Abstract

The safety of systemically administered sex steroids continues to be a major focus of researchers. The negative results of the Women's Health Initiative study (WHI), and follow-up reports published in JAMA, evaluating the safety of estro-progestogen in postmenopausal women, elicited an unprecedented reaction in the press by women and doctors alike. From these publications, it is clear that research should focus on new progestogens and on alternative administration routes to minimize adverse drug effects. One approach to the improvement of safety, efficacy, and acceptability of steroid hormones, including patient compliance, is to develop long-acting implantable methods that deliver the lowest possible dose to the key target tissues. This therapeutic concept of "minimal intervention" has been known for several decades, but the practical applications of the method were lacking. Intrauterine drug-delivery systems can be developed to achieve minimal intervention fertility control without influencing normal ovarian function and/or causing adverse hormonal effects. With hormone replacement therapy in postmenopausal women, research suggests that progestogens delivered directly to the uterine mucosa could reduce side effects and minimize reversal of the beneficial effect of estrogens. Various "frameless" and "framed" intrauterine systems are currently being clinically evaluated. They are less troublesome than the available intrauterine systems and could therefore be suitable for use in the majority of women for contraception and treatment purposes (e.g., menorrhagia, hormone replacement). These systems require a single short office procedure, and have a low morbidity, which is undeniably linked with more invasive methods and systemic hormonal contraceptives. Due to the technological progress miniature, low-dose, long-term intrauterine drug-delivery systems offer enhanced effectiveness, reduced side effects, and optimal user compliance. Although there is minimal absorption in the systemic circulation, they deserve the status of a locally acting method that should be regarded as fundamentally advantageous, if effective, to systemically applied medications that may have potentially inherent ill side effects