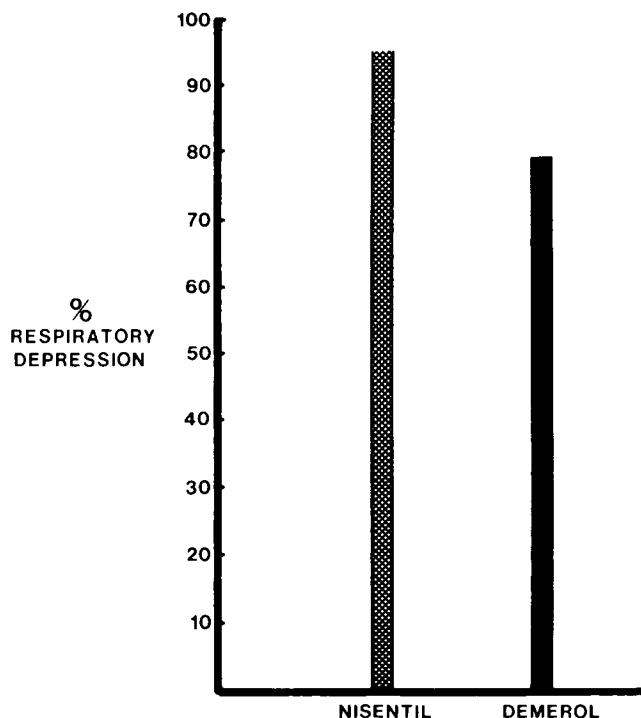
An analysis of the child-related variables showed the following: the typical adverse reaction occurred in healthy children between the ages of 2-4 years with body weights between 25 and 45 pounds. There was no sex predilection.

Analysis of the clinician variables showed the following: the clinician most likely to experience a problem was a pedodontist in his second decade of sedative use, and who sedated greater than 10% of his patient population. The pedodontist's educational background had no influence on adverse reaction incidence.

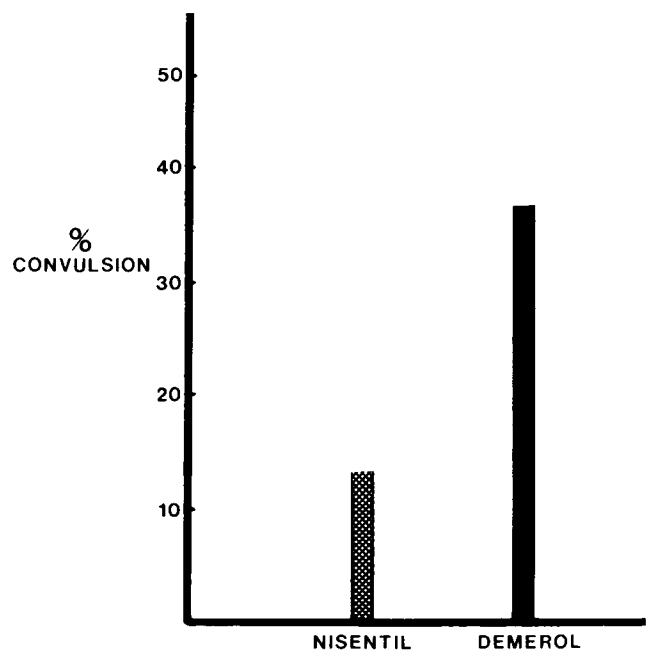
Graph 9 shows the rate of respiratory depression in case reports in which alphaprodine and meperidine were the major sedatives. Statistically, in those reports in which alphaprodine was used, the clinician was more likely to have commented about severe respiratory depression than those cases in which meperidine was used.

Case reports in which meperidine was used had a much higher occurrence of convulsion when compared to alphaprodine, as shown in graph 10. This was a significant difference.

This difference in the type of sedative complication produced by these two popular child sedation techniques is of paramount importance. First, convulsive episodes within the case reports tended to be more



