PERIOPERATIVE SEIZURES AND FLUVOXAMINE

Sir,—We recently anaesthetized a healthy, 50-kg, 38-yr-old woman for extraction of wisdom teeth as an outpatient. Apart from taking fluvoxamine 200 mg day\(^{-1}\) for depression, her pre-operative assessment was unremarkable.

She received no premedication. Anaesthesia was induced with propofol 150 mg, fentanyl 0.1 mg and droperidol 1.25 mg. After suxamethonium 100 mg, the trachea was intubated with a nasotracheal tube. The lungs were ventilated by a Penlon 200 ventilator and Bain system delivering 66% nitrous oxide in oxygen at a fresh gas flow of 6 l min\(^{-1}\). Anaesthesia was maintained with 2% enflurane, reducing to 1% during the procedure, which lasted 45 min. No additional neuromuscular blockers were required.

At the end of surgery the pharynx was suctioned and 100% oxygen and doxapram 40 mg administered. Shortly after this, the patient coughed on the tracheal tube, became rigid and began a series of dramatic generalized tonic-clonic movements, with opisthotonos typical of a grand-mal type seizure. She was given midazolam 2 mg and 100% oxygen. The seizure subsided over about 1 min, although she continued to have generalized increased muscle tone with marked ankle clonus which resolved gradually over the next 30 min. The patient was drowsy initially, but thereafter made a full and unremarkable recovery.

Although she was keen to go home that day, she was admitted to the ward for overnight observation. She remained well, with no further neurological symptoms or signs, and was discharged the following morning without any sequelae.

Perioperative seizures in apparently normal patients may be multifactorial and it is clearly not possible to identify one cause with certainty when several agents have been used.

Fluvoxamine maleate is a selective inhibitor of serotonin re-uptake. Such drugs are increasingly being used to treat a wide variety of psychiatric disorders. One reason for their popularity is an apparent relative lack of side effects and toxicity in overdose compared with the tricyclic antidepressants or monoamine oxidase inhibitors [1]. Among the listed side effects of fluvoxamine are agitation, tremor and convulsions. The drug reduces the threshold for convulsion and is contraindicated in patients with a history of epilepsy [2].

The ability of enflurane to induce epileptiform activity and grand-mal seizure patterns is well established and has been reviewed comprehensively [3]. The situation with regard to propofol is more controversial, with reports of both pro- and anticonvulsant activity in some circumstances [4]. The Committee on Safety of Medicines have received 54 reports of convulsive episodes (including generalized convulsions, myoclonic jerks, opisthotonous) associated with propofol (C. S. M.—personal communication).

The analeptic agent, doxapram, is sometimes used at the end of anaesthesia to stimulate ventilation and accelerate recovery from the effects of volatile agents without antagonizing anaesthesia [5, 6]. A modest dose (less than 1 mg kg\(^{-1}\)) was administered slowly to our patient, as surgery had been more prolonged than anticipated and ended rather unexpectedly. The drug has central stimulant activity, especially in large doses, and its use is not advised in known epileptics [7]. However, the Adverse Reaction Drug Analysis Information Service yielded only two reports of convulsions associated with doxapram in a 28-yr period (C. S. M.—personal communication).

It seems possible that this patient suffered an epileptiform seizure as a result of receiving a proconvulsant anesthetic sequence against a background of an antidepressant which decreases the threshold for convulsion. As the 5-hydroxytryptamine receptor inhibitors are a relatively new group of antidepressants which are increasing in popularity, it is important for us to be aware of possible interactions with anaesthetic agents. Any further reports of similar problems would be most helpful in establishing the role (if any) of fluvoxamine in the events that we witnessed.

K. M. SPIVEY
C. M. WAIT
Horton General Hospital
Banbury, Oxon


TRACHEAL INTUBATION WITHOUT NEUROMUSCULAR BLOCK

Sir,—Drs Davidson and Gillespie [1] have shown that tracheal intubation is frequently possible in healthy patients, using propofol with alfentanil and lignocaine, without the use of neuromuscular blocking agents. Their induction regimen included alfentanil given 1 min before induction with propofol. Both propofol [2] and alfentanil [3] have the capacity to produce apnoea and do so significantly in combination [4].

The authors do not state if the patients' lungs were pre-oxygenated, but they noted that monitoring included continuous pulse oximetry, although they did not record the results of oximetry. They did not comment on the presence or duration of apnoea associated with this technique. It is documented that desaturation may occur at induction of anaesthesia [5, 6]; when administering drugs that produce apnoea in association with anaesthesia or in patients in whom intubation may be difficult, preoxygenation should be used routinely.

It would seem sensible to preoxygenate the lungs of all patients before intubation attempts with Davidson and Gillespie's technique. It is also worth noting that one of the advantages of intubation without neuromuscular paralysis is that a patient may breathe spontaneously after intubation; if the technique is associated with prolonged apnoea, this advantage is lost.

