

# facts and opinion

## Estrogens + Patient Package Insert = Confused Patients

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*A brief review of the patient package inserts concept and estrogen pharmacology is presented. Then the need for patient education is discussed along with recommendations for a team approach to managing patient anxiety by helping patients understand the estrogen-containing products they are using.*

A postpartum patient, elated at the birth of her child, relaxes in the recovery room. Since she has decided not to breastfeed, her physician has prescribed an estrogen-containing drug which may help avoid painful postpartum breast engorgement. In accordance with a recently enacted law, she is given a patient package insert (PPI) entitled "Information for the Patient—What you should know about estrogens". She appears apprehensive as she reviews the section entitled "The Dangers of Estrogens". There, she reads that she could be susceptible to endometrial cancer, tumor of the breast, cervix, liver, gallbladder disease, and abnormal clotting if she takes the drug. By this point, our previously elated patient is not only apprehensive but the information provided in the PPI has left her with numerous unanswered questions and concerns about her own personal health.

The above example, while melodramatic, is in fact, realistic. Realizing that PPI's are required by law and may be beneficial in many cases, what can be done to alleviate some of the patient's apprehension concerning estrogens? One approach to handle potential problems generated by the estrogen PPI law was developed jointly by the departments of Nursing and Pharmacy at Crozer-

Chester Medical Center, Chester, Pennsylvania.

### The PPI Concept

Are patients adequately informed about the medications they are taking? Are patients allowed to participate in the decision to prescribe a certain drug? Many patients and proponents of consumer interests feel that the answer to both these questions is no. In addition, they indicate that the present system of providing drug information to patients is totally inadequate. The PPI is most often suggested as a possible answer.

The first PPI was created in 1970 when the FDA mandated that a patient-oriented insert be provided to the patient each time an oral contraceptive was dispensed. Its inception grew out of concern over the safety of these agents as a result of reports published in the 1960's. More recently, on October 18, 1977, the FDA implemented regulations dictating mandatory dispensing of PPI's along with all estrogen-containing drugs.<sup>1</sup> In community pharmacy practice, the law states that, when a patient has a prescription filled for an estrogen-containing product, a PPI must be provided to the patient at the same time.

In the hospital setting, a PPI must be given to the patient before ad-

ministration of the first dose of estrogen and every 30 days thereafter as long as the therapy continues. The intent of the law and the concept of the PPI would appear, on the surface, beneficial to all. The primary purposes of the PPI are to inform the patient why a drug is used, what help it can provide, why it should be taken as directed, what the adverse effects of the drug can be, and what to do if a side effect occurs.

However, before proceeding, we must ask if we aren't forging ahead too hastily. Additionally, will PPI's really improve compliance, reduce the incidence of adverse drug reactions, and reduce costs solely as a result of giving the patient information? Are we giving adequate attention to the potential for the undesirable side effect of confusing the patient or discouraging the use of an often prescribed drug? This is a difficult set of questions for which no answers are readily available.

Realizing that a PPI must be given to the patient, it would appear necessary that nurses and pharmacists review and develop their own pharmacological information banks concerning estrogens in order to be able to handle some of the questions that patients may initiate.

Over the past few years, the literature published on estrogens and associated side effects has grown at a tremendous rate. Much controversy and confusion has surfaced so that it is mandatory that one continually review the literature for new developments.

The following review is not to be comprehensive, but it can give the nurse and the pharmacist a basic foundation to build on.

### Estrogen Review<sup>2-4</sup>

Estrogens are hormones secreted primarily by ovarian follicles and also by the adrenals, corpus luteum, placenta, and testes, or are synthetic steroidal and non-steroidal compounds.

Estrogens have important effects on uterine development and cyclic endometrial changes associated with ovulation. They are also responsible for providing sex characteristics in

the female. Estrogens are secreted at varying rates during the menstrual cycle. During pregnancy, the placenta becomes the main source of estrogens. At menopause, ovarian secretion of estrogens declines at varying rates. There is a complex feedback system which results in the cyclic phenomenon of ovulation and menstruation. This and other mechanisms of action are beyond the scope of this review. However, the reader is referred to Goodman and Gilman<sup>2</sup> for detailed information.

### Uses

Estrogens are used widely for menopausal disturbances, atrophic vaginitis, inhibition of lactation, menstrual disturbances, osteoporosis, and some types of prostatic and mammary carcinoma. More specifically, they are administered therapeutically for replacement therapy in several conditions, including the following.

**Menopausal Syndrome.** The purpose of therapy in this case is to relieve the various physiological and psychological effects of a decline in natural hormone production. The doses required for relief vary due to the variation in individual response to estrogens. They should be used in minimal doses during menopause to lessen the undesirable effects of the transition period but not to prolong the natural body adjustment, which must be made eventually.

**Estrogen Deficiency.** Here estrogens are used to prevent symptoms of estrogen deficiency when a woman's ovaries have been removed surgically before the natural menopause. Estrogen therapy is also used in sexual infantilism because it promotes the development of the uterus and the secondary sex characteristics.

