EFFECTS OF DOXAPRAM ON POSTOPERATIVE PULMONARY COMPLICATIONS FOLLOWING THORACOTOMY

P. S. SEBEL, E. J. KERSHAW AND W. S. RAO

SUMMARY

An i.v. solution of 5% dextrose with doxapram 2 mg ml\(^{-1}\) or 5% dextrose alone was administered to 53 patients following lateral thoracotomy. Estimations of arterial \(P_{O_2}\), \(P_{CO_2}\), and pH were made before operation, during infusion and 7 days after operation. Respiratory function tests were carried out before and 7 days after operation. There were no significant differences in arterial \(P_{O_2}\), \(P_{CO_2}\), and pH or in respiratory function tests between those who received doxapram and those who did not. In this study doxapram did not affect the frequency of postoperative pulmonary complications.

Doxapram hydrochloride is a respiratory stimulant which has an action both centrally and on the peripheral chemoreceptors (Kato and Buckley, 1964; Wang and Hirsch, 1973; Scott, Whitwam and Chakrabarti, 1977). The administration of doxapram has been shown to reduce respiratory complications and hypoxaemia in fit patients after abdominal surgery (Gupta and Dundee, 1974; Gawley, Dundee and Jones, 1975; Gawley et al., 1976; Downing et al., 1977). Lees and others (1976) suggested that reduction in hypoxaemia may be a result of a sparing effect on functional residual capacity (FRC). However, not all investigators agree that the drug is of value after surgery (Andersen and Krohg, 1976).

We have investigated the effects of an infusion of doxapram on postoperative pulmonary complications and on arterial \(P_{O_2}\), \(P_{CO_2}\), and pH in a group of patients with pre-existing lung disease undergoing lateral thoracotomy.

PATIENTS AND METHODS

Fifty-three patients admitted to the same surgical unit for thoracotomy gave informed consent to investigation. Patients with severe hypertension (>112 mm Hg diastolic), severe coronary artery disease and those requiring repeat operation on the chest were excluded from the study.

Before operation arterial blood was sampled from the femoral or radial artery into a heparinized syringe with the patient breathing room air. The sample was analysed within 10 min for hydrogen ion activity ([H\(^+\)], \(P_{O_2}\), and \(P_{CO_2}\) using a Corning pH/blood-gas 165 analyser previously calibrated using Corning buffer and calibration gas. Vital capacity (VC), the forced expiratory volume in 1 s (FEV\(_1\)) and the peak expiratory flow rates (PEF) were measured using a Vitalograph dry spirometer. The carbon monoxide transfer factor corrected for alveolar volume (\(K_CO\)) was measured by the single breath method using a P. K. Morgan Respirometer. A chest x-ray was taken before operation.

All patients were premedicated with papaveretum 10–20 mg and hyoscine 0.2–0.4 mg i.m. Anaesthesia was induced with a sleep dose of thiopentone. Following the administration of suxamethonium 100 mg, the trachea was intubated with an appropriate double-lumen tube. Ventilation was controlled throughout the operation with the aid of a non-depolarizing neuromuscular blocker and anaesthesia was maintained with a mixture of nitrous oxide in oxygen supplemented with fentanyl or phenoperidine. At the end of surgery, residual muscular paralysis was antagonized with neostigmine and atropine.

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<tr>
<th>TABLE I. Details of patients in the two groups</th>
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<td>Male</td>
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<td>Mean age (yr ± SD)</td>
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<td>Operation</td>
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<td>Pneumonectomy</td>
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<td>Lobectomy</td>
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<td>Pleurectomy</td>
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RESULTS

Before surgery there were no significant differences between the two groups in respect of arterial $P_{O_2}$, $P_{CO_2}$ or $[H^+]$ or respiratory function.

Two hours after operation, $P_{A O_2}$, $P_{A CO_2}$ and $[H^+]$ 2 h after the start of the infusion. All patients received ampicillin and flucloxacillin for 5-7 days. They also received physiotherapy (breathing exercises) twice a day for 3 days after operation, and then daily.

On the 7th day following operation, all the investigations carried out before operation were repeated.

Taking production of purulent sputum or severe cough, or both, as evidence of respiratory infection, the doxapram group had a reduced frequency of infection although the difference between the groups was not statistically significant (table IV).

There was no significant difference in the number of patients who had an increase in temperature of more than 1 °C (table V).

