Administering sedation: The controversy continues

The recent articles authored by Goodchild and Donaldson ("Calculating and justifying total anxiolytic doses of medication for in-office use," January-February 2006, pp. 54-57, and "Maximum cumulative doses of sedation medications for in-office use," March-April 2007, pp. 143-148), although timely, are likely to add to the controversy and uncertainty regarding the safety of multiple dosing regimens of triazolam in dentistry. The most important outcome of this controversy is the clear understanding within the profession that there is an unmet need for safe and effective pharmacologic strategies to manage the enormous number of anxious and fearful patients in the U.S who need dental care.

The authors present a rationale for a "cumulative maximum dose" that restricts triazolam to a total dose of 2.0 mg when it is administered repeatedly during dental treatment. Their example for the largest dosing scenario involves a healthy patient, weighing 200 lb and receiving 0.5 mg triazolam initially with subsequent doses of 0.25 mg triazolam administered every 90 minutes for up to nine hours (plus some unknown time for recovery and discharge). Unfortunately, I believe the rationale for this 2.0 mg triazolam recommendation is both arbitrary and flawed.

The rationale Goodchild and Donaldson present in their first article is based on an equivalency calculation relative to lorazepam's use for alcohol withdrawal, a comparison that obviously is not appropriate to fear and anxiety management.[1] Cumulative diazepam doses of more than 2,000 mg over two days may be required to control the seizures and delirium that occur following alcohol withdrawal.[2]

The justification Goodchild and Donaldson present in their second article is based on a pharmacokinetic calculation that often is applied to establish "steady state" blood levels with multiple fixed-interval drug administration. Unfortunately, the initial dose of 500 mg was not based on failure of the lower doses, as recommended by the manufacturer, but on the authors' belief that blood levels following triazolam administration are body weight-dependent, a belief that may not be valid.[3] The dosing interval the authors selected was 15 minutes more than the mean values presented for T_{max} (1.25 hours). A safer and more conservative interval of 120 or 150 minutes (to allow for individual patient variability) could have been selected just as easily. Similarly, the authors' recommendation to restrict interval dosing to a maximum of 0.25 mg could just as easily have been 0.125 mg.

Dosing recommendations for conscious and deep sedation are not based on "steady state" pharmacokinetic calculations but on pharmacodynamic dose-response data—a determination of the maximum level of central nervous system (CNS) depression seen following a given dose. With intravenous conscious sedation in dentistry, the therapeutic dose may vary tenfold.[4] Reliable dose-response efficacy and safety data are not available for the higher "off label" enteral doses recommended currently.

I am pleased that the authors recommend repeated doses of triazolam only when blood levels have probably reached the drug's maximum blood level (beyond 75 minutes). The study by Jackson *et al*, which used a total triazolam dose of 1.0 mg (referenced by the authors and contractually funded by the Oral Sedation Research Fund of the Dental Organization for Conscious Sedation), clearly demonstrates the potential for deep sedation when shorter dosing intervals are used.[5]

I appreciate that single-dose oral triazolam is an extremely safe anxiolytic agent, and I recognize that prescribing oral triazolam can offer a great benefit to many fearful dental patients. Our published experience with the use of 0.25 mg of triazolam prior to venipuncture clearly demonstrated its sedative and amnesic efficacy.[6] I applaud the authors' recognition that additional research is needed. However, I am not convinced that advocating a maximum cumulative triazolam dose of 2.0 mg makes any sense unless a dentist has advanced anesthesia training, has an intravenous line in place, and is prepared to manage deeper levels of sedation. Case series analyses that document loss of consciousness and deaths of pediatric patients when repeated doses of sedatives are used dictate that dosing recommendations for oral and sublingual sedation be provided cautiously and conservatively.[7,8]

Training in conscious sedation, deep sedation, and general anesthesia has not been readily available for students and dentist. The ADA Commission on Dental Accreditation's recent decision to accredit postgraduate programs in dental anesthesiology may increase the supply of trained individuals who are capable of teaching and administering these advanced anesthetic modalities. Currently, only six graduate programs in the U.S. are eligible to apply for this important credential. The ADA's recognizing dental anesthesiology as a specialty of dentistry would advance the availability of educational opportunities for advanced anesthesia training.

It is my opinion that enteral anxiolysis is an extremely

safe and effective pharmacologic treatment modality, is appropriate for use by general dentists, should be required curriculum in all dental schools, and should be available to all of our anxious and fearful patients. Proposals to justify high "off label" doses of triazolam to induce conscious and deep sedation will create additional safety concerns among our patients and our colleagues. Such controversies are likely to restrict the availability of this important treatment modality for patients who would benefit from this safe treatment modality.

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Response from Drs. Goodchild and Donaldson—

We appreciate Dr. Moore's comments, given the consonance in our points of view stated in his final paragraph "that enteral anxiolysis is an extremely safe and effective pharmacologic treatment modality, is appropriate for use by general dentists, should be required curriculum in all dental schools, and should be available to all of our anxious and fearful patients." Until this education is universally available in dental school curriculums, it is vital to have conservative guidelines for the practice of anxiolysis by pharmacological means to help meet the tremendous need for this treatment modality.

We are further encouraged that our recently proposed guidelines have been included in another publication to help provide practical oral sedation protocols for California.[1] As the body of evidence continues to develop in support of this practice, articles such as these will help to address both the clinical and regulatory concerns of proponents and critics so that the greatest number of patients may be served safely. We are sure that all of the individuals who reviewed that article join us in commending the AGD for taking a leadership role by drafting a White Paper on this important topic at the end of last year.[2]

As to the safety of multiple dosing regimens of triazolam in dentistry: until unanimity exists among all state dental boards, some dentists will be required to obtain an IV/conscious sedation permit before they are allowed to titrate (dose) oral medication. In those states where general dentists have fewer restrictions on their practice, our article "Maximum cumulative doses of sedation medications for in-office use" is the first to introduce guardrails for this practice. Cumulative maximum doses of triazolam up to 2.0 mg should never be a goal, nor should they be reached. We have suggested that only in a "worst case scenario" (where the 200 lb, ASA 1 patient is treated for nine hours) would this even be possible. We are neither advocating nor encouraging that dentists attempt an oral sedation procedure for such a long period. In addition, we agree with Dr. Moore's assertion that repeated dosing of oral sedatives to maintain patient comfort should be based on direct patient assessment.

Our equivalency calculation for lorazepam was not taken from only the article on its use in alcohol withdrawal, but also from Jackson and Johnson's article on inhalational and enteral conscious sedation as well as from a pharmacy compendium.[3-5] Presenting evidence from the medical, dental, and pharmaceutical literature was intended to stress the safety of these medications in different settings and at a variety of doses when suggesting guardrails for the off-label use of the drug for oral conscious sedation.

It is important to emphasize that factors such as patient age and medical complexity will impact both the recommended starting dose of triazolam and the potential maximum cumulative dose. Again, a cumulative maximum dose of 2.0 mg would apply only to healthy individuals weighing more than 200 lb. Because we advocate a dosing interval of no less than 90 minutes, total sedative doses used in practice should be far more conservative.

References

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