T. M. COOK
Bristol Royal Infirmary
Bristol

throughout the procedure. No significant changes from baseline were noted in any of the groups after either induction or intubation.

With regard to the occurrence and duration of apnoea after induction, although several patients continued to breathe spontaneously, most became apnoeic after administration of the combination of propofol, alfentanil, and lignocaine. However, the study was designed to determine the feasibility of laryngoscopy and tracheal intubation using this regimen, and consequently measurement of apnoeic period was felt to be of lesser importance in the first instance. Having demonstrated that this technique can provide adequate intubating conditions in up to 93% of patients, we are at present undertaking additional studies to assess the duration of apnoea using this approach.

A. MAIN
Killingbeck Hospital
Leeds

SIR,—The investigation by Haynes and colleagues [1] of the accuracy of coagulation studies using arterial cannula samples raised the interesting question of contamination with heparin flush. They cited Lew, Hutchinson and Lin [2], stating that accurate results may be obtained when 5 ml of blood is withdrawn and discarded before sampling. Consequently, they withdrew 5.6 ml of blood before collecting the sample.

In unpublished observations made on cardiothoracic surgical patients in theatre before heparinization, we found that, after the deadspace was discarded, sampling from a proximal port at 15 cm from the cannula necessitated 3 ml of blood to be wasted before achieving a “clean” sample. If blood was sampled at 150 cm from the cannula, deadspace plus 7 ml of blood had to be wasted to give an uncontaminated sample. We also used heparin 2 iu ml−1 in our flush; the coagulation tests in this small study were activated partial thromboplastin time and thrombelastography.

In the light of Haynes and colleagues’ conclusion that “a blood sample from an arterial cannula may give clinically misleading information because of contamination with small amounts of heparin”, it would seem inevitable that contamination would occur if sampling was made at a distance of about 200 cm from the cannula. However, their point of sampling was not stated.


Sir,—The choice of reagent used for measuring activated partial thromboplastin time has a significant bearing on the degree to which heparin contamination prolongs the result [1]. This was not considered adequately by Lew, Hutchinson and Lin [2]. The reagents used in our study are used widely in haematology laboratories in Great Britain, and we feel that the results of our study are of direct relevance to clinicians in this country. Dr Main does not mention the reagent used in his unpublished work. The samples in our study were taken 15 cm distant from the arterial cannula.

Thrombelastography is a useful technique for rapid diagnosis of a coagulopathy, but its interpretation is open to a degree of subjectivity. At present, it is use remains confined to specialized units such as those involved in the provision of liver transplantation.

We believe that, unless shown otherwise in carefully conducted studies, the only practical solution to the problem is to accept the results of our work? That is, that heparin contamination in minute amounts may occur unpredictably in blood samples taken from arterial cannulae.

S. R. HAYNES
Victoria Infirmary
Glasgow


EFFECT OF PEEP ON HYPERINFLATION

SIR,—We congratulate Dr Tan and colleagues on their well designed and informative study concerning the effects of PEEP in patients with obstructive airways disease [1].

While we have no argument with their findings or the conclusions drawn, we have noted a fundamental statistical error. Two methods were used to measure intrinsic PEEP; these were airway pressure at the onset of inspiratory flow (Paw,0) and airway pressure obtained with expiratory port occlusion at end-expiration (Poc). The authors then calculated a correlation coefficient between the two variables and concluded they were “[in] reasonable agreement (r = 0.87”). Having reached this conclusion, they referred to only one measurement (Poc) in further analyses.

The misleading use of correlation coefficients in the comparison of two measurements that has been highlighted by Bland and Altman [2]. Regression analysis is used to predict one variable from another (i.e. y from x), whereas correlation measures the strength of a relation between two variables. This is not the same as agreement, nor does it describe accuracy.

Bland and Altman then described a method of measuring agreement between two measurement techniques. This involves using the average of the two measurements as the best estimate of the true value, and then obtaining the difference between this average and each of the measured values. A mean difference and SD are then obtained. These are the “bias” and “limits of agreement” of the measurement techniques.

C. B. BERRY
P. S. MYLES
Alfred Hospital
Prabhan, Victoria, Australia


Sir,—The method of estimation of PEEP was not a prime consideration of our study, but merits further comment. Paw,0 is a measurement of end-expiratory alveolar pressure under dynamic conditions, while Poc is measured under static conditions. To average the two variables to obtain the “best estimate of the true value”, as suggested, would be misleading. Nonetheless, the data have been examined by the method of Bland and Altman [1] and the two measurements are in “reasonable agreement”. The bias mean difference is 0.06 (so 0.17) kPa (fig. 1).

Poc (as a measure of whole-lung static PEEP) was used in our study to analyse the data of hyperinflation and effects of PEEP in patients with obstructive airways disease. While we have no argument with their findings or the conclusions drawn, we have noted a fundamental statistical error.

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T. E. ON
Chinese University of Hong Kong
Hong Kong