**Inhibition of Lactation.** With high blood concentrations, estrogens produce a reflex inhibition of the lactogenic hormone, thus suppressing lactation. They are employed in instances in which a mother prefers not to nurse her infant. Therapy is most effective if started immediately after delivery and has little value once lactation has been established.

**Prostatic and Mammary Carcinoma.** In prostatic carcinoma, estrogens may alleviate local discomfort and may bring about a regression of the primary tumor and soft tissue metastases, although malignant cells do not completely disappear. Estrogen therapy may be useful in palliative treatment of mammary carcinoma in women who are at least 5 years past the menopause; however, therapy should be limited to those patients who do not respond to surgery or radiation therapy.

**Inhibition of Pregnancy.** Estrogens in combination with progestogens successfully inhibit ovulation, thus preventing conception.

While there are numerous other uses of estrogens, these are the most common.

### Adverse Reactions, Cautions and Side Effects

Patients receiving estrogen therapy should be under continuous medical supervision. Since estrogens are prescribed for many symptoms which differ from the symptoms of genital tract malignancies, the breast and pelvic organs should be examined before initiating therapy and periodically thereafter, to rule out neoplastic lesions.

The most frequent side effect associated with estrogen therapy is nausea, which usually disappears with continued therapy and rarely necessitates discontinuation of the drug. Other gastrointestinal side effects include vomiting, abdominal cramps, anorexia, diarrhea, and thirst. Additional side effects include purpura, hypersensitivity reaction, edema, leg cramps, and following prolonged therapy, hypercalcemia.

Continuous estrogen therapy for prolonged periods may produce endometrial hyperplasia and uterine bleeding; in most cases, this may be prevented by using minimum dosage and administering the drug cyclically. Intravaginal application of estrogens may produce a vaginal discharge due to mucous hypersecretion. Thromboembolic disease has been associated with the use of oral contraceptives containing an es-

trogen. Also, there may be an association between the use of oral contraceptives and death from pulmonary embolism or heart attacks in previously healthy women.

In men, gynecomastia, loss of libido, arrest of spermatogenesis, and testicular atrophy may occur with prolonged therapy.

Because estrogen therapy may increase fluid retention, the drugs should be administered with caution to patients with asthma, epilepsy, migraines, cardiac failure, hypertension, hyperlipoproteinemia, or renal dysfunction. Estrogens should also be carefully administered to patients with bone diseases or other diseases involving calcium or phosphorus metabolism, since estrogens are known to affect this metabolic process. Caution should also be observed when estrogens are administered to women who smoke, are of advanced age, or have a history of thrombophlebitis or thromboembolism.

### Cooperative Approach

The PPI attempts to present some of the complex pharmacology, indications, and dangers of estrogens in lay terms. This task is not easy when one considers the wide variance of ability to interpret and comprehend that exists among the general population. It is too early to determine what effect the PPI's will have. However, in the case of oral contraceptives, there have been some experiences which can be reviewed.

Fleckstein, *et al.*,<sup>5</sup> attempted to assess, via a questionnaire survey, patients' attitudes, knowledge, views, and sources of drug information on oral contraceptives, with particular attention to the role of the patient-oriented package insert. One of the conclusions made from this survey was that professional sources (physician, nurse, pharmacist) were preferred over nonprofessional and media sources. In addition, it would appear from their data, that patients desire *direct communication* with a professional in addition to the printed matter. We concur with this approach since our patients seem to

prefer to have a professional explain the PPI. A team approach was developed that meets the law *and* takes into account the patient's psychological well-being.

Basically, the Pharmacy and Therapeutics Committee recommended the following: 1) Standardization of all estrogens on the Formulary. 2) A pharmacist will be responsible for presenting the PPI to the patient and explaining it. 3) Ob/Gyn patients' charts will contain signed consent forms after the presentation of the PPI, prior to hospital admission, since the patients are often sedated when estrogens are administered. 4) The pharmacist's activities will be documented in the patient's record.

In addition, the Pharmacy and Nursing Committee recommended that the pharmacist and nurse consult with each other to ascertain if any special approaches might be needed before the estrogen information is given to the patient. Briefly, the procedure utilized by the pharmacy is as follows:

1. Upon request of an order for an estrogen-containing product, the pharmacist will obtain the appropriate PPI. (Note that to avoid liability of misbranding, each prescription for a specific manufacturer's product should be dispensed only with that particular manufacturer's Patient Information Insert).

2. The pharmacist will review the patient chart, noting the indication for which the estrogen is to be used. *If the indication differs from those enumerated in the PPI, the prescribing physician will be contacted and a clarification as to what the patient is to be told will be made.*

3. The pharmacist will then give the patient the PPI explaining its purpose and answer any questions according to accepted guidelines for patient consultation.

4. Upon completing this, an entry in the progress notes of the chart will be made as follows: "The PPI for the drug \_\_\_\_\_ (drug name) has been given to the patient. The patient indicated comprehension of the content". Name of Pharmacist \_\_\_\_\_ Date & Time \_\_\_\_\_

In unusual circumstances, where the PPI has to be given to a family mem-

ber or guardian, the name of that person will be included in the entry.

