

Anticoagulants Are Safe for Most Skin Ca Surgery

BY JEFF EVANS
Senior Writer

NAPLES, FLA. — The use of anticoagulants during and after skin cancer surgery involves a low risk of bleeding complications for most patients, especially aspirin users, but the risk may be greater in the elderly, warfarin users, and those on multiple agents, according to the results of two studies presented at the annual meeting of the American College of Mohs Surgery.

“It’s been said by many that . . . bleeding from skin surgery is never life threatening. Well, that was certainly what we noticed,” said Dr. Anthony J. Dixon, a dermatologic surgeon who practices in Belmont, Australia.

He and his colleagues conducted a prospective study of bleeding complications in skin cancer surgery on 5,990 lesions. During the 44-month enrollment period, 40 bleeding events (26 hemorhages and 14 hematomas) occurred.

Analysis showed that, at the time of surgery, age 67 years or older and warfarin use were significant and independent risk factors for bleeding complications.

A large age difference in the rate of bleeding complications was “perhaps the most surprising feature we found,” said Dr. Dixon, who also is director of research for Skin Alert Skin Cancer Clinics, a network of 13 clinics in Australia.

In surgery for 2,947 lesions in patients younger than 67 years, there were only

5 bleeding complications, compared with 35 complications in 2,939 lesions in patients 67 years or older.

Bleeding events developed in 8 (2.5%) of 320 lesions in patients who were taking warfarin. Patients who were using warfarin prior to surgery were included in the study unless their international normalized ratio (INR) was greater than 3 in the days immediately before surgery. Two patients on warfarin were the only ones to have late bleeding events in the study. Their INRs were less than 3 at the time of surgery but then increased after surgery.

It is important to measure INR not only in the days before surgery, but also in the days afterward, Dr. Dixon suggested. In all, warfarin should only be stopped in “very limited circumstances” and definitely not if the patient had a deep vein thrombosis or a pulmonary embolism within 1 month of the surgery.

Aspirin users developed bleeding complications in 9 (1%) of 890 total cases. All patients who were taking aspirin at the time of surgery were included. “Aspirin is not a risk factor. It’s just that older people take aspirin, and older people are more likely to be on a combination of warfarin and aspirin,” he said.

Among patients who took both anticoagulants, bleeding complications occurred in 2 (6%) of 35 lesions.

In a separate presentation at the meeting, Ikue Shimizu reported that the use of multiple anticoagulants may increase the risk of bleeding complications. She and her colleagues at Brown University in Providence, R.I., found that only four bleeding complications developed in 760 patients who were undergoing Mohs surgery, but that three of these occurred in patients who were taking two or more oral anticoagulants.

Patients who took two or more anticoagulants were significantly more likely to have bleeding complications than were those who took no agent or only one, she said.

The investigators reviewed the charts of patients who underwent the procedure and received postoperative care at one center during a 1-year span. Patients who received outside postoperative care or had incomplete data were excluded from the trial.

Most of the patients (62%) were not taking any anticoagulants at the time of surgery; the others took one (30%) or two or more agents (8%).

Other studies that have examined the risk of developing bleeding complications after dermatologic surgery have analyzed the effect of using only one anticoagulant agent and not two or more, said Ms. Shimizu, a medical student at the university.

For patients who are on multiple anticoagulants, surgeons at the Brown University Mohs surgery unit try to use extra caution in obtaining hemostasis, and they decrease the use of epinephrine during repair and follow up with patients the next day.

“We feel that there is a need for more prospective studies with increased numbers to properly assess the risks of different complications,” Ms. Shimizu said. ■

Tretinoin Cream, USP (Emollient) 0.05%

Brief Summary of Full Prescribing Information

DESCRIPTION

Tretinoin is available as TRETINOIN CREAM, USP (EMOLLIENT) at a concentration of 0.05% w/w in a water in oil emulsion formulation consisting of light mineral oil, NF; sorbitol solution, USP; hydroxyoctacosanyl hydroxystearate; methoxy PEG-22/dodecyl glycol copolymer; PEG-45/dodecyl glycol copolymer; stearytrimethylsilane and stearyl alcohol; dimethicone 50 cs; methylparaben, NF; edetate disodium, USP; quaternium-15; butylated hydroxytoluene, NF; citric acid monohydrate, USP; fragrance; and purified water, USP.

INDICATIONS AND USAGE

TRETINOIN CREAM, USP (EMOLLIENT) 0.05% is indicated as an adjunctive agent for use in the mitigation (palliation) of fine wrinkles, mottled hyperpigmentation, and tactile roughness of facial skin in patients who do not achieve such palliation using comprehensive skin care and sun avoidance programs alone (see bullet point 3 for populations in which effectiveness has not been established). TRETINOIN CREAM, USP (EMOLLIENT) DOES NOT ELIMINATE WRINKLES, REPAIR SUN DAMAGED SKIN, REVERSE PHOTO-AGING, or RESTORE A MORE YOUTHFUL or YOUNGER DERMAL HISTOLOGIC PATTERN. TRETINOIN CREAM, USP (EMOLLIENT) should only be used under medical supervision as an adjunct to a comprehensive skin care and sun avoidance program that includes the use of effective sunscreens (minimum SPF of 15) and protective clothing when desired results on fine wrinkles, mottled hyperpigmentation, and roughness of facial skin have not been achieved with a comprehensive skin care and sun avoidance program alone. Neither the safety nor the efficacy of using TRETINOIN CREAM, USP (EMOLLIENT) daily for greater than 48 weeks has been established, and daily use beyond 48 weeks has not been systematically and histologically investigated in adequate and well-controlled trials.

