SHORT REPORTS

Absence of uterine neoplasia in patients on bromocriptine

Bromocriptine is a dopamine agonist which is used to suppress prolactin secretion postpartum and in men and women with gonadal dysfunction; to suppress growth hormone secretion in acromegaly; and to treat Parkinsonism. Initial toxicological studies in rats showed no adverse effects over 53 weeks except for the presence of endometrial hyperplasia with squamous metaplasia and cystic ovarian follicles.¹ The preliminary results of a 100-week study in rats have now shown, however, that the endometrial changes have progressed in some animals to malignant tumours.² For this reason we have screened gynaecologically all of our available patients who have received bromocriptine.

Patients and methods

Of the 108 women, 21 were acromegalic; 49 had hyperprolactinaemic gonadal dysfunction (29 pituitary tumours); 19 had normoprolactinaemic infertility or galactorrhoea, or both; 18 had polycystic ovarian disease (16 with hyperprolactinaemia); and one had Cushing's disease. Ten of these patients were pregnant and 10 had had hysterectomies; these had been for benign conditions except in one patient who had an endometrial carcinoma removed before starting bromocriptine. Eleven of the remaining 88 were postmenopausal, and all 88 patients were assessed gynaecologically. Bromocriptine treatment had lasted for four to six years in six patients; two to four years in 24; one to two years in 37; and less than one year in 21. The dose of bromocriptine varied from 1.25 mg to 60 mg daily; 64 patients received 5 to 10 mg daily. Twenty women had stopped treatment for between six months and three years. As an outpatient each patient underwent a gynaecological examination, cervical smear, and endometrial suction curettage using a Vabra aspirator without sedation or anaesthesia. The endometrial aspirate and cervical smears were stained for cytological examination by the Papanicolaou method, and when sufficient material was available endometrium was fixed, embedded in paraffin wax, and sectioned for histological examination using haematoxylin and eosin staining.

Cervical and endometrial assessment was not possible in the 10 pregnant patients and the 10 who had had hysterectomies. No gross gynaecological abnormalities were found in the remaining 88 patients, except uterine fibroids in one. No cytological or histological evidence of endometrial neoplasia, metaplasia, or hyperplasia or cervical abnormalities were found in any of the tissues studied (see table).

Results of gynaecological assessment in 88 women* treated with bromocriptine

	No (%) of women with enough tissue for assessment		Evidence of neoplasia, hyperplasia, hyperplasia or metaplasia
	Pre-menopausal	Post-menopausal	
Cervical cytology	77 (100)	9 (82)	0
Endometrial cytology	74 (96)	5 (45)	0
Endometrial histology	61 (79)	1 (9)	0

*These women were left after 10 pregnant women and 10 women who had had hysterectomies had been excluded.

Comment

Unlike the rat, our patients on bromocriptine showed no evidence of hyperplasia, metaplasia, or neoplasia of the uterine mucosa. This is not surprising since the rat is a poor endocrine model of the human. Long-term prolactin suppression with bromocriptine in the rat is associated with loss of the normal oestrus pattern. In women of reproductive age, however, normal menstrual cycles return or remain when bromocriptine is administered, particularly in hyperprolactinaemic patients. The abnormalities seen in rats on bromocriptine are associated with exposure of the animals to oestrogen effects inadequately opposed by progesterone; the progressive rise in progesterone secretion normally seen during the aging process in the rat is inhibited when prolactin is suppressed. This endocrine alteration does not occur in women, since bromocriptine induces regular and normal ovulation with regular endometrial shedding. The induction of regular menstruation in women with amenorrhoea or irregular cycles by bromocriptine may indeed protect against the possible adverse

effects of prolonged unopposed actions of oestrogens, possibly including an increased risk of the development of endometrial carcinoma.^{3,4}

While there is no evidence that bromocriptine induces uterine abnormalities, it is advisable that patients on long-term treatment should undergo gynaecological assessment, preferably with cervical and endometrial examination, every year during treatment until enough data are accumulated. Any associated malignancies should be evaluated for any possible relation with bromocriptine therapy. We have ourselves seen one acromegalic patient, not included in this series, whose ovarian adenocarcinoma was diagnosed eight months after starting bromocriptine, although in retrospect symptoms had been present for 11 months.

