LETTERS TO THE EDITOR

Intravenous midazolam in small bowel biopsy

EDITOR,—Small bowel biopsy has an important role in paediatric gastroenterology. The diagnosis of coeliac disease, the second most common chronic disease in Swedish children, is fully based for instance on the findings of serial small bowel biopsies. In Sweden most paediatric centres perform biopsies using peroral capsule instruments and without general anaesthesia. This biopsy procedure is uncomfortable to children. Optimal sedation is thus essential. Moreover, in a well sedated child the radiation dose can be minimised.[1] We have previously found intravenous midazolam to be effective and superior to other sedatives given orally.[2] The recommended intravenous dose of midazolam in children is 0·10–0·20 mg/kg body weight.[3] However, with increasing experience of the preparation it became obvious to us that the dosage must be adjusted according to the age of the child.

During the period between April 1991 and April 1994, 269 peroral small bowel biopsies were performed. Twenty nine patients were excluded from the study because they had received no sedation, or an alternative to intravenous midazolam. The remaining 240 children (table 1) were sedated with intravenous midazolam immediately before the biopsy procedure. The midazolam was given repeatedly with five minute intervals until the sedation was at least grade 3 on a five grade scale according to Karl *et al*,[4] grade 1 being agitated, 2 anxious, 3 calm, 4 drowsy, and 5 asleep. The total amount of midazolam given before the biopsy was recorded. In addition metoclopramide 0·30 mg/kg body weight (maximum dose 10 mg) was given intravenously immediately before the midazolam was administered. If the biopsy procedure was more time consuming an additional reduced dose of midazolam was given if sedation was considered inadequate, that is, less than grade 3 on the five grade scale.

The biopsy was performed on an outpatient basis but the children remained under observation in the hospital after the biopsy until they were fully awake and had eaten a light meal. The paediatric Storz capsule (Karl Storz KG, Germany) was used in 208 cases and the paediatric Watson capsule (Ferraris Development and Engineering) with angiography catheter in 32 cases. The procedure was performed under intermittent fluoroscopy. The total fluoroscopy time and the procedure time, measured from the moment the child had swallowed the capsule and the fluoroscopy was started to the moment the capsule was fired, were registered.

Table 1 Data on 240 patients and doses of midazolam given

No of patients	*Age (years)*	*Mean (SD) intravenous midazolam (mg/kg body weight)*
25	0–0·9	0·25 (0·10)
77	1·0–1·9	0·30 (0·10)
55	2·0–2·9	0·30 (0·10)
17	3·0–3·9	0·30 (0·15)
20	4·0–5·9	0·25 (0·10)
17	6·0–9·9	0·20 (0·10)
29	10·0–17·9	0·10 (0·05)

Table 2 Recommended dosage of midazolam for intravenous administration to paediatric patients

Age (years)	*Dose of intravenous midazolam (mg/kg body weight)*
0–0·9	0·25
1·0–3·9	0·30
4·0–5·9	0·25
6·0–9·9	0·20
10·0–17·9	0·10

The benzodiazepine antagonist flumazenil 0·20 mg was given intravenously to 15 children (median age 11·0 years; range 10 months–17·3 years) after the biopsy for practical purposes (n=10) or because of unnecessarily deep residual sedation (n=5), including two children with Down's syndrome, one child with juvenile diabetes mellitus, and one infant with a newly diagnosed coeliac disease in a rather bad general condition. Resuscitative equipment was immediately available at the bedside.

The midazolam doses given before biopsy to children of various ages are presented in table 1. Children between 1·0 and 3·9 years of age required significantly higher doses (mean (SD) 0·30 (0·10) mg/kg body weight) than did adolescents over 10 years (0·10 (0·05) mg/kg body weight) ($p<0·001$; Student's t test). The median biopsy time was 5 (range 1–45) minutes and the median fluoroscopy time was 5 (range 1–48) seconds. Bronchial hypersecretion was observed in 15 children including three children with Down's syndrome, but there was no serious adverse effect.

