Anaphylactoid reactions following propofol-atracurium sequence

To the Editor:

In a letter to the editor Mohamed Naguib states, the "combination of propofol and atracurium may be followed by frequent anaphylactoid reactions and bronchospasm."[1] Although anaphylactoid reactions with this drug combination are possible, I believe Dr. Naguib has unfairly represented the frequency of this potential side effect. His observations, in my estimation, more likely represent a worst case scenario and result from potential clinical mismanagement.

To summarize the clinical technique utilized by Dr. Naguib, thirteen ASA Class I patients undergoing elective surgical procedures had anaesthesia induced with propofol (2.5 $mg \cdot kg^{-1}$) administered IV over 15 sec followed by atracurium (0.5 $mg \cdot kg^{-1}$) administered IV over 5 seconds. The author observed erythema and wheals along the path of the injected vein in 11 patients (85 per cent) and bronchospasm in three (23 per cent).

Propofol's manufacturer recommends that propofol be administered IV in a dose of 2.0–2.5 $mg \cdot kg^{-1}$, but at a rate of 40 $mg \cdot 10\ sec^{-1}$.[2] In a large clinical trial, when propofol was properly administered at the suggested speed of initiation, flushing and cutaneous manifestations at the injection site occurred, but only with an incidence of 1–3 per cent. Bronchospasm was not observed in clinical trials, but has been reported with an incidence of less than one per cent. Dr. Naguib's induction technique employed a dose of propofol at the upper end of the suggested range (2.5 $mg \cdot kg^{-1}$). Had that dose been administered at the rate suggested by the manufacturer, for an average 70 kg patient (Dr. Naguib's patients ranged from 50 to 78 kg), an approximate 175 mg dose should have been administered over 50 sec, rather than the 15 sec described.

Atracurium when employed to facilitate tracheal intubation is suggested by its manufacturer to be administered as an IV bolus in a dose of 0.4–0.5 $mg \cdot kg^{-1}$. In controlled clinical studies of 875 patients, atracurium administered in this recommended dose range resulted in skin flush, hives, and wheezing in 8.7, 0, and 0.3 per cent of patients, respectively.[3] Hypotension requiring treatment occurred in only five of 875 patients. Although not formally articulated in the product insert, it is well known that cutaneous manifestations and hypotensive side effects associated with intravenous adminstration of atracurium relate to the speed of injection. For example, Scott *et al.*[4] have demonstrated that atracurium in a dose of 0.6 $mg \cdot kg^{-1}$ administered over five seconds resulted in an approximate doubling of the plasma histamine concentration which was accompanied by hypotension. However, when the same dose was titrated over 75 seconds, no changes in plasma histamine concentration or cardiovascular variables were observed.

As Dr. Naguib suggests, many of the described side effects from administration of propofol and atracurium are assumed to relate to their stimulation of histamine release. Histamine release and associated anaphylactoid reactions are related to the speed of injection of these drugs. It may be true as Dr. Naguib suggests, that the co-administration of propofol and atracurium potentiate each other's effects and result in an exaggerated histamine release with the potential for an anaphylactoid reaction. However, to generalize about the frequency of this complication after administration of these drugs in combination by a technique peculiar to the clinical practice of a sole user and in a way different from that recommended by the manufacturers and in a way likely to cause complications seems unfair. Before we implicate these drugs in the production of unwanted side effects, at the very least, this drug combination deserves to be studied scientifically with measurement of histamine levels while the drugs are co-administered in the proper dose range and by a techniqe recommended by the manufacturers.

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REFERENCES

1 *Naguib M.* Anaphylactoid reactions following propofol-atracurium sequence. Can J Anaesth 1989; 36: 358–9.
2 Product insert for diprivan.
3 Atracurium product insert.
4 *Scott RPF, Savarese JJ, Basta SJ, et al.* Atracurium: clinical strategies for preventing histamine release and attenuating the haemodynamic response. Br J Anaesth 1985; 57: 550–3.

REPLY

We share Dr. McLeskey's concern regarding the increased incidence of anaphylactoid reactions if IV drugs (especially those capable of releasing histamine) are administered as bolus doses over 5–15 sec. The focus of our report was to point out a potential danger following a propofol-atracurium sequence as described. At the time of the study propofol was still in the phase II trials and we were using the coded drug (ICI 35,868). The manufacturer's recommendations regarding the rate of injection appeared at a later stage. It was not our intention, however, to represent any dramatic scenario of drug interactions.