ELSEVIER

EJC Supplements Vol 2 No. 9 (2004) 81–83

EJC Supplements

www.ejconline.com

E29. Management of the menopause in breast cancer patients

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1. Introduction

It has been reported that breast cancer patients often have a higher prevalence of menopausal symptoms than women in the general population [1]. This is even more marked when the onset of the menopause is sudden or occurs at an early age (premature menopause) [1]. An exacerbation of menopausal symptoms can certainly be partially explained by the distress linked to the disease. It is also more frequent when using hormonal chemotherapy [2].

In the 1990's, it was generally believed that hormone replacement therapy (HRT) prevents many chronic diseases, such as coronary heart disease, or even Alzheimer's disease [3]. As a consequence, the question was raised as to whether HRT is really contraindicated in breast cancer patients [4].

The aim of this presentation is to review critically the therapeutic strategies reducing the menopausal symptoms in breast cancer patients and to focus on their efficacy or safety.

2. Methods

A systematic review of available data concerning HRT after breast cancer has been searched. In this presentation, some of these articles are discussed. Comments on the efficacy and safety of other drugs used in such patients (clonidine, serotonin re-uptake inhibitors) or alternative medicine (phyto-oestrogens) are also presented.

3. Results and discussion

Several observational trials in breast cancer patients reported no increase in breast cancer recurrences using HRT [5–8]. In addition, two meta-analyses supported this notion [9,10]. We conducted a systematic review of these trials and observed that none were randomised and that most are retrospective and often hampered by a huge heterogeneity, lack of statistical power and, possibly, by selection biases. Nevertheless, these trials have justified the onset of several double-blind studies regarding the efficacy and safety of HRT or of tibolone, a tissue-specific steroid in breast cancer patients. Some of these trials are still ongoing. However, very recently, one of them "the HABITS-trial", was stopped because it revealed an increased risk of breast cancer recurrence (Rlative Hazards = 3.5; 95% Confidence Interval 1.5–8.1) [11].

Today, many breast cancer patients also use so-called alternative medication, such as phyto-oestrogens. There is substantial commercial promotion of these so-called "natural" medications, with claims of efficacy and an absence of harm. However, most well-designed randomised trials have failed to report relief of symptoms higher than that observed for placebo [12]. Furthermore, the safety of these drugs remains to be proven, since there is some evidence that certain isoflavones can stimulate breast cancer growth and interfere with the antitumour activity of tamoxifen [13]. We therefore believe that, at this time, the use of phyto-oestrogens, as well as that of HRT or other tissue-specific steroids, should be restricted to protocols in breast cancer patients.

Finally, many breast cancer patients can be treated for their vasomotor symptoms with non-hormonal drugs, such as clonidine or serotonin re-uptake inhibitors, which have a modest beneficial effect (compared with placebo), but can also have side-effects

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1359-6349/$ - see front matter
doi:10.1016/j.ejcsup.2004.08.034

[14–16]. Furthermore, the safety of these drugs remains to be proven, since Stearns and colleagues [17] showed a diminution of the metabolisation of tamoxifen when the latter is co-administrated together with serotonin reuptake inhibitors. Vaginal moisteners and, if necessary, weak oestrogen vaginal gels are used for the relief of vaginal atrophy [18].

Although some publications reported that women with increased bone density have an increased risk of breast cancer, breast cancer patients are also susceptible to suffering from osteoporosis [19–21]. Osteoporosis can be prevented in breast cancer patients by promoting healthy lifestyle habits, which include regular exercise. It has also been reported that exercise reduces the risk of breast cancer recurrence [22]. Some of these patients will be treated by tamoxifen, which has been shown to also have some bone-sparing action, while, by contrast, Gonadotrophin-releasing hormone (GnRH) agonists and aromatase inhibitors induce bone loss [23, 24]. Women with low bone mass, should receive a calcium and vitamin D supplementation, and those with osteoporosis may be treated with biphosphonates or, alternatively, with raloxifene (when they are not using tamoxifen).

4. Conclusions

Breast cancer patients often suffer more from menopausal symptoms than other postmenopausal women. Nevertheless, before treating them, one has to be certain about the safety and efficacy of the treatments given.

Unfortunately, most observational studies conducted using HRT in breast cancer patients are of insufficient quality to provide information about its safety. Furthermore, the only randomised trial showed an increase in cancer recurrence using HRT.

The other drugs which can be used for menopausal symptoms are less effective than HRT and only few data are available about their safety in breast cancer patients. There is a strong need for protocols in assessing the safety and efficacy of treatments for menopausal symptoms in breast cancer patients.

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