These results indicate that midazolam given intravenously in the age related dosage recommended in table 2 gives short procedure and fluoroscopy times and is an effective and safe means of sedation for paediatric patients undergoing peroral small bowel biopsy.

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1 Persliden J, Pettersson HBL, Stenhammar L. Fälth-Magnusson K. Small intestine biopsy of children with coeliac disease: influence of X-ray equipment on radiation dose. *European Radiology* 1994; **4**: 458–61.
2 Stenhammar L, Wärngård O, Lewander P, Nordvall M. Oral versus intravenous premedication for small bowel biopsy in children: effect on procedure and fluoroscopy times. *Acta Paediatr* 1993; **82**: 49–51.
3 Cole WHJ. Midazolam in paediatric anaesthesia. *Anaesth Intensive Care* 1982; **10**: 36–9.
4 Karl HW, Keifer AT, Rosenberger JL, Larach MG, Ruffle JM. Comparison of the safety and efficacy of intranasal midazolam or sufentanil for preinduction of anaesthesia in pediatric patients. *Anesthesiology* 1992; **76**: 209–15.

Jet nebulising systems for recombinant human DNase I

EDITOR,—Recombinant human DNase I (rhDNase, dornase alfa, Pulmozyme) has been shown to be beneficial in improving lung function and reducing infective episodes in cystic fibrosis patients with mild to moderate lung disease.[1] In all the clinical trials, weak compressor nebulising systems (Hudson T Updraft II nebuliser/Pulmo-aide compressor, Marquest Acorn II nebuliser/Pulmo-aide compressor, and Pari LC nebuliser/Proneb compressor) were used as there is worry that more powerful nebulising systems may excessively inactivate the enzyme product. In Britain, the manufacturer also recommends the use of Medic-aid Sidestream nebuliser/CR50 compressor (which is provided with a drug). Interestingly, none of the trials so far have used this combination.

In our cystic fibrosis clinic, more powerful compressors (either Medic-aid CR60 or Medix Turboneb) coupled with either Life-care MicroNeb III or Medic-aid System 22 Acorn nebulisers are used routinely for the delivery of inhaled antibiotics, amiloride etc. We have carried out a pilot study to assess their performance in delivering active DNase aerosol by comparing them with two of the recommended systems (Hudson T Updraft II nebuliser/Pulmo-aide compressor and Medic-aid Sidestream nebuliser/CR50 compressor). A sample of 2·5 mg (2·5 ml) rhDNase was nebulised with each system. Particle size was measured by a Malvern 2600 laser particle sizer. The released aerosols were dissolved in 0·15 M sodium chloride by drawing it through an 'underwater' seal. The DNase activity was measured immediately by spectrophotometric method as described by Sigma Chemical Company based on the Kunitz unit.[2] One Kunitz unit will produce a ΔA_{260nm} of 0·001 per minute per ml at pH 5·0 at 25°C using DNA as the substrate.

The results are shown in the table. Our data do not suggest excessive inactivation by our nebulising systems (Turboneb and CR60) when compared with the recommended systems (CR50 and Pulmo-aide). In terms of particle size, CR60 or Turboneb coupled with MicroNeb III is comparable to the recommended systems. For the Sidestream nebuliser, a nebulisation time of around three minutes may be too brief for children with smaller minute volumes.[3] A duration of five to 10 minutes is likely to be less wasteful. The nebulisation time of the Sidestream nebuliser can be increased by using a mouthpiece which blocks off the Venturi vent at the outlet top.

The preliminary trial results in patients with severe lung disease (forced vital capacity <40% predicted) are not impressive.[4] This may be partly because the severely distorted airways prevent the relatively large aerosol particles from reaching the intended target sites. The use of more powerful systems,[5] for example CR60 coupled with Sidestream, to generate small aerosol particles, is likely to improve drug delivery to the patients. It is now our policy that patients should continue to use their existing compressors for the nebulisation of rhDNase and clinical improvement in our patients has been detected regardless of the systems used. This also avoids the need to use two compressor systems at home.