Integrative medicine in gynaecological cancers

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Gynaecological cancers are the fifth most common cause of cancer death in women in Australia. This article reviews three studies investigating nutritional aspects relating to gynaecological cancers.

Micronutrients, folic acid and cervical cancer

Several lifestyle factors can increase the risk of cervical cancer, such as cigarette smoking, whereas specific micronutrients such as folic acid have been documented to reduce this risk. Cervical dysplasia is a common diagnosis in women aged 25–40 years and is aetiologically related to infection with the human papillomavirus (HPV). There has been uncertainty as to whether particular nutrients may reduce the rate of acquisition of a high risk HPV or whether they facilitate the clearance of high risk HPV.

A recent prospective 2 year follow up study[1] investigated high risk HPV infection (with follow up at 6 monthly intervals) to test the hypothesis that systemic concentrations of folate were associated with the occurrence and duration of high risk HPV infections. The study controlled for numerous micronutrients and known risk factors for high risk HPV infections and cervical cancer. The cohort consisted of 345 women who were at risk of developing cervical intraepithelial neoplasia and had blood micronutrient levels investigated for folate, vitamins B12, A, E, C, and total carotene. Results showed that women with a higher folate status were inversely associated with a positive high risk HPV test when compared with lower folate status during the study period (OR: 0.27, 95% CI: 0.08–0.91; p=0.04). Women with higher folate status were significantly less likely to repeatedly test positive (OR: 0.33, 95% CI: 0.13–0.86; p=0.02) and more likely to become test negative during the study period (OR: 2.50, 95% CI: 1.18–5.30; p=0.02).

This is the first long term prospective follow up study demonstrating a micronutrient has an independent protective role (ie. high folate status) on several aspects of the natural history of high risk HPV after controlling for known risk factors and other micronutrients. The authors concluded that improving folate status in patients at risk

of getting infected or who already are infected with high risk HPV may have a beneficial impact in the prevention of cervical cancer with folate supplementation.

Even with folate food fortification, the data from this study suggests that the current level of fortification would be inadequate to provide an optimally protective effect against cervical cancer.

Previously, a large case controlled study found that serum homocysteine was strongly and significantly predictive of cervical cancer risk.[2] This association could reflect folate, B12 and or B6 inadequacy, or genetic polymorphisms affecting the 1-carbon metabolism cycle.

Endometrial cancer – soya food intake

Endometrial cancer (EC) is the second most common cancer of the female genital tract in western societies. It occurs most often in women aged 50–70 years. Consuming unopposed oestrogen for a prolonged period increases the risk, with the increased risk appearing to persist for 10 years or more following exposure.

Phytoestrogens, which are weak oestrogens found in plant foods, may have anti-oestrogenic effects. Seven case controlled studies and one prospective study in 2003 examining the role of diet and EC, reported that consumption of wholegrains, fresh fruit and vegetables was associated with decreased risk of EC. It was thought that plant foods favourably alter the hormonal profiles of women.[3]

A population based controlled study in China reported the consumption of soya foods, a known rich source of phytoestrogens.[4] The design of the study utilised the face-to-face interview food frequency questionnaire, as well as collecting detailed information about soya food intake, menstrual and reproductive history, hormone use, disease history, tobacco and alcohol use, weight history, and family history of cancer were obtained. Current weight, height, waist and hip circumferences were measured. Soya products included: soya milk, tofu, processed soya products, dried soya bean seeds, fresh soya beans and soya bean sprouts. Participants in the study included 832 women with EC, aged 32–69 years, and 146 matched randomly selected control women.

Women with EC had a lower intake of soya foods, and almost every individual soya food investigated, as well as total soya protein and soya isoflavones, than did controls. The adjusted odds ratio of EC of women with the lowest quarter of intake was reduced from 0.93–0.85 and 0.67 with increasing quarter of soya protein intake (p=0.01).

A similar inverse association was observed for soya isoflavones and soya fibre intake. Women with high body mass index (BMI) and waist-hip ratio had an inverse association that was more pronounced. There was a similar inverse association among pre- and post-menopausal women. This study would have been more complete if oestrogen concentrations had been measured.

