

'Chemobrain' Not Seen in Breast Cancer Therapy

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Assistant Editor

CHICAGO — Chemotherapy-related cognitive impairment was infrequent in a small study of 30 patients who underwent adjuvant chemotherapy for non-metastatic breast cancer.

"People could be making decisions about whether or not to have chemotherapy based on stories they've heard about 'chemofog' or 'chemobrain,'" said Dr.

David G. Darby, "We hope this information will help people make informed decisions."

Dr. Darby and his colleagues looked at a total of 30 women who had already undergone either lumpectomy or mastectomy and were scheduled to undergo either the chemotherapy regimen known as AC (n = 15) or CEF or CMF regimens (n = 15).

► The AC regimen involves doxorubicin 60 mg/m² and cyclophosphamide 600 mg/m² intravenously, repeated every 21 days for a total of four cycles.

► The CEF regimen involves cyclophosphamide administered orally in doses of 75 mg/m² on days 1-14; epirubicin 60 mg/m² by IV on days 1 and 8; and 5-fluorouracil 500 mg/m² by IV on days 1 and 8, repeated every 28 days for six cycles.

► The CMF regimen involves cyclophosphamide 100 mg/m² given orally on days 1-14; methotrexate in doses of 40 mg/m² via IV on days 1 and 8; and 5-fluorouracil 600 mg/m² given by IV on days 1 and 8, repeated every 28 days for a total of six cycles.

The women were compared with 30 age-matched controls.

Women took several tests designed to measure cognition as well as mood a few days before initiating chemotherapy (but after the diagnosis had been given and treatment course was decided); again at the start of each new treatment cycle; and for the last time 28 days after the final treatment cycle had begun in each group. Patients were assessed on the National Institute of Mental Health's Center for Epidemiologic Studies Depression (CES-D) scale, the State-Trait Anxiety Inventory (STAI) scale, and a test of Dr. Darby's own design, which measures detection speed, identification speed, working memory, and learning ability in a 10- to 12-minute battery.

Dr. Darby is the chief medical officer of a company he formed, called CogState, which produces and scores these tests. It is based in Australia and partly funded this study.

"The first finding of interest was that prior to the first cycle of chemo there was impairment in learning of moderate amplitude, and that was also associated with a mild reduction on mood scales or depressive scales," said Dr. Darby in an interview. No women were clinically depressed (clinically depressed patients were excluded from the study) and none of the women were on antidepressants at baseline or throughout the study. However, he said, "There may have been an impairment there initially, prior to chemo."

Two other findings also emerged, both good and bad. "There was an improvement of some of the learning aspects of their performance and a mild improvement on scores on anxiety scales, but there was also a mild deterioration in aspects of concentration and psychomotor speed [as the study progressed]." There was also evidence that patients' mood was declining slightly throughout the treatment.

Individual patients showed "quite a lot of variation—in particular, some patients would have impairment on only one occasion and then improve, and others would have impairment on two or more occasions," he said. Persistent impairment, that occurring on two consecutive occasions, was seen in only three patients, or 10% of the total, Dr. Darby reported at the annual meeting of the American Academy of Neurology.

Impairment in concentration was not severe, "equivalent to the sort of jet-lag that I'm feeling now, having travelled from Australia." He also likened it to the sort of impairment one would feel after being awake for about 17 hours.

Dr. Darby found no significant differences in the risk for cognitive impairment based on the women's age, menopausal status (pre-, peri-, or post-), or time from surgery.

As for the practical applications of his results, Dr. Darby said, "When women are confronting breast cancer, coming to terms with the many different aspects of it, and trying to take advice and understand what's happening to them, the issues of quality of life are important. They should realize that these sorts of changes seem to be very mild." ■

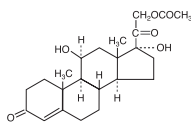
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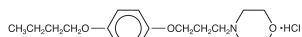
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Topical corticosteroids are anti-inflammatory and anti-pruritic agents. The structural formula, the chemical name, molecular formula and molecular weight for active ingredients are presented below.



hydrocortisone acetate
Pregn-4-ene-3,20-dione, 21-(acetoxy)-11, 17-dihydroxy-, (11-beta)-
C₂₃H₃₂O₆; mol. wt. 404.50



pramoxine hydrochloride
4-(3-(p-butoxyphenoxy)propyl)morpholine
hydrochloride
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CLINICAL PHARMACOLOGY: Topical corticosteroids share anti-inflammatory, anti-pruritic and vasoconstrictive actions.

The mechanism of anti-inflammatory activity of topical corticosteroids is unclear. Various laboratory methods, including vasoconstrictor assays, are used to compare and predict potencies and/or clinical efficacies of the topical corticosteroids. There is some evidence to suggest that a recognizable correlation exists between vasoconstrictor potency and therapeutic efficacy in man.

Pramoxine hydrochloride is a topical anesthetic agent which provides temporary relief from itching and pain. It acts by stabilizing the neuronal membrane of nerve endings with which it comes into contact.

Pharmacokinetics: The extent of percutaneous absorption of topical corticosteroids is determined by many factors including the vehicle, the integrity of the epidermal barrier, and the use of occlusive dressings.

Topical corticosteroids can be absorbed from normal intact skin. Inflammation and/or other disease processes in the skin increase percutaneous absorption. Occlusive dressings substantially increase the percutaneous absorption of topical corticosteroids. Thus, occlusive dressings may be a valuable therapeutic adjunct for treatment of resistant dermatoses. (See DOSAGE AND ADMINISTRATION.)