### Case Study

Subsequent to the presentation, what happens to the patient? The following is a representative case study of the possible therapeutic interaction the pharmacist and the nurse can have.

Mrs. S., a 25-year-old white woman, has been receiving prenatal care from a private physician. It was her first pregnancy and she had tried to read available literature carefully. During her 28th-30th week of pregnancy, her physician asked her to begin to think of the type of anesthesia and delivery she would prefer (i.e., epidural versus local; childbirth with her husband present, etc.). Her physician, Dr. M., also asked her to sign the various hospital and physician consent forms. Among these was a consent for estrogen-containing products concerned with suppression of lactation. When Dr. M. presented the consent to be signed, he also gave her the Patient Package Insert, asked her to read it, and informed her that he would answer any questions. Mrs. S. became very quiet as she read the insert describing contraindications of estrogen usage. She asked the doctor if there was anything else she could take to suppress lactation as she really did prefer to bottlefeed. Dr. M. responded that there was nothing else. She then refused to sign the consent form and desired more time to consider this medication.

Mrs. S. is admitted to the labor and delivery suite in active labor, 9-10 weeks later. She signs more hospital consent forms and is again approached to complete the estrogen consent. She again refuses. Subsequently, she delivers a 6 lb, 5 oz, baby girl with Apgar scores of 8 and 9. Her postpartum course is uneventful except for engorged breasts. All methods of treatment are employed to relieve her discomfort including binding of her breasts, icepacks, etc. She is discharged home, still with extreme breast discomfort along with the responsibility of caring for a newborn, accepting the new role of mothering, and resuming her relationship with her husband.

What other approach can be utilized to better provide clear patient education? We feel that the best approach is to have the physician first present the patient with the PPI and consent form. If it is not possible to complete the process prenatally and the physician does not do the follow-up teaching, the pharmacist and nurse can work together as a therapeutic team. The patient's chart can be reviewed by the pharmacist, and when it is determined that the estrogen is to be used for milk suppression, the appropriate PPI will be chosen. We have elected to have one type of estrogen available for use, eliminating confusion with many different brands. The pharmacist then notifies the nurse caring for the patient of his plan and receives information concerning the patient's present postpartum condition, physically and emotionally. The pharmacist then will give the patient the PPI explaining its purpose and will answer any questions he is able to. The nurse will later approach the patient and reinforce the teaching.<sup>6,7</sup> It is extremely important for all information to be consistent. We therefore urge the collaboration of the physician, pharmacist, and nurse.

### Other Recommendations

The issue remains as to whom the consents and PPI truly protect.<sup>8</sup> One would hope that the furor over estrogens originated with consumer groups concerned with patient education and protection. However, it has become apparent to the health professionals who deal with many confused and frightened patients that the protection is, perhaps, for the drug company producing the product. If we are genuinely motivated to patient education, the PPI's should be written in language that is readily understandable to the literate layperson. It should also be presented in the context of its usage. The previously cited case study was specifically related to an obstetrical service. But, what of the situations where estrogens are adjunct therapy to radiation for patients with prostatic carcinomas? Furthermore, what if the attending physician has chosen not to inform the patient of his true prognosis? The pharmacist and the

nurse are put in the uncomfortable position of educating patients while at the same time implementing the physician's orders.

What is an appropriate nursing/pharmacy intervention which can successfully educate the patient as well as provide a milieu for intelligent decision-making? One method would be for each medical center, in a combined nursing-pharmacy-medical approach, to plan, write, and implement a PPI for their particular needs. Federal law at this time does not allow individual medical centers to write their own PPI's. But our recommendation is for health centers to design information packets from data distributed by drug companies.

For example, if we always deal with postpartum women who will be given estrogens for milk suppression and perhaps for birth control, our packets will deal specifically with that aspect. We will delete the warnings concerning menopause, continuous treatment for genital tract malignancies, etc. The postpartum woman will have her fears allayed greatly because the insert deals directly with her present physical condition. Second, the pharmacist, nurse, and physician must consistently present the same information, and be available for any questions the patient has. Third, the patient should be informed that the consent merely indicates that she has read information pertaining directly to the estrogen product she will be given. It does not release anyone from liability associated with dispensing of information nor of the product itself.

### Conclusion

The issues presented for discussion give nurses and pharmacists some al-

ternatives. A collaborative approach to patient drug education is invaluable. It is not difficult to coordinate as long as all health professionals involved will standardize the estrogen drug to be used, establish in writing a clear policy regarding the PPI process, and involve themselves in a therapeutic teaching plan for the patient. The nurse should have a general base of information concerning estrogens and their effects on all systems of the body. She/he should also be acquainted with contraindications, side effects, and adverse reactions. Nurses should also be given guidelines for teaching the material and presenting it to the patient and family. Finally, documentation of the nurse's activities as well as the pharmacist's must be clearly delineated in the patient's record. The documentation should include not only the information given, but a verbalization of understanding and the resultant decision made by the patient.

It is hoped that nurses and pharmacists will persist in their consumer-oriented approach concerning estrogens. By cooperating in writing and implementing programs of product information that deal directly with the individual patient problem, they will deliver higher than the minimum care as outlined by government standards.

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