CONTRAINDICATIONS:

This drug is contraindicated in individuals with a history of sensitivity reactions to any of its components. It should be discontinued if hypersensitivity to any of its ingredients is noted.

WARNINGS

TRETINOIN CREAM, USP (EMOLLIENT) is a dermal irritant, and the results of continued irritation of the skin for greater than 48 weeks in chronic, long term use are not known. Safety and effectiveness of TRETINOIN CREAM, USP (EMOLLIENT) in individuals with moderately or heavily pigmented skin have not been established. TRETINOIN CREAM, USP (EMOLLIENT) should not be administered if the patient is also taking drugs known to be photosensitizers (e.g., thiazides, tetracyclines, fluoroquinolones, phenothiazines, sulfonamides) because of the possibility of augmented phototoxicity.

Because of heightened burning susceptibility, exposure to sunlight (including sunlamps) should be avoided or minimized during use of TRETINOIN CREAM, USP (EMOLLIENT). Patients must be warned to use sunscreens (minimum of SPF of 15) and protective clothing when using TRETINOIN CREAM, USP (EMOLLIENT). Patients with sunburn should be advised not to use until fully recovered. Patients who may have considerable sun exposure due to their occupation and those patients with inherent sensitivity to sunlight should exercise particular caution when using and assure that the precautions outlined in the Patient Package Insert are observed. TRETINOIN CREAM, USP (EMOLLIENT) should be kept out of the eyes, mouth, angles of the nose, and mucous membranes. Topical use may cause severe local erythema, pruritus, burning, stinging, and peeling at the site of application. If the degree of local irritation warrants, patients should be directed to use less medication, decrease the frequency of application, discontinue use temporarily or discontinue use altogether.

Tretinoin has been reported to cause severe irritation on eczematous skin and should be used only with utmost caution in patients with this condition.

PRECAUTIONS

General: If a drug sensitivity, chemical irritation, or a systemic adverse reaction develops, use should be discontinued.

Drug Interactions: Concomitant topical medication, medicated or abrasive soaps, shampoos, cleansers, cosmetics with a strong drying effect, products with high concentration of alcohol, astringents, spices or lime, permanent wave solutions, electrolysis, hair depilatories or waxes, and products that may irritate the skin should be used with caution in patients being treated because they may increase irritation with use. Tretinoin Cream USP (Emollient) should not be administered if the patient is also taking drugs known to be photosensitizers (e.g., thiazides, tetracyclines, fluoroquinolones, phenothiazines, sulfonamides) because of the possibility of augmented phototoxicity.

Carcinogenesis, Mutagenesis, Impairment of Fertility

There was no evidence of carcinogenic potential when tretinoin was administered topically at a dose 5 times the average recommended human topical clinical dose. The mutagenic potential of tretinoin was evaluated in the Ames assay and in the in vivo mouse micronucleus assay, both of which were negative.

Pregnancy: Pregnancy Category C.

There are no adequate and well-controlled studies in pregnant women. TRETINOIN CREAM, USP (EMOLLIENT) **should not be used during pregnancy.** Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, **caution should be exercised when administered to a nursing women.**

Pediatric Use: Safety and effectiveness in patients less than 18 years of age have not been established.

Geriatric Use: Safety and effectiveness in individuals older than 50 years of age have not been established.

ADVERSE REACTIONS

(See WARNINGS and PRECAUTIONS sections.)

Local reactions such as peeling, dry skin, burning, stinging, erythema, and pruritus were reported by almost all subjects during therapy. These signs and symptoms were usually of mild to moderate severity and generally occurred early in therapy.

OVERDOSAGE:

Application of larger amounts of medication than recommended has not been shown to lead to more rapid or better results, and marked redness, peeling, or discomfort may occur. Oral ingestion of the drug may lead to the same side effects as those associated with excessive oral intake of Vitamin A.

DOSAGE AND ADMINISTRATION

TRETINOIN CREAM, USP (EMOLLIENT) should be applied to the face **once a day** before retiring using only enough to cover the entire affected area lightly. Patients should gently wash their face with a mild soap, pat the skin dry, and wait 20 to 30 minutes before applying. The **patient should apply a pea-sized amount of cream** to cover the entire face lightly. Special caution should be taken when applying the cream to avoid the eyes, ears, nostrils, and mouth. With discontinuation of therapy, a majority of patients will lose most mitigating effects on fine wrinkles, mottled hyperpigmentation, and tactile roughness of facial skin; **however, the safety and effectiveness of using TRETINOIN CREAM, USP (EMOLLIENT) daily for greater than 48 weeks have not been established.**

HOW SUPPLIED

TRETINOIN CREAM, USP (EMOLLIENT) is available in these sizes:

NDC 66530-24740 gram tube

NDC 66530-24760 gram tube

Storage: Store at 20-25° (68-77°F) [see USP Controlled Room Temperature]. DO NOT FREEZE.

Manufactured by DPT Laboratories, San Antonio, TX 78215
Distributed by Spear Dermatology Products, Randolph, NJ 07869

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