¹ Griffith, R W, *IRCS*, 1974, **2**, 1661.

² Griffith, R W, 1977, Sandoz Ltd, Basel, personal communication.

³ Vellios, F, in *Genital and Mammary Pathology Decennial 1966-75*, ed S C Sommers, p 55. New York, Appleton-Century-Crofts, 1975.

⁴ Nordqvist, S R B, in *Genital and Mammary Pathology Decennial 1966-75*, ed S C Sommers, p 85. New York, Appleton-Century-Crofts, 1975.

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Carinal granuloma after endotracheal intubation

Tumours of the trachea are uncommon, and present problems of combined anaesthetic and surgical management if removal is attempted.¹

Case report

An Indian boy had his patent ductus arteriosus divided and coarctation of aorta resected at the age of 11 days. It was necessary to leave a 3.5-mm Portex nasotracheal tube in situ for eight days postoperatively. For all that time he breathed spontaneously with oxygen-enriched, humidified air, with constant positive airway pressure. Serial x-ray films showed that the tip of the endotracheal tube was too low, often at, or near, the carina, so the tube was partially withdrawn on several occasions. He was discharged a week after extubation, apparently well.

At the age of 10 weeks he was re-admitted with what was thought to be bronchospasm secondary to bronchitis, with mild cardiac failure. He was given antibiotics, hydrocortisone, digoxin, and diuretics, and was fit for discharge a week later. After only another week he was readmitted with similar signs, and was treated as before. After some initial improvement, his bronchospasm got much worse, and he developed severe respiratory distress, with diminished air entry to both lungs. On the tenth day of admission it was noted that the breath sounds had returned to normal over the left lung, but remained reduced on the right side. A chest x-ray film showed a hyperinflated right lung with shift of the mediastinum to the left, and bronchial obstruction was diagnosed. The child was anaesthetised for bronchoscopy by the Sanders technique,² and was found to have a pedunculated tumour arising from the carina, flopping into both main bronchi. Attempted removal caused too much bleeding, and was abandoned.

Four days later, at the age of 15 weeks, he was reanaesthetised, and the bronchoscopic findings confirmed. An uncut, 3.5-mm Portex nasotracheal tube was passed, and as ventilation was easy he was given alcuronium and intermittent positive pressure ventilation with nitrous oxide and oxygen. The trachea was exposed via a right thoracotomy, and then incised vertically. Ventilation then being impossible, the surgeon tried unsuccessfully to pull the endotracheal tube down the trachea and push it into the left main bronchus. Instead, he wedged a 12FG Warne tube into the open end of the left bronchus; connected a sterile, Jackson-Rees modified Ayres T-piece circuit to the tube; and passed the other end of the circuit to the anaesthetist. One-lung anaesthesia was continued without difficulty until the trachea was repaired after complete excision of the tumour. At the end of the operation the child was extubated, and made an uneventful recovery.

The solid tumour was confirmed to arise from the carina and to prolapse into the right main bronchus. It measured 6.4 × 3 mm, the internal diameters of the trachea at his age being roughly 6–7 mm. The histological diagnosis was postintubation granuloma, the alternative diagnosis of pre-existing capillary haemangioma being considered unlikely.

Comment

Endotracheal intubation is now a well-recognised and accepted aid in the treatment of cardiac and respiratory failure and after some forms of major surgery. Postintubation granulomata are not uncommon, but usually occur on the arytenoids or in the subglottic region, where trauma from the tube is greatest.^{3,4} Probably the long tube used after the child's first operation damaged the carinal mucosa leading to granuloma formation, but possibly also suction catheters used for routine bronchial toilet were responsible.⁵

This case illustrates yet another rare hazard of modern treatment, and the need for careful preparation and co-operation between surgeons and anaesthetists when operating in the presence of airway obstruction.

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¹ Carden, E, and Ferguson, G B, *Annals of Otolaryngology, Rhinology, and Laryngology*, 1975, **84**, 233.

² Sanders, R D, *Delaware Medical Journal*, 1967, **39**, 170.

