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Abstract: P8

Short term results of a computerised program for breast carcinoma risk analysis

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1. Introduction

New selective modulators of the oestrogen receptor (ER) that are protective against the development of breast cancer will soon be proposed for use as mamma-protective preventive medication in women with a high risk for breast cancer. We present the short-term results of a computerised mass screening programme that enables calculation of the individual risk of breast carcinoma.

2. Objective

To test the predictive value of a newly developed computerised program for the assessment of individual risk for breast cancer. Calculation of risk of 943 women participating in a mammography screening programme was compared with the results of mammography and pathology of biopsies.

3. Methods

An interactive d-Base program requests input from women who present for early breast cancer screening. Basic risk according to age is adjusted for most known risk factors. The program returns: (a) a summary of the protective and risk-enhancing factors of the individual; (b) a crude risk for developing breast cancer expressed in number per 100 000 woman-years (crude breast carcinoma risk score — CBCRS); (c) the relative risk compared with other women of the same age. An individualised advice for further follow-up or use of preventive mamma-protective medication can easily be incorporated.

4. Results

From April 1992 to February 1993 detailed information of 943 women presenting for mammographical screening was obtained. 13 women had suspect lesions on mammography and required further analysis. 6 of these had cancer, while the remaining 7 had a negative biopsy or a negative supplementary diagnostic work-out. The mean CBCRS was 989 versus 153 in the 6 women with suspected mammography and breast cancer (true-positive mammography), 462 versus 128 in the 7 women with suspected mammography and no breast cancer (false-positive mammography) ($P = 0.02$) and 430 versus 312 in the 778 women with normal mammography and no breast cancer ($P = 0.0003$).

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PII: S0959-8049(00)00254-9

5. Conclusions

Preliminary data show an increased risk in women with undiagnosed cancer at initial screening. The program was designed for calculating the remote risk for breast cancer, but these data are not available yet. The risk analysis may reduce the cost-price of follow-up, increase the women's motivation to improve some of their risk factors and make her more likely to focus on follow-up mammographic examination and preventive medication. After further refining, the risk profile may contribute to the correct interpretation of mammograms.

Abstract: P9

Determination of tamoxifen and its metabolites in endometrial tissue of long-term treated women

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1. Introduction

The need for large samples (usually recovered from surgical specimens) for chromatographic methods has limited the determination of tamoxifen and its metabolites in human endometrial tissue. Instead, mass spectrometry allows the study of drug distribution even in very small specimens.

2. Objective

We have, therefore, studied 23 postmenopausal breast cancer patients on chronic tamoxifen treatment to measure tamoxifen, N-desmethyltamoxifen (metabolite X), N-didesmethyl-tamoxifen (metabolite Z) and 4-hydroxytamoxifen (metabolite B).

3. Materials and methods

Hysteroscopically-directed endometrial biopsy was taken with microforceps (mean: 2 mg of tissue immediately frozen) together with a sample of blood. Endometrial and serum samples were conveniently processed, homogenated and then analysed with mass spetrometry to measure tamoxifen, N-desmethyltamoxifen (metabolite X), N-didesmethyl-tamoxifen (metabolite Z) and 4-hydroxytamoxifen (metabolite B). Quantitative determinations of tamoxifen and its metabolites were made and expressed as ng per ml of serum or g of endometrial tissue. Endometrial concentrations of tamoxifen and its compounds were also expressed as percentage increase of tissue toward serum concentrations, assuming that 1 ml of serum is equivalent to 1 g of tissue.

4. Results

Metabolite X was by far the most concentrated compound both in serum (mean: 318±158 ng/ml) and in the endometrium (mean: 4240±1642 ng/g) but with a serum/tissue gradient of only a 17-fold increase. B metabolite had the highest gradient (more than 400-fold increase with serum concentration of 7.5±5.3 ng/ml and tissue concentration of 1952±1283 ng/ml). Tamoxifen was less detectable in serum (mean: 102.3±44.8 ng/ml) than X metabolite, and was the least concentrated in tissue (mean: 1887±762 ng/g) with a gradient of 22-fold increase. Z compound had an inter-

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PII: S0959-8049(00)00255-0