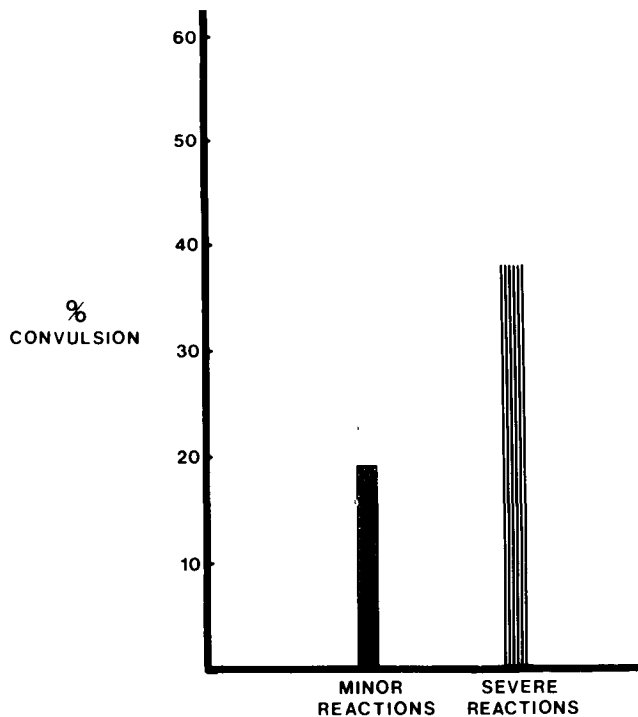
Graph 9. Rate of respiratory depression in cases in which alphaprodine and meperidine were the major sedatives.



Graph 10. Comparison of convulsion rates between alphaprodine and meperidine.

severe in nature as shown in graph 11. Secondly, of these two complications, the respiratory depression is reversible with a narcotic antagonist whereas the convulsive complication is not. Thirdly, there are collaborative animal studies which have shown this same trend in sedative complications for alphaprodine and meperidine as well as the lack of responsiveness of the convulsive complication to a narcotic antagonist.

Another important factor which was found in the



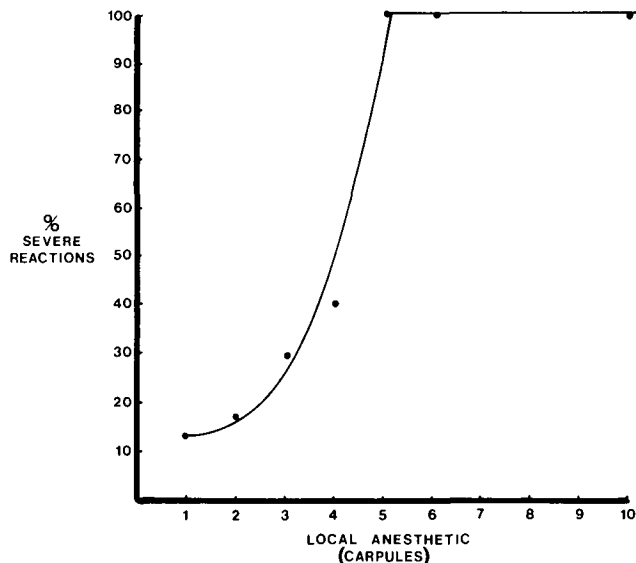
Graph 11. Severity of convulsive episodes.

case report analysis was the probability that the local anesthetic helped precipitate the adverse reaction. Graph 12 plots the rate of severe adverse reaction as a function of the number of carpules of local anesthetic administered. In those case reports in which only one carpule of local anesthetic was administered, about 12% reported a severe reaction. As the number of carpules were increased, the rate of severe reaction also increased.

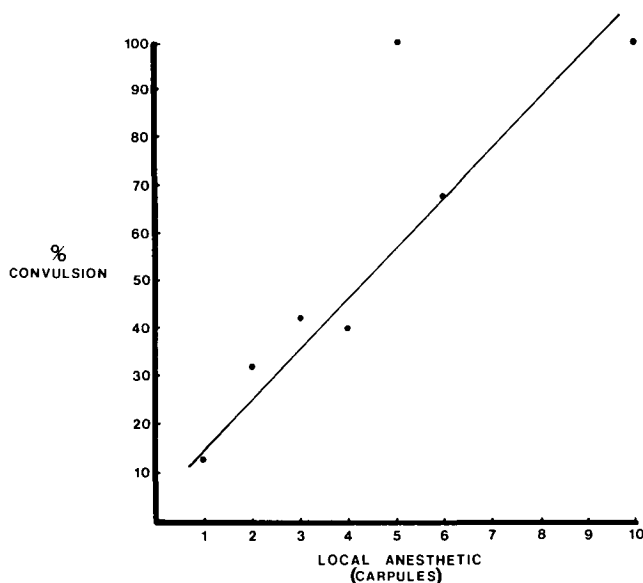
Graph 13 shows a direct linear relationship between the number of carpules of local anesthetic administered and the rate of convulsion, and, as noted earlier, convulsions are generally associated with severe reactions. In Graph 14 the rate of convulsion was related to the type and concentration of local anesthetic. The more concentrated the local anesthetic, the more likely would the case report indicate a convulsive episode.