Once absorbed through the skin, topical corticosteroids are handled through pharmacokinetic pathways similar to systemically administered corticosteroids. Corticosteroids are bound to plasma proteins in varying degrees. Corticosteroids are metabolized primarily in the liver and are then excreted by the kidneys. Some of the topical corticosteroids and their metabolites are also excreted into the bile.

INDICATIONS AND USAGE: Topical corticosteroids are indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.

CONTRAINDICATIONS: Topical corticosteroids are contraindicated in those patients with a history of hypersensitivity to any of the components of the preparation.

PRECAUTIONS: General: Systemic absorption of topical corticosteroids has produced reversible hypothalamic-pituitary-adrenal (HPA) axis suppression, manifestations of Cushing's syndrome, hyperglycemia, and glucosuria in some patients. Conditions which augment systemic absorption include the application of the more potent steroids, use over large surface areas, prolonged use, and the addition of occlusive dressings.

Therefore, patients receiving a large dose of a potent topical steroid applied to a large surface area and under an occlusive dressing should be evaluated periodically for evidence of HPA axis suppression by using the urinary free cortisol and ACTH stimulation tests. If HPA axis suppression is noted, an attempt should be made to withdraw the drug, to reduce the frequency of application, or to substitute a less potent steroid.

Recovery of HPA axis function is generally prompt and complete upon discontinuation of the drug. Infrequently, signs and symptoms of steroid withdrawal may occur, requiring supplemental systemic corticosteroids. Children may absorb proportionally larger amounts of topical corticosteroids and thus be more susceptible to systemic toxicity. (See Precautions-Pediatric Use.)

If irritation develops, topical corticosteroids should be discontinued and appropriate therapy instituted.

In the presence of dermatological infections, the use of an appropriate antifungal or antibacterial agent should be instituted. If a favorable response does not occur promptly the corticosteroid should be discontinued until the infection has been adequately controlled.

Information for the Patient: Patients using topical corticosteroids should receive the following information and instructions:

1. This medication is to be used as directed by the physician. It is for external use only. Avoid contact with the eyes.
2. Patients should be advised not to use this medication for any disorder other than for which it was prescribed.
3. The treated skin area should not be bandaged or otherwise covered or wrapped as to be occlusive unless directed by the physician.
4. Patients should report any signs of local adverse reactions especially under occlusive dressings.
5. Parents of pediatric patients should be advised not to use tight-fitting diapers or plastic pants on a child being treated in the diaper area, as these garments may constitute occlusive dressings.

Laboratory Tests: The following tests may be helpful in evaluating the HPA axis suppression: Urinary free cortisol test
ACTH stimulation test

Carcinogenesis, Mutagenesis, and Impairment of Fertility: Long-term animal studies have not been performed to evaluate the carcinogenic potential or the effect on fertility of topical corticosteroids. Studies to determine mutagenicity with prednisolone and hydrocortisone have revealed negative results.

Pregnancy: Teratogenic Effects: Pregnancy Category C: Corticosteroids are generally teratogenic in laboratory animals when administered systemically at relatively low dosage levels. The more potent corticosteroids have been shown to be teratogenic after dermal application in laboratory animals. There are no adequate and well-controlled studies in pregnant women on teratogenic effects from topically applied corticosteroids. Therefore, topical corticosteroids should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Drugs of this class should not be used extensively on pregnant patients, in large amounts, or for prolonged periods of time.

Nursing Mothers: It is not known whether topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable amounts in breast milk. Systemically administered corticosteroids are secreted into breast milk in quantities NOT likely to have a deleterious effect on the infant. Nevertheless, caution should be exercised when topical corticosteroids are administered to a nursing woman.

Pediatric Use: Pediatric patients may demonstrate greater susceptibility to topical corticosteroid induced HPA axis suppression and Cushing's syndrome than mature patients because of a larger skin surface area to body weight ratio.

Hypothalamic-pituitary-adrenal (HPA) axis suppression, Cushing's syndrome, and intracranial hypertension have been reported in children receiving topical corticosteroids. Manifestations of adrenal suppression in children include linear growth retardation, delayed weight gain, low plasma cortisol levels, and absence of response to ACTH stimulation. Manifestations of intracranial hypertension include bulging fontanelles, headaches, and bilateral papilledema.

Administration of topical corticosteroids to children should be limited to the least amount compatible with an effective therapeutic regimen. Chronic corticosteroid therapy may interfere with the growth and development of children.

ADVERSE REACTIONS: The following local adverse reactions are reported infrequently with topical corticosteroids, but may occur more frequently with the use of occlusive dressings. These reactions are listed in an approximate decreasing order of occurrence:

Burning	Hypertrichosis	Maceration of the skin
Itching	Acneiform eruptions	Secondary infection
Irritation	Hypopigmentation	Skin atrophy
Dryness	Perioral dermatitis	Striae
Folliculitis	Allergic contact dermatitis	Miliaria

OVERDOSAGE: Topically applied corticosteroids can be absorbed in sufficient amounts to produce systemic effects. (See PRECAUTIONS.)

DOSAGE AND ADMINISTRATION: Topical corticosteroids are generally applied to the affected area as a thin film three to four times daily depending on the severity of the condition. Occlusive dressings may be used for the management of psoriasis or recalcitrant conditions. If an infection develops, the use of occlusive dressings should be discontinued and appropriate antimicrobial therapy instituted.

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