Abstract

Anti-estrogen therapy is used for treatment of hormone (estrogen) receptor positive breast cancer. The rise of this type of cancer is associated with a prolonged exposure to these hormones throughout life. Tamoxifen is one of the most used hormonal drugs, which blocks the effects of these hormones in breast cancer tissue by competitive binding to hormonal receptors. The affinity of tamoxifen to these receptors is not sufficient, therefore it has to be activated to metabolites having greater affinity, namely 4-hydroxytamoxifen and endoxifen. The formation of these intermediates is catalysed by cytochromes P450. In the second phase of its biotransformation hydroxylated metabolites of tamoxifen are primarily sulphated by sulphotransferases and eliminated from the body. In addition to these active intermediates, which inhibit the growth of breast tumor tissue, there are metabolites causing negative effects in the others. The most important metabolite is α-hydroxytamoxifen, which forms covalent DNA adducts in liver tissue of rats and endometrium of females. Tamoxifen therapy is associated with numerous side effects, but the greatest attention is focused to formation of endometrial cancer and induction of tumor´s resistance to this therapy. Effects of tamoxifen therapy are dependent on the activity of enzymes, which are associated with its biotransformation. This activity is inter-individually different as a consequence of genetic polymorphisms of such enzymes. In addition, the effects of other drugs used, which can interact with tamoxifen and caused reduced efficiency of tamoxifen therapy, should also be considered. (In Czech)