

Full-Body Exam Finds More, Thinner Melanomas

BY MARY ANN MOON

In patients attending a general dermatology practice, most melanomas diagnosed during a 3-year period were not the presenting complaint, but were only discovered because a dermatologist performed a full-body skin examination, according to a recent report.

Such melanomas, discovered incidentally during an unrelated office visit, were more likely to be thinner or in-situ lesions than those that were inquired about by the patient or someone who observed them on the patient, said Dr. Jonathan Kantor and Deborah E. Kantor, C.R.N.P., of North Florida Dermatology Associates, Jacksonville.

The U.S. Preventive Services Task Force has stated that current evidence is insufficient to recommend either for or against routine full-body melanoma screening, and previous studies of patients in tertiary referral centers have reported that physicians detect only 14%-34% of melanomas.

More than half of melanomas were discovered by a dermatologist and had not been noted by the patient or another physician.

“Our aim was to determine the proportion of patients in a private dermatology practice in whom melanoma was detected but was not the presenting complaint. If a substantial proportion of melanomas are detected only after a dermatologist’s examination,

this may suggest that FBSE [full-body skin examination], and not simply a problem-focused approach, should at least be considered for selected patients,” the researchers said (Arch. Dermatol. 2009;145:873-6).

The findings also “may help to promote education and encourage future patients to avail themselves of full-body skin examination,” they added.

The investigators performed a retrospective case series of all patients diagnosed as having melanoma (51 cases) or melanoma in situ (75 cases) during a 3-year period. Patients were aged 15-92 years (mean age, 60 years).

A total of 56% of melanomas were discovered by a dermatologist and had not been noted by the patient, a spouse,

a friend, or another physician. Similarly, 60% of the melanomas in situ were discovered by a dermatologist, they said.

“Moreover, we found that dermatologist detection was associated with thinner melanomas and an increasing likelihood of the melanoma being in-situ,” they said.

“Thus, full-body skin examinations confer both an absolute benefit (detecting most melanomas) as well as a clinically sig-

nificant marginal benefit (detecting melanomas with less tumor thickness). We hope that these findings will help spur large population-based studies in high-risk populations to develop an evidence-based approach to determining appropriate screening practices and intervals,” the investigators added.

The researchers reported no financial disclosures. ■

Study Disputes Link Between Melanoma and Antioxidants

BY MARY ANN MOON

Antioxidant supplements do not appear to increase the risk of melanoma, according to a large, population-based study.

None of the exposure variables examined—overall antioxidant use, duration of use over the past 10 years, total dosage expressed in pill-years, or years of adult use during adulthood—correlated with melanoma risk in either men or women, said Dr. Maryam M. Asgari of Kaiser Permanente Northern California, Oakland, and her associates.

They undertook this study because the Supplementation in Vitamins and Mineral Antioxidants (SUVIMAX) study, a primary prevention trial published in 2007, found that daily oral supplementation with a combination of antioxidants raised the incidence of melanoma in women. The SUVIMAX findings were alarming, given that an estimated 48%-55% of American adults use supplements regularly, Dr. Asgari and her colleagues wrote.

They further examined the issue in a cohort of 69,671 adults who answered a 24-page questionnaire regarding health history, lifestyle factors, diet, supplement use, and cancer risk factors. They focused on the five antioxidants assessed in the SUVIMAX trial: vitamin C, vitamin E, zinc, beta carotene, and selenium.

Most of the study subjects (66%) were either current or former users of multi-

vitamins. During 7 years of follow-up there were 461 incident cases of cutaneous melanoma.

Antioxidants were not associated with the disease. “Specifically, in the highest dose category of multivitamins ... there was no increased risk of melanoma. Results were similar in men and women,” the investigators wrote (Arch. Dermatol. 2009;145:879-82).

Moreover, since many people take multivitamins plus additional beta carotene and selenium supplements, comparably high doses of these two nutrients were tested in a separate analysis. Again, no increased risk of melanoma was found and the results were the same for women and men.

