CORRESPONDENCE

BRITISH STANDARD FOR VENTILATORS

Sir,—I read with interest the letter by Drs Davis and Shaw (1977) on British standards for automatic ventilators. They state that “past attempts to achieve a basic standard have failed” and indicate that a new standard is in preparation by the International Organization for Standardization. “As this new document is longer and more complex” (than the old British Standard), they suggest that it may suffer the same obscurity.

As secretary of the International Organization for Standardization Committee that prepared this new complex and comprehensive standard, I am glad that this standard is now accepted for publication by the International Organization for Standardization. Since international bureaucracy works slowly, it might be easier to purchase, for $5.75, essentially the same document: American National Standard for Breathing Machines for Medical Use, ANSI Z79.7-1976, Secretariat—American Society of Anesthesiologists, published by the American National Standards Institute, 1430 Broadway, New York, New York 10018.

John Hedley-Whyte
Boston, U.S.A.

REFERENCE

ORPHENADRINE AND POSTOPERATIVE PAIN

Sir,—After major operations on the abdomen or large joints some patients develop severe pain and muscle spasm which is not relieved by standard doses of narcotic analgesics. This pain may be appreciated soon after recovery from anaesthesia or 1–3 h later, and may persist for several hours or for as long as 2 days. Fear and anxiety aggravate pain after operation by inducing muscle spasm, the purpose of which is to splint the site of operation. This leads to a self-perpetuating cycle of increased pain, fear and muscle spasm (Wylie and Churchill-Davidson, 1973).

During the past year the author has seen 16 patients with pain and muscle spasm which was not relieved by papaveretum 14–30 mg i.v. (six patients) or papaveretum 20 mg i.m. 2-hourly to a total of 40 mg. Two of the 16 patients suffered severe pain for 2 days despite receiving papaveretum 20 mg i.m. 4-hourly. In eight of the other 14 patients orphenadrine (Norflex) 60 mg i.v. relieved the pain and muscle spasm within a few minutes. These patients remained comfortable and required reduced doses of analgesic drugs. Orphenadrine was repeated in a dose of 60 mg i.m. after 10–12 h. The remaining six patients were more comfortable after the first injection of orphenadrine, but their pain was not relieved fully until a second dose had been given 12 h later.

Orphenadrine acts centrally at medullary and mesencephalic levels to reduce muscle tone without impairing the force of voluntary contractions (Biflisma et al., 1956). It possesses weak analgesic, euphoric and parasympatholytic actions (Cass and Frederik, 1964). Caution should be exercised in patients with tachycardia or residual neuromuscular blockade.

Orphenadrine may be a useful drug in the management of postoperative pain which is unresponsive to standard narcotic analgesic therapy.

E. N. S. Fry
Stockton-on-Tees

REFERENCES


INTERACTIONS BETWEEN MORPHINE AND DOXAPRAM

Sir,—It is not surprising that Gregoretti and Pleuvry (1977) found that single doses of doxapram in the presence of morphine are without effect on respiration in rodents, since it has been shown that these animals do not respond well to stimulation by doxapram even in the absence of morphine (Ward and Franko, 1962). The data on the interaction between morphine and doxapram in rodents reported by Gregoretti and Pleuvry, who suggested this combination may be toxic in man, are at variance with those reported previously by others who studied this combination of drugs.

Gupta and Dundee (1974a) studied 140 patients following upper abdominal surgery. Using a double-blind technique, these investigators found that doses of 1–1.5 mg kg⁻¹ of doxapram, which effectively inhibited morphine-induced respiratory depression, had no significant effect on the analgesic action of morphine. The concomitant administration of doxapram 1 mg kg⁻¹ permitted the safe use of a mean i.v. dose of morphine 27 mg.

Following the report by Bruce and his colleagues (1965) indicating that doxapram is metabolized rapidly, Gupta and Dundee (1974b) repeated their studies using an infusion of doxapram. Morphine was given to 40 patients soon after surgery. The patients then received an infusion of either 5% dextrose solution or doxapram 2 mg ml⁻¹ in 5% dextrose at a rate of 100 ml h⁻¹. Each treatment was continued for 120 min in a double-blind fashion. This study confirmed that doxapram reduced significantly the respiratory depression induced by effective doses of morphine without interfering with the analgesic action of the opiate. These large doses of doxapram produced no complications.