Obesity and ovarian cancer

The prevalence of obesity in Australia is one of the highest in the western world and continues to increase. Excess weight is known to be a risk factor for cancers of the large bowel, breast, endometrium, kidney (renal cell), and oesophagus. In the USA it is estimated that overweight and obesity account for 1:7 cancer deaths in men and 1:5 in women.[5]

Although epidemiological studies suggest that obese women are more likely to die of ovarian cancer than those of ideal body weight, it is not known whether increased incidence, comorbidities common to obese women, or altered tumour biology is responsible for this difference.

This study examined the influence of excess body weight on ovarian cancer survival, disease progression, and clinicopathologic factors.[6] The investigators reviewed the records of patients undergoing surgery for epithelial ovarian cancer at Cedars Sinai Medical Centre for 6.5 years. Epithelial ovarian cancer is the most common type of ovarian cancer originating from the surface of the ovary. The authors analysed data on height, weight, age, comorbidities, and treatment specific details using the Fisher Exact Test, Kaplan-Meier survival, and Cox regression analysis. Of the 216 patients identified, 8% were underweight, 50% were ideal body weight, 25% were overweight, and 16% were obese.

Obese women were also more likely to have mucinous and nonserous tumours compared with normal weight women. Stage 1 disease was present in 29% of the obese patients compared with 10% of the patients with a BMI less than 30 kg/m^2 (p=0.01).

In a subcohort of 159 patients with stage 3 or 4 disease, BMI was an independent negative factor for disease free (p=0.02) and overall (p=0.02) survival. Increasing BMI was associated with significantly increased risk for mortality with body mass indices more than 25 at shorter disease free times and higher chances of death. In this study, the cause of death was assumed to be ovarian cancer if the patient had recurrent disease at the time of death.

Other studies have supported the association between ovarian cancer and obesity.[7,8] A direct association has been found between dietary glycaemic index and glycaemic load with ovarian cancer risk, and consequently of a possible role of hyperinsulinaemia/insulin resistance in ovarian cancer development.[9] The assemblage of factors that define the metabolic syndrome may confer a high risk for this cancer.

Conflict of interest: none declared.

References

1. Piyathilake CJ, Henao OL, Macaluso M, et al. Folate is associated with the natural history of high risk of human papilloma viruses. Cancer Res 2004;64:8788–93.
2. Weinstein SJ, Ziegler RG, Selhaub J, et al. Elevated serum homocysteine levels and increased risk of invasive cervical cancer in US women. Cancer Causes Control 2001;12:317–24.
3. Folsom AR, Demissie Z, Harnack L. Glycemic index, glycaemic load and incidence of endometrial cancer: the Iowa women's health study. Nutr Cancer 2003;46:119–24.
4. Xu WH, Zheng W, Xiang YB, et al. soyaa food intake and risk of endometrial cancer among Chinese women in Shanghai: population based case controlled study. BMJ 2004;328:1285–90.
5. Calle EE, Thun MJ. Obesity and cancer. Oncogene 2004;23:6365–78.
6. Pavelka JC, Brown RS, Karlan BY, et al. Effect of obesity on survival in epithelial ovarian cancer. Cancer 2006;107:1520–4.
7. Rodriguez C, Calle EE, Fakhrabadi-Shokoohi D, Jacobs EJ, Thun MJ. Body mass index, height, and risk of ovarian cancer mortality in a prospective cohort of postmenopausal women. Cancer Epidemiol Biomarkers Prev 2002;11:822–8.
8. Schouten LJ, Goldbohm RA, Van den Brandt PA. Height, weight, weight change, and ovarian risk in Netherlands. Cohort study on diet and cancer. Am J Epidemiol 2003;157:424–33.
9. Augustin LSA, Bosetti JP, Kendall CWC, et al. Dietary glycaemic index, glycaemic load and ovarian cancer risk: a case controlled study in Italy. Ann Oncol 2003;14:78–84.

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