Again, animal studies tend to collaborate this observation. Several animal studies have demonstrated an increased toxicity to the combined use of local anesthetic and narcotic drugs over that which would have been predicted when these drugs were used alone.

The relationship between the alphaprodine dosage and the occurrence of the adverse reactions is not straightforward. In general, the cases fell into two categories: (1) those cases in which the alphaprodine dose would be considered high, or the combined dose of alphaprodine plus cosedatives would be considered high, and (2) those cases in which the alphaprodine dosage was relatively low, well within the typical



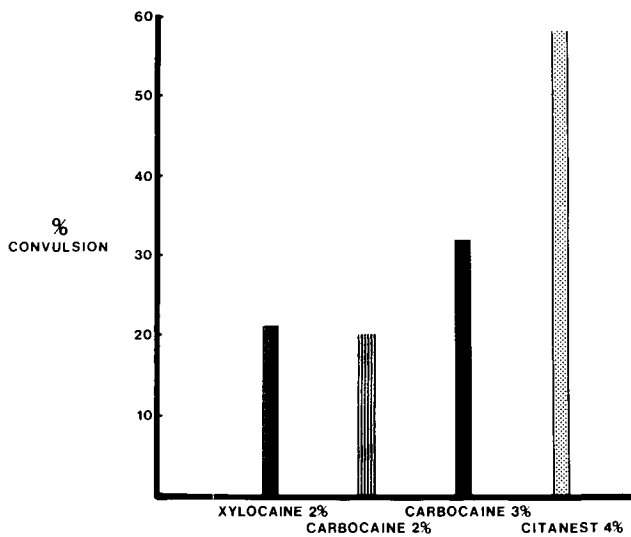
Graph 12. Rate of severe adverse reaction as a function of the number of carpules of local anesthetic administered.



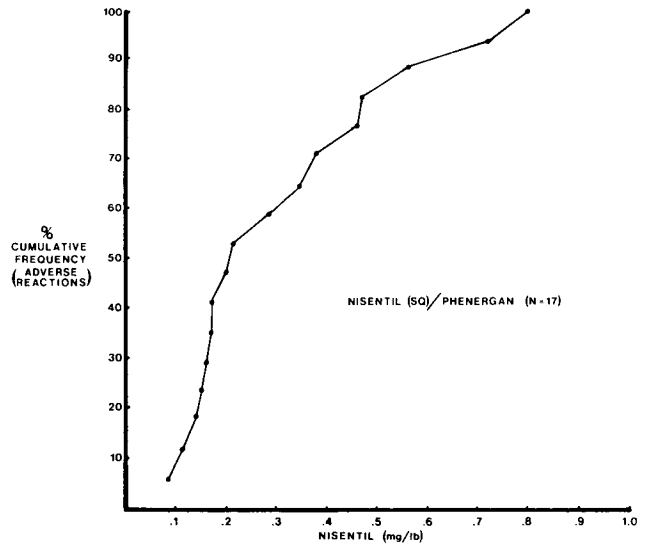
Graph 13. Relationship between number of carpules of local anesthetic administered and the rate of convulsion.

dosages being used. Both categories had a significant number of adverse reactions and represent a third major finding of the case report analysis. That is, any plausible explanation for these alphaprodine adverse reactions must account for both the adverse reactions occurring at both the high dose and the low dose ranges.

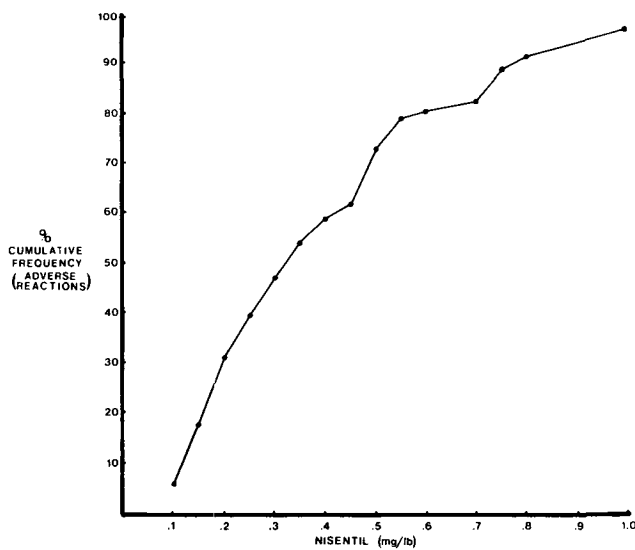
Graph 15 shows the percent cumulative frequency for all adverse reactions in which alphaprodine was used as the major sedative. As can be seen from this graph, the median occurred at about 0.35 mg/lb. That is, one half of the total cases reporting the use of alphaprodine had an adverse reaction at 0.35 mg/lb or less. Graph 16 separates these alphaprodine cases into severe (bottom line) and minor adverse reactions.