Ramamurthy, Steen and Winnie (1975) studied pethidine and doxapram in six volunteers. When doxapram 2 mg kg⁻¹ and pethidine 1 mg kg⁻¹ were given in combination i.m. there was a slight shift to the right of the carbon dioxide...
response curve. However, this shift was less than half that seen with pethidine alone and it was not statistically significant. The antagonism of pethidine-induced depression provided by doxapram lasted as long as the depressant effect of pethidine. As doxapram is metabolized rapidly this finding was unexpected.

The projection of the findings of Gregoretti and Pleuvry (1977) to man is unwarranted. Furthermore the studies in man described above support this conclusion.

ALON P. WINNIE
Chicago
WILLIAM H. FUNDERBURK
A. H. Robins Ltd.,
Richmond, Virginia, U.S.A.

REFERENCES


Sir,—Before replying to the letter from Drs Winnie and Funderburk, I should like to restate the final paragraph of our paper (Gregoretti and Pleuvry, 1977).

"It is hoped that this interaction is murine-specific, but in view of the current vogue for morphine–doxapram mixtures and reports of doses in excess of 1 g being used in man (Newell et al., 1969) it may be advisable to limit doses until the situation has been clarified."

We have not suggested that this interaction does occur in man. However, we do not have any evidence that it does not, and this was the reason for the note of caution in our paper.

Toxicology.

The fact that morphine and doxapram mixtures have been used by many workers with no apparent toxic effects does not prove that our data in the mouse are necessarily irrelevant to man. The lethal dose of doxapram in mice depended upon the dose of morphine given. Thus, if our results are relevant to man, I would expect to see problems only when large doses of doxapram are used to reverse large doses of narcotic analgesics.

In their letter, Drs Winnie and Funderburk have discussed interactions between doxapram and narcotic analgesics with respect to respiration and analgesia in man. I have no evidence from my rodent studies that the site of the toxic interaction between morphine and doxapram is the respiratory system. Indeed, more recent studies in this laboratory have shown that the cardiovascular system is a more likely site of the interaction. In mice and rats morphine, by a mechanism which is as yet unclear, increases the intrinsic ability of doxapram to produce conduction defects in the heart. In sub-lethal doses these effects may be seen only by monitoring the e.c.g. The cardiotoxicity of high doses of doxapram has been reported also in the cat (Polak and Plum, 1964).

BARBARA J. PLEUVRY
Manchester

REFERENCES


ANAESTHESIA WITH PROFOUND HYPOTENSION FOR MIDDLE EAR SURGERY

Sir,—I have read with interest the article on this subject by Dr A. R. Kerr (1977), but I was surprised that the e.c.g. was not used as part of the monitoring technique to detect dangerous arrhythmias, myocardial ischaemia and the onset of cardiac arrest during profound induced hypotension, even in the physically fit patient.

While the critical closing pressure of healthy coronary arteries may be as little as 15 mm Hg, which may be reduced during induced hypotension according to the Law of Laplace, I do feel that some reserve should be retained and in my view the systolic arterial pressure should not decrease below 50 mm Hg at the level of the heart except for very brief periods such as to facilitate the clipping of a cerebral aneurysm.

Should the systolic arterial pressure be allowed to decrease to 30 mm Hg it will be no greater than that in the pulmonary artery or that at the arteriolar end of a capillary, and all reserve will have been lost.

In my experience, it is possible to obtain dry operating fields for middle ear surgery using halothane to produce arterial systolic pressures of 55–60 mm Hg at heart level, provided posture and IPPV are utilized and practolol used to correct tachycardia or ventricular arrhythmias.

If the very high PaCO₂ values mentioned in some of the patients in the series were higher than the arrhythmia threshold for halothane, it is possible that some patients developed dangerous ventricular arrhythmias which passed unnoticed but which could have been prevented by IPPV or treated with a cardioselective beta-blocking drug.

The total absence of morbidity or mortality in the series is commendable, but it may lead some anaesthetists into a false sense of security.

W. N. ROLLASON
Aberdeen

REFERENCE

Printed in Great Britain by John Wright and Sons Ltd. at The Stonebridge Press, Bristol BS4 5NU © Macmillan Journals Ltd 1978