SHORT COMMUNICATION

Oophorectomy has no effect on experimental pancreatic carcinogenesis in the Syrian hamster

J.F. Chester, R.I. Nicholson1, J.V. Lever, A.R. Turnbull & D.C. Britton

Departments of Surgery and Cellular Pathology, Royal United Hospital, Bath BA1 3NG, and the Tenovus Institute for Cancer Research, University of Wales College of Medicine, The Heath, Cardiff CF4 4XX, UK.

The finding of high concentrations of oestrogen receptors in the cytoplasm and nucleus of both human and experimental animal pancreatic adenocarcinoma cells (Greenway et al., 1981; Satake et al., 1982), and subsequent demonstration of an apparent dependence of pancreatic cancer cells on circulating sex steroids (Greenway et al., 1982; Iqbal et al., 1983) has led to a series of human and animal studies of hormonal manipulation as a possible new approach to the treatment of pancreatic cancer (Crowson et al., 1986, 1987; Greenway, 1982, 1987, 1988; Kloppel et al., 1986; Redding et al., 1984; Theve et al., 1983; Tonnos et al., 1986; Wong et al., 1987).

Because pancreatic cancer induced in the Syrian hamster by N-nitrosobis-(2-oxopropyl) amine (BOP) resembles human pancreatic cancer in many ways (Pour et al., 1981), we studied the effect of surgical oophorectomy in this animal model. Female Syrian hamsters (Bantin and Kingman Ltd, The Field Station, Grimston, Hull, n = 60; age, 5 weeks) were housed with a 12-h light/dark cycle and were given free access to Purina Laboratory Chow and water. Following acclimatisation, one group of 30 hamsters underwent laparotomy and bilateral oophorectomy through a midline incision, while a second group (n = 30) underwent sham operations where the ovaries were simply touched before closure of the abdomen. All animals were anaesthetised using intraperitoneal Hypnorm (Fentanyl citrate with Fluanisone) and Midazolam (1 part Hypnorm, 2 parts water and 1 part Midazolam; 4.5 ml kg⁻¹). Two weeks postoperatively all hamsters received a course of four weekly subcutaneous injections of BOP (Ash Stevens, Detroit, MI, USA) (10 mg kg⁻¹, made up fresh in normal saline solution). Thirty weeks following the first BOP injection, all surviving animals were killed by an overdose of carbon dioxide. Each pancreas was removed by dissection of its three lobes from surrounding structures, and after trimming of peripancreatic fat, each organ was weighed. The anatomical surfaces of each liver and lung were also examined, and any abnormal areas were removed and fixed in 10% formalin for histological examination. Sections through each pancreas were cut at 5 μm intervals, the number of sections varying according to the size of the pancreas and any tumours within it. All tissues were stained with Haematoxylin & Eosin for histological examination on coded slides. The χ² test was used to compare the incidence of pancreatic cancer.

All animals gained weight equally following surgery (Table I) and 57 (95%) survived to the end of the experiment. There was no difference in the incidence of pancreatic cancer between the two groups: 45% in the oophorectomy group and 50% in controls (Table I). One hamster in the control group developed an islet cell pancreatic carcinoma in addition to an adenocarcinoma, but there were no other instances where multiple tumours occurred. The incidence of hamsters bearing bronchial neoplasms was similar in all animals (9/29 (31%) in the oophorectomy group, and 8/28 (28%) in controls). Although a number of hamsters developed hepatic cysts, there were no hepatic cancers.

In experimental animals, hormonal manipulation using long-acting gonadotrophin antagonists has been found to be effective in inhibiting the growth of cancers in the prostate, mammary glands, pituitary and connective tissues (Schally et al., 1984). Furthermore, the agonistic analogue of luteinising hormone-releasing hormone (which paradoxically inhibits pituitary and gonadal function after chronic administration) decreases the weight and volume of chemically induced, transplanted pancreatic cancers in both rats and hamsters (Redding, 1984). In addition, gonadal ablation inhibits azaserine-induced pancreatic carcinogenesis in male rats, although opposite effects have been seen in female rats undergoing oophorectomy (Lhoo et al., 1986). Despite these findings, we found no effect of bilateral oophorectomy on BOP-induced pancreatic carcinogenesis in the Syrian hamster.

Recent studies on the effect of the anti-oestrogen tamoxifen on inhibition of the growth of inoperable pancreatic adenocarcinomas in human beings have been conflicting (Crowson et al., 1986, 1987; Greenway, 1987, 1988; Theve et al., 1983; Tonnos et al., 1986; Wong et al., 1987), but the results of further studies are awaited (Greenway, 1987). In our study, the lack of effect of oophorectomy on experimental pancreatic carcinogenesis has been documented, but the contribution of the adrenals to oestrogen production has not been assessed. In addition, the presence of, or any change in, oestrogen receptor status of the developing pancreatic cancers has not been determined. The effect of ovarian ablation or of tamoxifen on the development of established pancreatic cancers in this animal model, together with an investigation of the steroid receptor status of these experimental tumours now merits further investigation.

Table I Body weights, pancreatic weights and incidence of pancreatic cancer for hamsters undergoing oophorectomy or sham operations and receiving N-nitrosobis-(2-oxopropyl) amine (BOP)

| Treatment            | No. of animals | Body wt (g) (± s.e.) | Pancreatic wt (mg) (± s.e.) | Pancreatic/body wt (mg g⁻¹) (± s.e.) | No. animals with pancreatic cancer |
|----------------------|----------------|----------------------|-----------------------------|--------------------------------------|-----------------------------------|
|                      | Week 1 | Week 30 | Week 1 | Week 30 |                                    |                                    |                                    |
| Oophorectomy + BOP   | 30     | 29      | 114.1 ± 1.3 | 129.5 ± 3.8 | 658 ± 25 | 5.13 ± 0.17 | 13                           |
| Sham operation + BOP | 30     | 28      | 108.8 ± 1.5 | 126.4 ± 2.0 | 672 ± 32 | 5.31 ± 0.16 | 14                           |
| Total                | 60     | 57      |            |          |                                    |                                    | 27                           |

Correspondence: J.F. Chester, St George’s Hospital, Blackshaw Road, London SW17 0QT, UK.

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