Acitretin Plus Diabetes Drug May Calm Psoriasis

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**PRAGUE** — The diabetes drug pioglitazone significantly improved psoriasis control when added to oral acitretin, data from a small clinical trial found.

The combination led to a 64% reduction in psoriasis severity, compared with 52% for acitretin alone, Dr. Sunil Dogra of the Postgraduate Institute of Medical Education and Research in Chandigarh, India, and colleagues reported at the International Congress of Dermatology.

"From our study results it is apparent that the addition of pioglitazone [Actos] to acitretin [Soriatane] therapy can enhance antipsoriatic efficacy," he reported in a poster presentation. Initial worsening of disease severity occurred less often with the combination, but the difference did not achieve statistical significance.

"In comparison to other antipsoriatic drugs used in combination with acitretin, pioglitazone may offer a safer alternative, as it has been used in patients with diabetes mellitus for several years, and most placebo-controlled trials have shown the incidence of side effects due to pioglitazone to be approximately equal to that found with placebo," he reported.

The rationale for using a thiazolidinedione drug to treat psoriasis came from evidence that activation of peroxisome-proliferator activated receptor-gamma (PPAR-gamma) may inhibit proliferation and promote cell differentiation, according to the investigators.

Experience with tazorotene showed reduced disease activity and normalized histologic features of psoriatic skin, Dr. Dogra noted. And, studies of pioglitazone in psoriasis have shown response rates as high as 50%.

Given that acitretin and PPAR-gamma activators decrease proliferation, reduce differentiation, and have anti-inflammatory activity, the investigators combined the drugs to try and achieve therapeutic synergy. They hypothesized that pioglitazone might counter acitretin-induced lipid abnormalities.

Dr. Dogra and colleagues randomized 41 patients with plaque psoriasis requiring systemic therapy. Patients received acitretin 25 mg/day plus either pioglitazone 15 mg/day or placebo.

Patients had follow-up visits at 2, 4, 8, and 12 weeks. The primary efficacy endpoint was the change in Psoriasis Area and Severity Index (PASI) from baseline to 12 weeks.

The baseline PASI score averaged 19.3 in the acitretin-placebo group and 17.5 in the acitretin-pioglitazone group. The mean PASI score had worsened at 2 weeks in 37% of the acitretin-pioglitazone group and 50% of the acitretin-placebo group.

At 12 weeks, the median PASI score in the pioglitazone group was 6.0, a reduction of 11.5 from baseline. That compared with a mean difference of 10.0 in the placebo group and a reduction of 9.2 from baseline. The difference translated into a statistically significant advantage in favor of acitretin-pioglitazone.

No unexpected adverse effects or interactions were noted in either treatment group, and no patients had any laboratory abnormalities during the study.

The investigators acknowledged the small size of the study, that they used the lowest available dose of pioglitazone, and that women of child-bearing potential were excluded from the study.

"PPAR-gamma agonists are known on a pressor array of beneficial effects, including decreased blood pressure, increased HDL, and improved fibrinolysis," the investigators said. "Moreover, the occurrence of diabetes, hypertension, and metabolic syndrome in patients with psoriasis is not uncommon. These conditions may co-exist more often than predicted from the prevalence of either disorder alone. Pioglitazone may be particularly useful in these subsets of patients."

The results warrant additional studies of the combination, including evaluations of the safety and efficacy combining higher doses of pioglitazone with acitretin.

The investigators declared having no relevant conflicts of interest.

Coal Tar Found as Effective As Tazarotene for Psoriasis

**PRAGUE** — For psoriasis patients who can handle the smell and mess, coal tar remains an effective, inexpensive treatment option for stable disease, according to Dr. Uma Kumar.

Coal tar proved just as effective as topically tazarotene (Tazorac) in a small randomized study of patients with stable plaque psoriasis. All patients in both groups had either marked or moderate improvement after 12 weeks of treatment.

"Our results indicate that tazarotene 0.1% gel and coal tar 5% ointment appear to have comparable efficacy in stable psoriasis," Dr. Kumar of the Postgraduate Institute of Medical Education and Research in New Delhi reported at the International Congress of Dermatology.

