

## Alphaprodine in twenty years of sedation experience

Robert L. Creedon, DDS

Alphaprodine was first used for premedication of dental patients at the Cincinnati Children's Hospital Medical Center in 1966 following the discovery of an article published that year in the Journal of the American Society of Dentistry for Children by Maurice C. Corbett. Prior to that time a variety of medications had been used.

My own personal experience with premedication began over twenty years ago with a phenothiazine called promazine hydrochloride (Sparine<sup>®</sup>). It was unforgettable in that we ended up resuscitating our patient, who was an adult male, on the floor of the operatory. Promazine was used often, however, and that one case was our only major complication.

Since that time we have employed a wide variety of drugs alone and in combination; and sometimes in large doses. I can recall an instance in which 1.5cc of Mepergan<sup>®</sup>, which is 75 mg of meperdine and 75 mg of promethazine in the 50 mg/cc concentration, was used for a seventeen-year-old profoundly retarded patient. The only effect produced was nausea and emesis; almost no sedation. Other drugs used over the years have been promethazine, hydroxazine, chloral hydrate, and diazepam. Many types and combinations have been used since we have so many physically handicapped and mentally retarded patients who are large, severely involved adolescents.

Yet another combination used has been the "lytic" or "cardiac" cocktail consisting of meperidine, promethazine and a phenothiazine. It is a very effective combination as one might expect, but it also has many serious side effects. It is most often used for cardiac catheterization and occasionally will produce respiratory depression of some magnitude, and even arrest.

In order to put our early use of premedication into proper prospective, one needs to have an appreciation for the patient types and the situations that we were working under in those days. Our facilities were in satellite operations spread around the city of Cincinnati. We were not able to bring patients to the Children's Hospital for general anesthesia unless they were patients of record of the hospital for at least the preceding year. There were many that did not fit that category.

We have always had a large population of older, profoundly retarded patients. We have been associated for twenty years with the Hamilton County Diagnostic Center for Mental Retardation, now the Cincinnati Center for Developmental Disabilities. We also have a large population of cerebral palsy patients from the very young to the adult who many times cannot find dental service in our community.

We quickly discovered that alphaprodine was the best agent we had tried for children between the ages of  $2\frac{1}{2}$  to 6 years. We have used the drug in younger children, but only rarely, for very short procedures such as the extraction of anterior primary teeth or for trauma management in the emergency room. Alphaprodine has been used in adolescent and young adults, but the objectives were somewhat different as were the responses obtained.

We have always used alphaprodine via the buccal vestibular or retromolar pad injection. We would estimate that over the 20 years we have probably sedated approximately 5,500 to 6,000 patients, but it is impossible to say how many of those were given alphaprodine. Alphaprodine became a favorite agent of all who have worked with us. In fact, a local pedodontist on our attending staff began using the drug at the same time we did and has treated approximately 1,500 to 2,000 patients, with about 400 cases in the year prior to its withdrawal from the market. We were able to document only 75 cases since we did not keep a record of past patients from the general patient population who might have received alphaprodine.

In all of our patients treated by whatever means, we have had only one case of apnea. That occurred in a three-year-old child one minute after the injection of alphaprodine. The patient became apneic following injection and was reversed immediately with an antagonist. With the antagonist and oxygen, the patient regained consciousness quickly and had no further problem. We have had many cases where alphaprodine was ineffective. It is the best agent we have used in all of these years, but it is still not effective for everyone.

A Foldes, Zedick, et al. report in the American Journal of Medical Sciences in 1957, studied the effects of narcotic analgesics and narcotic antagonists on respiration. These investigators reported that the respiratory depression caused by meperidine and alphaprodine could be prevented by either giving levalorphan tartrate (Lorfan®) or nalorphine (Nalline®) prior to, or in combination with, the narcotic. Because of that discovery, we began to utilize this method occasionally, until naloxone became available. Naloxone works better than levalorphan tartrate or nalorphine. We abandoned the routine reversal techniques shortly thereafter, simply because we felt it was unnecessary.

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Prior to 1973 we did not employ nitrous oxide/oxygen to supplement our sedation techniques, because it was not available. Now it is the only agent we use in combination with alphaprodine, with the possible exception of cases in which we desire extending the clinical effects to about 1 to  $1\frac{1}{2}$  hours. In these cases promethazine is used, in the amounts of 0.15 to 0.25 cc of the 50 mg per cc concentration, injected into the retromolar pad. We prefer the administration of promethazine to repeating the dose of alphaprodine.

Our criteria for the use of sedation is the same today as it was 20 years ago. Our age range for alphaprodine use is 21/2 to 6 years and we consider its use with the combative child in particular. We also use alphaprodine in recalcitrant, frightened, hysterical children in whom we have tried voice control and nitrous oxide to no avail. The drug is used in patients requiring extensive restorative treatment which is to be completed in one sitting. It is useful in patients requiring extractions, suturing of lacerations, and restoration of anterior primary teeth, as in nursing bottle caries. The dosage employed has always been 1.1 mg per kg (0.5 mg/lb.). There are those occasions when, with a  $2\frac{1}{2}$  year-old, the dose would be reduced. We inject the drug submucosally into the retromolar pad area, the site of mandibular block injection or in the buccal vestibule of the maxilla. No combinations are used. Nitrous oxide/oxygen is used adjunctively.