³ Epstein, S S, and Winston, P, *Journal of Laryngology and Otolaryngology*, 1957, **71**, 37.

⁴ Hatch, D J, *Lancet*, 1968, **1**, 1272.

⁵ Fisk, G C, and Baker, W de C, *Anaesthesia and Intensive Care*, 1975, **3**, 209.

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Does antibiotic spray reduce wound infection?

Antibiotic sprays are now widely used during surgical wound closure, although their value is not universally accepted. During our six-month tenure as house officers in two surgical wards we found that their use in a small series during abdominal surgery reduced postoperative wound infection.

Patients, methods, and results

The survey was conducted on 115 patients from two surgical wards (one male, one female) who had had operations in one of two theatres between February 1975 and July 1975. Wounds were classified as "clean," "contaminated," or "dirty." In "clean" wounds endodermal cavities were not entered—for example, plastic surgery, hernia operations, mastectomies, and vascular surgery. In "contaminated" wounds endodermal cavities were

Antibiotic spray and prevention of wound infections

Treatment	Clean wounds		Contaminated wounds		Dirty wounds	
	Total No	No infected (%)	Total No	No infected (%)	Total No	No infected (%)
(a) Antibiotic spray	45	3 (7)	28	2 (7)	3	1
(b) No antibiotic spray	21	1 (5)	17	6 (35)	1	1

entered—for example, routine abdominal surgery. In "dirty" wounds there was extensive contamination of the surgical field—for example, perforated, infected, or gangrenous viscera. We excluded from the survey those patients with preoperative wound infections or those who died within three post-operative days.

Wounds were treated during closure in one of two ways: (a) they were sprayed with Polybactrin or Rikospray, both preparations containing neomycin sulphate, bacitracin zinc, and polymyxin B sulphate; (b) the wound was washed with either sterile saline (for "clean" wounds) or chlorhexidine 1 in 5000 aqueous solution (for "contaminated" or "dirty" wounds). Two surgeons routinely used treatment (a), one treatment (b). Each surgeon performed a similar spectrum of operations. The table shows that the wound types were in approximately 2:1 ratio between groups, as were the sex ratio (treatment (a) 41 male, 35 female; treatment (b) 21 male, 18 female), while the mean age of each group was 55 years. The theatre suite, theatre and ward staff (for each ward), pre-, intra-, and post-operative care was the same in each treatment group.

For the purpose of this study a "wound infection" was described as a purulent wound exudate from which bacteria were isolated. Postoperative wound infections developed in eight (20.5%) of the 39 wounds not receiving antibiotics, compared with six (7.9%) of the 76 wounds receiving antibiotics. For the "contaminated" wounds the difference is significant ($\chi^2 = 3.97$, $P < 0.05$).

Comment

Several reports have stated that application of certain antibiotics in powder or solution form during wound closure significantly decreased postoperative wound infection.^{1,2} Nevertheless, we could find only two recent reports on the incidence of wound infections after the use of combination antibiotic sprays: Jackson *et al*,³ using the same wound grouping as we, reported no significant decrease in wound infections when Rikospray was used; Gilmore⁴ showed that a similar antibiotic spray reduced postoperative wound infections, particularly with "contaminated" wounds. Although the numbers in our study were small, the results suggest that the use of this antibiotic spray during closure of "contaminated" wounds reduced the incidence of subsequent wound infection.

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¹ Logan, C J H, *British Journal of Surgery*, 1973, **60**, 355.

² Scherr, D D, *et al*, *Journal of Bone and Joint Surgery*, 1972, **54A**, 634.

³ Jackson, D W, *et al*, *British Journal of Surgery*, 1971, **58**, 564.

⁴ Gilmore, O J A, *British Journal of Surgery*, 1973, **60**, 910.

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Reptilase time in cirrhosis and hepatocellular carcinoma

There have been several isolated case reports of dysfibrinogenemia in patients with hepatocellular carcinoma, but Barr *et al*¹ have now reported evidence of dysfibrinogenemia in a larger series of 28 Kenyan patients. In the presence of normal amounts of fibrin(ogen) degradation