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The luteinising hormone–releasing hormone analogue triptorelin with or without the aromatase inhibitor formestane in premenopausal breast cancer: effects on bone metabolism markers

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Abstract

Background: the combination of a luteinising hormone–releasing hormone (LH–RH) analogue and an aromatase inhibitor (AI) induces greater oestrogen suppression than the analogue alone in premenopausal breast cancer. However, very few data on the biological effects of such a combination are currently available. *Aim of the study:* the short-term effects of treatment with the LH–RH analogue triptorelin alone or in association with the AI formestane on bone metabolism were investigated in premenopausal breast cancer. Circulating levels of the bone formation markers carboxy-terminal and amino-terminal propeptides of type I procollagen (PICP and PINP) and the bone resorption marker cross-linked carboxy-terminal telopeptide of type I collagen (ICTP) were assessed. In addition, serum levels of insulin-like growth factor (IGF)-I, IGF binding protein (IGFBP)-3 and interleukin 6 (IL-6) were evaluated. *Patients and methods:* twenty-one patients with advanced breast cancer were randomly given triptorelin monthly alone ($n = 10$, arm A) or in combination with formestane fortnightly ($n = 11$, arm B). Blood samples were collected over a 3-month period. *Results:* serum PICP and PINP levels increased significantly over time ($P = 0.0065$ and 0.0197 in arm A and B, respectively); no change in ICTP levels was observed. A rise in IGF-I and IGFBP-3 levels was seen in each treatment group, but only the increase in IGF-I was significant ($P = 0.0138$, always). The on-treatment levels of the bone turnover markers and IGF-system components were inversely correlated with serum oestrogens. Neither treatment modalities significantly affected serum IL-6 levels over time. No difference in the behaviour of any of the assessed biomarkers was observed between patients with or without skeletal metastases. *Conclusion:* it is worth noting that complete oestrogen depletion, at least in our case series, seems to increase only osteoblastic activity markers. The observed modifications appear to be related to oestrogen depletion per se rather than the degree of oestrogen suppression or the different therapeutic regimen administered.

Keywords: Breast cancer; Bone metabolism markers; Growth factors; Cytokines; Oestrogens; Gonadotrophin releasing-hormone; Aromatase inhibitors

1. Introduction

The goal of endocrine therapy in breast cancer is to inhibit the oestrogen-stimulated growth of tumour cells. This can be accomplished in two major ways — by blocking the oestrogen receptor (ER) at the target cell or by inhibiting the oestrogen supply to tumour tissue [1]. The latter approach relies on the suppression of oestrogen biosynthesis by means of inhibitors of the aromatase enzyme complex [2,3]. Although the role of aromatase inhibitors (AIs) in the management of post-menopausal breast cancer is well established, a high degree of ovarian aromatase activity together with the

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