When alphaprodine was withdrawn from the market, we began using fentanyl or a combination of meperidine and chloral hydrate. Both of these regimens work, but they have many different considerations which still make alphaprodine the drug of choice in our opinion. There were more treatment failures with fentanyl than we ever had with alphaprodine.

The drug does not help with combative patients. There are great individual variations of response. Because of the small concentration, large volumes must be used which can be a problem with buccal vestibule injection. This injection tends to be more toward an intravascular type than subcutaneous. Large doses given intravenously have been reported to result in rigidity of the chest wall. Respiratory depression is a known side effect of fentanyl.

The meperidine and chloral hydrate combination works well. The problem here is that the patients are sedated for a long period of time and one has to deal with the problem of sending a sedated patient home with the parent. When these patients are awakened, an important criteria for sending them home, we try to make sure that they can ambulate and that they can hold their heads erect.

Our choice of drugs is based solely on personal preference, observed patient behavior, utilization, and the need to avoid postoperative problems occurring when the patient is no longer in our hands. The only prejudice we would profess would be against promethazine whether it is used preoperatively or in combination with another drug. It is our feeling that it is an unpredictable agent, particularly in children. Our anesthesiology department has reported many instances of hypotensive side effects and extrapyramidal experiences with promethazine.

The considerations for premedication are as follows:

- 1. preoperative informed consent,
- 2. patient must not have eaten for three or four hours prior to appointment,
- 3. patient must be healthy without respiratory ailments (such as colds),
- 4. accurate weight of the patient must be established,
- 5. baseline vital signs must be determined (though they are sometimes difficult to obtain),
- 6. the parent must remain in the office for the duration of procedure and recovery.
- The intraoperative considerations are as follows:
- 1. mild restraint, e.g., the Pedi-Wrap<sup>a</sup> or Papoose Board,
- 2. a quiet treatment environment,
- 3. nitrous oxide induction,
- 4. a fully stocked crash cart available with a team trained in CPR,
- 5. patient monitoring by carotid or temporal pulse, respiration (rate and depth) and blood pressure,

<sup>a</sup>Clark Associates, Worcester, MA.

6. making sure that the restraints are not confining the patient's capability to breathe and that an airway remains absolutely patent at all times.

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Post-treatment considerations are:

- 1. not releasing the patient until he is able to hold his head erect, verbalize and ambulate,
- 2. cautioning the parent to frequently observe the airway and color of the patient and keep he or she turned on one side,
- 3. cautioning the parent to give solid foods only when the patient asks to be fed.

Accurate patient monitoring is essential to good premedication management. This is especially true in the dental setting where the operator oftimes does the patient monitoring. The dental assistant can be trained to monitor the sedated patient of course. Some type of mechanical, automatic patient monitoring system is preferable.

One such device is the Dynamap Monitor<sup>®</sup>.<sup>b</sup> The monitor gives a digital readout of systolic and diastolic blood pressure, heart rate, and mean arterial pressure. Determinations are made at automatic preset intervals, from one to five minutes apart, utilizing an inflatable cuff controlled by the monitor. An automatic alarm system which is either visual or auditory is built into the instrument. The operator presets the limits for the alarm prior to the procedure.

<sup>b</sup>Critikon Corp., Tampa, FL.

One excellent feature is that the monitor is capable of producing readings of mean arterial pressure even at very low blood pressures.

A trend recorder is also available for use with the monitor. This is a thermal printer which relies on software stored in the monitor. It must be connected via an interface cable to the monitor in order to function.

We use a precordial stethoscope along with the Dynamap<sup>®</sup> monitoring device. We would suggest the use of a Dynamap<sup>®</sup> or some automatically inflatable cuff and a spring loaded sphygmomanometer. Systolic pressure can be read from a needle jump and you do not have to listen to it with a stethoscope. If you are in a situation where a quick determination of the cardiac status of your patient is needed, the systolic pressure is the important consideration.

It is of course very nice to have all of these mechanical devices, but I'd like to stress that it is also very easy to come to rely too heavily on mechanical equipment. The more you deal with them, the more you tend to rely on them. You need to keep reminding yourself that devices need to be checked and calibrated often.

By way of summary, I would like to say that in all of these years of experience, I still feel that Roche has the best agent for us at this time. Generally, the results with alphaprodine have been excellent. We have not had situations that we couldn't handle. It is my own personal opinion that those reported cases of problems could have been avoided. Obviously, some cases require general anesthesia and we will continue to utilize general anesthesia when necessary. Alphaprodine is merely another modality for pediatric dentists.

Dr. Creedon is professor and director, dental department, Children's Hospital Medical Center, 240 Bethesda Avenue, Cincinnati, OH 45229. Reprint requests should be sent to him.