Considering the overall cost to benefit ratio, tazarotene is a more expensive disease like psoriasis, coal tar ointment is still an effective treatment modality for patients with stable plaque psoriasis, especially in developing countries where the treatment/handling costs are borne by patients themselves," he said.

The findings came from a comparison of tazarotene gel and crude coal tar in 30 patients with stable plaque psoriasis. The patients had limited disease, defined as involvement of less than 20% of body surface area. Disease duration averaged about 9 years. Before the initiation of randomized treatment, patients completed a 4-week washout period for systemic therapy—2 weeks for topical therapy.

Each patient was treated simultaneously with both agents in an unblinded manner: tazarotene on the right side of the body and coal tar on the left. Treatment continued for 12 weeks, and patients were assessed at 2-week intervals. Response was determined by change in an erythema, scaling, and induration (ESI) score, which averaged about 28 at baseline.

The ESI scores did not differ significantly between treatments at any of the assessments. At 12 weeks, ESI scores averaged 7.1 with tazarotene treatment and 5.9 with coal tar. The mean ESI score for lesions treated with coal tar were lower at 6 and 10 weeks, in addition to the end of the study.

Dr. Kumar reported that 27 patients completed the trial. Psoriasis lesions improved by at least 50% in all patients on both sides of the body. Investigators rated the improvement as marked in 41% of tazarotene-treated areas and 59% of areas treated with coal tar. The figures were reversed for moderate improvement.

"Coal tar is one of the commonest conventional treatment modalities for psoriasis," Dr. Kumar said. "Various studies have proved its effectiveness time and again.

"Patient acceptability is the major problem with coal tar. The preparations are usually greasy and unpleasant smelling, and they can stain clothing," he noted.

Dr. Kumar and his colleagues reported having no relevant conflicts of interest.

**Mind-Body Connection Plays Role in Coping With Disease**

**PRAGUE** — A mind-body connection may play a role in a psoriasis patients’ disease adaptation, study data suggest.

Lipoprotein levels and the amino-terminal fragment of pro-brain natriuretic peptide (NT-proBNP) correlated with various psychosocial aspects of psoriasis, Dr. Aldona Pietrzak of the Medical University of Lublin, Poland, reported at the International Congress of Dermatology.

Higher levels of certain lipoproteins correlated with disease acceptance and quality of life problems. Quality of life decreased as levels of NT-proBNP increased, particularly among men.

"Parameters of cardiovascular abnormalities, such as NT-proBNP and lipid levels, are associated with psychological dimensions of adjustment to psoriasis," Dr. Pietrzak said. "The mechanisms elucidating these associations require further studies."

Epidemiologic data have shown that psoriasis patients have an increased risk of cardiovascular disease. Explanations for the increased risk are incomplete but likely involve conventional and unconventional cardiac risk factors, she said.

Lipid abnormalities have a well-documented association with coronary heart disease, and elevated NT-proBNP has been linked to worse outcomes in heart failure. Both metabolic parameters have been implicated in psoriasis severity, she continued.

Expanding the associations to psychosocial aspects of psoriasis, Dr. Pietrzak and her colleagues studied 104 patients with psoriasis. The cohort had a mean Psoriasis Area and Severity Index score of about 24 and body surface involvement of about 30%.

The patients’ lipid profiles and NT-proBNP levels were compared with scores derived from three psychosocial assessment tools: the Skindex 29 measure of disease-related quality of life, the Acceptance of Disease Scale, and a disease-related social support scale.

The lipid profile comprised total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides, apolipoprotein-A1 (apo-A1) and apo-B.

The analysis showed that higher LDL levels were associated with a lower acceptance of life with disease, and higher NT-proBNP levels were associated with a lower quality of life.

Among men, higher NT-proBNP levels also correlated with increased physical symptoms and emotional stress.

In women, the degree of acceptance of life with disease correlated inverse with total cholesterol, LDL cholesterol, and apo-B levels. Levels of apo-B significantly influenced physical symptoms, emotions, and disease-related quality of life in women.

Perceived level of social support had a positive correlation with acceptance of life with disease. Dr. Pietrzak reported having no relevant conflicts of interest.