

**REDUCTION OF DOPAMINE RELEASE AND POSTOPERATIVE EMESIS BY BENZODIAZEPINES**

Sir,—We read with interest the study by Takada and colleagues [1] on the effects of midazolam and flunitrazepam on the release of dopamine from rat striatum.

Recently, we postulated that benzodiazepines may reduce the synthesis, release and postsynaptic effect of dopamine centrally [2]. This action at the chemo receptor trigger zone is a possible mechanism for the antiepileptic effect of benzodiazepines [2].

Anxiolysis mediated by benzodiazepine binding to the GABA- benzodiazepine receptor complex may also contribute to the antiepileptic effect by reducing the psychic input to the vomiting centre [2].

The study by Takada and colleagues [1] supports the hypothesis that benzodiazepines reduce dopamine release centrally. However, they suggest that the effect is mediated by benzodiazepine binding to the GABA- benzodiazepine receptor complex, causing inhibition of dopaminergic neuronal activity. The reason given for this conclusion is that the benzodiazepine effect on dopamine release was abolished by flumazenil.

It has been shown that flumazenil is also an adenosine antagonist [3]. Benzodiazepines block the re-uptake of adenosine and some of their central effects may be explained by an increased adenosine action [3]. Adenosine, a central neuromodulator, has been shown to inhibit nigrostriatal dopamine release by an adenosine-1 receptor mediated effect [4].

The alternative explanation for the reduced release of dopamine after administration of midazolam and flunitrazepam is that benzodiazepines block the re-uptake of adenosine, causing an adenosine-mediated reduction in dopamine release [2]. This effect can be blocked by flumazenil acting as an adenosine antagonist.

The regional differences in the effects of midazolam and flunitrazepam found by Takada and colleagues [1] may reflect the differing activities of the drugs on adenosine neuromodulation, the GABA- benzodiazepine receptor complex or both. Obviously, further studies are required to clarify this problem.

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di Florio and Goucke suggest that our results could be explained by an inhibitory effect of midazolam and flunitrazepam on adenosine uptake [1], because adenosine also inhibits dopamine release [1]. Given the lack of selectivity of benzodiazepines, benzodiazepine receptor antagonists [2-4] and the ability of benzodiazepines to modify adenosine A1 and A2 receptors [5], the suggestion of Drs Di Florio and Goucke merits further consideration. However, it is possible that the effect of adenosine on dopamine release may still be mediated by the GABA-B4 receptor chloride channel because of the close association of some adenosine receptors with this receptor complex [6].

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3. Morgan PF, Lloyd HGE, Stone TW. Inhibition of adenosine accumulation by CNS benzodiazepine antagonists (Ro-15-1788) and a peripheral benzodiazepine receptor ligand (Ro 05-4864). Neuroscience Letters 1983; 41: 183-188.


**ONSET OF BLOCK WITH VECURONIUM AND BODY MASS INDEX**

Sir,—I was interested in the demonstration by Drs Gill and Scott [1] that the onset of vecuronium 0.1 mg kg⁻¹ was faster after induction with etomidate compared with thiopentone or propofol.

I am concerned, however, that excessively heavy patients do not appear to have been excluded from the study.

It is stated that weights ranged from 50 to 110 kg. Body mass index is the weight divided by the height squared. According to a standard nomogram [2], in order to escape classification as "obese", a 110-kg male would have to be more than 190 cm (6'3") tall. Only if his height were to exceed 210 cm (6'11") would his weight be accepted as normal!

It has been shown that increasing the dose of vecuronium from 0.1 to 0.15 mg kg⁻¹ markedly decreases onset time in patients within 20% of ideal body weight [3]. The administration of a neuromuscular blocker to an obese patient on an mg kg⁻¹ basis constitutes an overdose. If the patient weighing 110 kg belonged to the etomidate group, the mean onset time would have been spuriously reduced.

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