It is likely that the SUVIMAX findings “could be explained by methodological shortcomings,” Dr. Asgari and her associates wrote.

In that study, subjects answered only a single question pertaining to their lifetime sun exposure, and “the analysis was based on only 16 cases” of melanoma. In addition, the incidence of melanoma in the SUVIMAX population was only 25 cases per 100,000 person-years—one-fifth the rate in the current study.

The work of Dr. Asgari and her associates was supported in part by the National Institute of Arthritis, Musculoskeletal and Skin Diseases and the National Cancer Institute. No financial conflicts of interest were reported. ■

BRIEF SUMMARY

(see package insert for full prescribing information)

Atralin™ (tretinoin) gel 0.05%

For topical use only

INDICATIONS AND USAGE

Atralin Gel is a retinoid indicated for topical treatment of acne vulgaris.

Important Limitations of Use

The safety and efficacy of the use of this product in the treatment of any other disorders have not been evaluated.

CONTRAINDICATIONS

None

WARNINGS AND PRECAUTIONS

Skin Irritation

The skin of certain individuals may become dry, red, or exfoliated while using Atralin Gel. If the degree of irritation warrants, patients should be directed to temporarily reduce the amount or frequency of application of the medication, discontinue use temporarily, or discontinue use altogether. Efficacy at reduced frequencies of application has not been established. If a reaction suggesting sensitivity occurs, use of the medication should be discontinued. Mild to moderate skin dryness may also be experienced if so, use of an appropriate moisturizer during the day may be helpful.

Tretinoin has been reported to cause severe irritation on eczematous or sunburned skin and should be used with caution in patients with these conditions.

Topical over-the-counter acne preparations, concomitant topical medication, medicated cleansers, topical products with alcohol or astringents, when used with Atralin Gel, should be used with caution. [See Drug Interactions (7)]

Ultraviolet Light and Environmental Exposure

Unprotected exposure to sunlight, including sunlamps, should be minimized during the use of Atralin Gel. Patients who normally experience high levels of sun exposure, and those with inherent sensitivity to sun, should be warned to exercise caution. Use of sunscreen products of at least SPF 15 and protective clothing over treated areas is recommended when exposure cannot be avoided.

Weather extremes, such as wind or cold, also may be irritating to patients under treatment with tretinoin.

Fish Allergies

Atralin Gel contains soluble fish proteins and should be used with caution in patients with known sensitivity or allergy to fish. Patients who develop pruritus or urticaria should contact their health care provider.

ADVERSE REACTIONS

Clinical Studies Experience

Because clinical trials are conducted under prescribed conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared with rates in the clinical trials of another drug and may not reflect the rates observed in practice.

In two randomized, controlled trials, 674 subjects received treatment for up to 12 weeks with Atralin Gel (see Clinical Studies (14)). In these studies, 50% of the subjects who were treated with Atralin Gel reported one or more adverse reactions; 30% of the subjects reported treatment-related adverse reactions. In the vehicle group, 29% of the 487 randomized subjects reported at least one adverse reaction; 5% of the subjects reported events that were treatment-related.

There were no serious, treatment-related adverse reactions reported by subjects in any of the treatment groups.

Selected adverse reactions that occurred in at least 1% of subjects in the two studies combined, are shown in Table 1 (below). Most skin-related adverse reactions first appear during the first two weeks of treatment with Atralin Gel, and the incidence rate for skin-related reactions peaks around the second and third week of treatment. In some subjects the skin-related adverse reactions persist throughout the treatment period.