The chest x-rays were reported by a radiologist who was unaware of the treatment group. He could detect no differences between the two groups.
Patients who underwent lobectomy showed some evidence of consolidation in the remaining lobe on the side of operation. Patients who underwent pneumonectomy, pleurectomy or who had no resection showed no evidence of collapse or consolidation that was not visible before operation.

During the study, one patient experienced facial sweating which was the only side-effect attributable to the administration of doxapram.

**DISCUSSION**

An infusion of doxapram 10 mg min\(^{-1}\) for 30 min following operation has been shown to cause an increase in \(P_{aO_2}\), and a decrease in \(P_{aCO_2}\) (Downing et al., 1977). Gawley and others (1976), using a dose of 2 mg min\(^{-1}\) for 2 h found the increase in \(P_{aO_2}\) to be sustained until the 5th day after surgery.

Lees and others (1976), who gave doxapram 250 mg over 2 h, found a significant increase in \(P_{aO_2}\) only on the 1st day after operation and not subsequently.

In this study, doxapram was not effective as a pharmacological stimulus to breathing. It was used in a dose of 2 mg kg\(^{-1}\) h\(^{-1}\) for 6 h, which should have been long enough to outlast any residual respiratory depression from anaesthesia. This is the first study reporting the use of doxapram following surgery in patients with pre-existing lung disease, and in this group of patients it appeared to have had no effect on ventilation, as measured by \(P_{aO_2}\) or \(P_{aCO_2}\).

The frequency of chest infections after abdominal surgery has been shown to be reduced by doxapram (Gupta and Dundee, 1974; Gawley, Dundee and Jones, 1975; Gawley et al., 1976). Although there was a reduced frequency of cough and spit in our study in patients receiving doxapram (4.5%) as compared with those not receiving doxapram (21.7%), the difference was not statistically significant. Downing and others (1977) found that doxapram only reduced respiratory sequelae in patients not treated with antibiotics. All our patients received prophylactic antibiotic therapy and this may have contributed to the overall result.

Lees and others (1976) have suggested that the effect of doxapram on hypoxaemia may be that of a sparing effect on FRC. FRC measurements would be impossible to interpret in patients in whom portions of lung had been removed, but we may speculate that the impaired lung function in our patients may have included such a large reduction in expiratory reserve volume that this limited the possible beneficial effects of doxapram.

We conclude that, although doxapram may reduce pulmonary complications after operation in fit patients, it has no effect on ventilation or postoperative respiratory complications in patients with lung disease undergoing thoracic surgery.

**ACKNOWLEDGEMENTS**

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**REFERENCES**


**EFFETS DU DOXAPRAM SUR LES COMPLICATIONS PULMONAIRES POSTOPERATOIRES APRES UNE THORACECTOMIE**

**RESUME**

On a administré par voie intraveineuse à 53 malades une solution à 5% de dextrose et de doxapram à raison de 2 mg ml\(^{-1}\), ou à 5% de dextrose seule après une thoracotomie latérale. On a procédé à des estimations de la \(P_{O_2}\) artérielle, de la \(P_{CO_2}\) et du pH avant l'opération, pendant l'infusion et 7 jours après l'intervention chirurgicale. On a effectué des tests sur la fonction respiratoire avant et
7 jours après l'opération. Il n'y a pas eu de différences importantes dans la Po₂ artérielle, la Pco₂ et le pH ou dans les tests de la fonction respiratoire, entre les malades qui avaient reçu du doxapram et ceux auxquels on n'en avait pas administré. Dans cette étude, le doxapram n'a pas affecté la fréquence des complications pulmonaires postopératoires.

ZUSAMMENFASSUNG

SUMARIO
Se administró una solución i.v. de 5% de dextrosa con 2 mg ml⁻¹ de doxapram o de 5% de dextrosa sola a 53 pacientes después de una toracotomia lateral. Antes de la operación, se hicieron estimaciones del Po₂, Pco₂ y del pH, así como durante la infusión y 7 días después de la operación. Se llevaron a cabo pruebas de la función respiratoria antes de la operación y 7 días después de la misma. No hubo diferencias significativas en el Po₂, Pco₂ y pH ni tampoco en las pruebas de la función respiratoria entre los que recibieron doxapram y los que no lo recibieron. En este estudio, el doxapram no afectó la frecuencia de las complicaciones pulmonares postoperatorias.