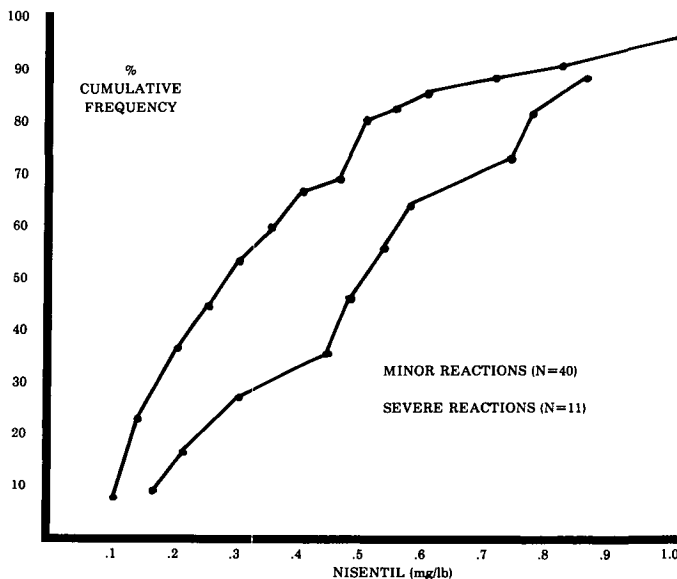
Graph 14. Rate of convulsion related to type and concentration of local anesthetic.



Graph 17. Alphaprodine dosages reported in which a specific alphaprodine technique was employed.



Graph 15. Percent cumulative frequency for all adverse reactions in which alphaprodine was used as the major sedative.



Graph 16. Severe and minor adverse reactions.

As might be expected, there was a shift toward the heavier alphaprodine doses for the more severe reactions. However, relatively low doses of alphaprodine have caused adverse reactions of a severe nature.

Graph 17 shows the alphaprodine dosages reported in the case histories in which a specific alphaprodine technique was employed. In these cases, alphaprodine was used as the major sedative and promethazine was used as a cosedative. The alphaprodine was administered submucosally at the dose specified in the graph. Neither the dosage of the cosedative nor its mode of administration was considered. At the 0.25 mg/lb dose level, one half of the alphaprodine adverse reactions were reported to have occurred. This is significant when one considers that the 0.25 mg/lb dose level has been the recommended dose of alphaprodine when cosedating with promethazine.

For the last part of this discussion, the work that is being done on various risk factors in the alphaprodine sedation technique will be described.

In the ASDC survey each respondent was asked to estimate the total number of sedations that he had given. From the other questions within the survey, it was possible to determine the sedation technique employed and the length of time that it was employed. From the 144 adverse reactions which were collected from the survey, it was also possible to determine the sedation technique employed in each case report. Using this information, it is theoretically possible to compute numerical values for various sedation procedures. The strategy is summarized in diagram 2. Statistical analyses were then used to compute significant differences between various sedation procedures and between variations in a given sedation technique.

The overall incidence of adverse reaction with

alphaprodine is about 1:6,781 sedations, and death and morbidity incidence about 1:194,714 sedations. Because the death and morbidity calculations had such a small n-value, probably a more realistic incidence value is 1:124,607 sedations — which was the incidence predicted for all narcotics sedations.

Because of the assumptions made in obtaining these figures, their absolute numerical value is suspect and should be used as a general order of magnitude. The comparative evaluations, however, should have a high degree of validity in that the same assumptions were made for all categories. Significant numerical differences should then reflect significant differences in risk factors.

Table 2 compares the influence of using cosedation on the risk factors with alphaprodine. The use of a cosedative did tend to improve the risk factors. This difference was shown to be statistically insignificant. However, if one considers the relative low n-value in the non-cosedation group, and that good statistical significance was shown when the same computations were made for all narcotic sedations, the use of a cosedative with alphaprodine will probably lessen the risks of adverse reactions.