Table 1. Number of Subjects with Selected Adverse Reactions (Occurring in At Least 1% of Subjects)

Event	Atralin Gel (n = 674)	Vehicle Gel (n = 487)
Dry Skin	109 (16%)	8 (2%)
Peeling/Scaling/Flaking Skin	76 (12%)	7 (1%)
Skin Burning/Sensation	53 (8%)	8 (2%)
Erythema	47 (7%)	1 (<1%)
Pruritus	11 (2%)	3 (1%)
Pain of Skin	7 (1%)	0 (0%)
Sunburn	7 (1%)	3 (1%)

DRUG INTERACTIONS

When treating with Atralin Gel, caution should be exercised with the use of concomitant topical medication, medicated or abrasive soaps and cleansers, products that have a strong drying effect, and products with high concentrations of alcohol, astringents, spices, or lime. Particular caution should be exercised with the concomitant use of topical over-the-counter acne preparations containing benzoyl peroxide, sulfur, resorcinol, or salicylic acid. Allow the effects of such preparations to subside before use of Atralin Gel is begun.

USE IN SPECIFIC POPULATIONS

Pregnancy

Pregnancy Category C. There are no well-controlled trials in pregnant women treated with Atralin Gel. Atralin Gel should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Atralin Gel at doses of 0.1, 0.3 and 1 g/kg/day was tested for maternal and developmental toxicity in pregnant Sprague-Dawley rats by dermal application. The dose of 1 g/kg/day was approximately 4 times the clinical dose assuming 100% absorption and based on body surface area comparison. Possible tretinoin-associated teratogenic effects (craniofacial abnormalities [hydrocephaly], asymmetrical thyroids, variations in ossification, and increased supernumerary ribs) were noted in the fetuses of Atralin Gel treated animals. These findings were not observed in control animals. Other maternal and reproductive parameters in the Atralin Gel treated animals were not different from control. For purposes of comparison of the animal exposure to human exposure, the clinical dose is defined as 2 g of Atralin Gel applied daily to a 50-kg person.

Oral tretinoin has been shown to be teratogenic in rats, mice, rabbits, hamsters and nonhuman primates. Tretinoin was teratogenic in Wistar rats when given orally in doses greater than 1 mg/kg/day (approximately 8 times the clinical dose based on body surface area comparison). In the cynomolgus monkey, fetal malformations were reported for doses of 10 mg/kg/day, but none were observed at 5 mg/kg/day (approximately 80 times the clinical dose based on body surface area comparison), although increased skeletal variations were observed at all doses.

Dose-related increases in embryolethality and abortion also were reported. Similar results have also been reported in pigtail macaques.

Topical tretinoin in a different formulation has generated equivocal results in animal teratogenicity tests. There is evidence for teratogenicity (shortened or kinked tail) of topical tretinoin in Wistar rats at doses greater than 1 mg/kg/day (approximately 8 times the clinical dose assuming 100% absorption and based on body surface area comparison). Anomalies (humerus: short 13%, bent 6%, os parietal incompletely ossified 14%) have also been reported when 10 mg/kg/day (approximately 160 times the clinical dose assuming 100% absorption and based on body surface area comparison) was topically applied. Supernumerary ribs have been a consistent finding in rats when dams were treated topically or orally with retinoids.

With widespread use of any drug, a small number of birth defect reports associated temporarily with the administration of the drug would be expected by chance alone. Cases of temporarily associated congenital malformations have been reported with use of other topical tretinoin products. The significance of these spontaneous reports in terms of risk to the fetus is not known.

Nonteratogenic effects on fetuses: Oral tretinoin has been shown to be fetotoxic in rats when administered in doses 20 times the clinical dose based on a body surface area comparison.

Topical tretinoin has been shown to be fetotoxic in rabbits when administered in doses 8 times the clinical dose based on a body surface area comparison.

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 Atralin Gel is administered to a nursing woman.

Pediatric Use

Safety and effectiveness in children below the age of 10 have not been established.

A total of 381 pediatric subjects (aged 10 to 16 years), treated with Atralin Gel were enrolled into the two clinical studies. Across these two studies, comparable safety and efficacy were observed between pediatric and adult subjects.

Geriatric Use

Safety and effectiveness in a geriatric population have not been established. Clinical studies of Atralin Gel did not include any subjects over age 65 to determine whether they respond differently than younger subjects.

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PAIN RELIEVERS



“Careful, it might be uninsured patients.”