Review and hypothesis

Western diet, early puberty, and breast cancer risk

Basil A. Stoll
Oncology Department, St. Thomas' Hospital, London SE1 7EH, UK

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Summary

The typical high fat, low fibre diet of the industrialised West, particularly when associated with inadequate exercise, is likely to advance the onset of puberty. This will manifest in girls as an earlier menarche, earlier onset of breast development, and an earlier growth spurt. Both earlier menarche and adult tallness are markers of increased risk to breast cancer. Earlier menarche in the West is usually associated with earlier onset of hyperinsulinaemia, and multiple case-control studies report that hyperinsulinaemia too is a marker of increased breast cancer risk.

Although the Western diet is linked both to earlier menarche and also to earlier hyperinsulinaemia, the mechanism involved is not necessarily the same. While menarche is likely to be triggered by a threshold level of fatness, manifestation of insulin resistance is genetically-determined and strongly influenced by the fatty acid profile of the diet. The putative mechanisms by which they influence mammary carcinogenesis also differ. Early menarche is reported to be associated with a raised oestriadiol level persisting into early adult life. On the other hand, hyperinsulinaemia is commonly associated with abnormal aromatase activity in the ovaries. In addition, the concomitant increase in bioactive levels of insulin like growth factor I may synergise with oestrogen in stimulating proliferative activity in mammary epithelium.

Dietary modification and exercise regimens are proposed in families at high risk to breast cancer. The measures have been shown to reduce insulin levels in both children and adults, and serial monitoring of insulin and sex steroid levels could be used to detect a metabolic-endocrine effect.

Introduction

Improving nutrition is generally assumed to be responsible for the secular trend to ever-earlier onset of menarche in Western industrialised countries. Most epidemiological studies in Western women confirm that the onset of menarche before the age of 13 is associated with increased risk of breast cancer, particularly in premenopausal women [1]. Studies have shown that the earlier onset of menarche is followed by an increased serum oestriadiol level which may persist into early adult life [2, 3] and this has been assumed to be the major factor responsible for the increased breast cancer risk.

An additional risk factor may be the hyperinsulinaemic insulin resistance commonly found in obese pubertal children [4]. Pubertal hyperinsulinaemia persists into adult life in some populations and multiple case-control studies have now confirmed it as a risk marker for postmenopausal breast cancer [5–15], although one study reports dissonant findings [16]. Both earlier menarche and earlier onset of hy-
perinsulinaemia are associated with the consumption of a Western diet, but different nutritional mechanisms may be involved. Whereas onset of menarche is likely to be triggered by a critical body fatness [17], there is increasing evidence that insulin sensitivity is strongly influenced by the fatty acid profile of the diet [18].

This review examines the mechanisms by which the dietary characteristics of the industrialised West favour not only an earlier onset of menarche but also the development of hyperinsulinaemia. It also examines possible effects on breast cancer risk from the effects of hyperinsulinaemia on ovarian steroidogenesis and the effect of an increased bioactive level of insulin-like growth factor IGF-1 on mammary epithelium. The findings may be relevant to recent observations that African-American girls show an earlier onset of menarche and thelarche than do Caucasian-American girls [19], and also more frequent insulin resistance, lower androstenedione levels, and a higher incidence of premenopausal breast cancer [20–22].

Early menarche, adult tallness, and breast cancer risk

In Western populations, the mean age of girls at the onset of menarche has fallen from about 16 to 13 since the beginning of the century. Nutritional factors are likely to be responsible and current opinion is that menarche is provoked by a critical accumulation of adipose tissue rather than through the effect of specific macronutrients [17]. Studies in the USA and Canada have found that earlier onset of menarche is associated with a greater height and weight for age and that after allowing for these variables, there was no association with energy-adjusted intake of fat, protein, or carbohydrate in the diet [23, 24]. Nevertheless, one prospective study in Germany concluded that a higher energy-adjusted fat intake was associated with accelerated menarche and might be responsible for earlier body fatness [25].

Most case-control and prospective studies in the USA and Europe have shown that taller women have a higher risk of breast cancer (reviewed in [26]). In one large study, the relative risk for women in the highest quartile was 2.1 times that of the lowest quartile. An earlier menarche is likely to be associated with an earlier growth spurt in adolescence, although not necessarily with adult tallness because of ‘catch up’ by the others. Nevertheless, the secular trend to earlier menarche in Western girls has been associated with increasing tallness in adult women [27].

Metabolic-endocrine signals in the hypothalamus initiate menarche and the major triggering factors is assumed to be a critical body mass/fat ratio [16]. The initiation of menarche is signalled by an increased amplitude of gonadotropin secretion. It is followed not only by increased ovarian production of sex steroids but also by increased circulating levels of growth hormone (GH) and insulin-like growth factor IGF-1 [28]. Growth hormone may synergise with gonadotropin in stimulating production of ovarian steroids and in increasing the rate of sexual maturation [29]. But while circulating IGF-1 levels are clearly related to the Tanner stages of genital development, high GH levels usually manifest only in late puberty when the rising oestriadiol level is thought to stimulate GH release [30].

Evidence of insulin resistance is common in children at the time of puberty but is found also before puberty in children with moderate or severe obesity [31]. The development of insulin resistance is likely to be favoured by obesity but it is seen also in lean children [32]. Hyperinsulinaemia persists after puberty in individuals who are genetically susceptible but its prevalence depends on diet. The fatty acid composition of cell membranes modulates insulin action, and in Western countries, insulin resistance is greater with a higher incorporation of saturated fatty acids and less with a higher incorporation of the n-3 group of polyunsaturated fatty acids (PUFAs) [17]. The latter are common in fish oils and this may be relevant to the observation that the very low breast cancer mortality in Japanese women increased by 35.5% between 1960 and 1980 [33] and has been ascribed to the increasing replacement of the traditional high fish oil intake by Western style foods [34].