Technique	Sedations	Incidence
Nisentil/cosedative	309,024	1:6,575
Nisentil/no cosedative	64,878	1:4,055

Table 2. Comparison of the influence of using cosedation on the risk factors with alphaprodine.

Table 3 compares the risk factors of the two most popular cosedatives being used with alphaprodine. The alphaprodine/hydroxyzine technique appeared to be less risky than the alphaprodine/promethazine technique. This observation was statistically significant.

Technique	Sedations	Incidence
Nisentil/Phenergan	204,522	1:6,391
Nisentil/Hydroxyzine	74,453	1:24,818

Table 3. Comparison of the risk factors of the two most popular cosedatives used with alphaprodine.

Table 4 compares the risk factors involved in the use of nitrous oxide/oxygen in conjunction with alphaprodine. These values were not statistically different, and because the n-values were relatively large, nitrous oxide/oxygen probably does not improve the risks involved with alphaprodine child sedations.

The influence of the mode of administration was evaluated for risk factors. As shown in table 5, a com-

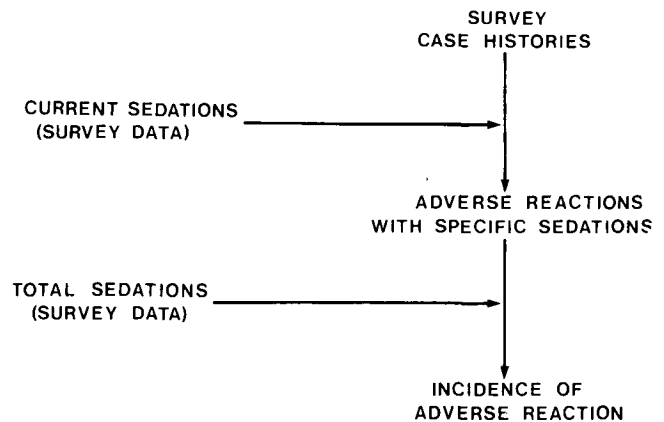


Diagram 2. Strategy for computing numerical values for various sedation procedures.

parison was made between the two most common methods of administering alphaprodine, that is, submucosal administration and intramuscular injection. Statistically the submucosal injection was safer. Further evaluation of the alphaprodine sedation technique for variables such as dosage, was impossible due to the rapid decrease in the n-values as specific sedation techniques were isolated from the data pool.

In summary, the following conclusions were reached in this ongoing project:

1. sedatives are an important aspect of child management in dentistry,
2. a narcotic sedative technique is the most common sedative technique used,
3. meperidine and alphaprodine are the chief narcotics being used in child sedation, and alphaprodine has been increasing in popularity relative to meperidine,
4. a narcotic sedation technique has an adverse reaction risk of about 1:5,000 compared to a risk of 1:20,000 to 1:30,000 for non-narcotic sedative techniques — the death and morbidity incidence

Technique	Sedations	Incidence
Nisentil/Nitrous Oxide	225,255	1:6,435
Nisentil/no Nitrous Oxide	142,604	1:5,093

Table 4. Comparison of the risk factors involved in the use of nitrous oxide/oxygen with alphaprodine.

Technique	Sedations	Incidence
Nisentil (SQ)	356,914	1:6,998
Nisentil (IM)	18,975	1:2,108

Table 5. Comparison of the two most common methods of administering alphaprodine, submucosal and intramuscular.

for narcotics is about 1:100,000 and is negligible for the non-narcotic techniques,

5. an alphaprodine sedative technique is as safe or safer than a meperidine sedative technique,
6. a narcotic/promethazine sedative is more risky than a narcotic/hydroxyzine sedative,
7. narcotic and local anesthetic combinations interact to increase the risk of adverse reaction,
8. no one explanation could account for the occurrence of the adverse reactions — the most probable causes are:
 - A. overdose,
 - B. hypersensitivity,
 - C. intravascular injection,
 - D. abnormal respiratory physiology,
9. a practitioner can lessen the occurrence of adverse reactions by:
 - A. minimal use of sedatives,
 - B. using low dose techniques,

- C. using minimal amounts of local anesthetic solution,
- D. having a narcotic antagonist available for narcotic sedations,
- E. careful patient monitoring,
- F. avoiding intravascular injection.

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