

Lab Monitoring and Isotretinoin: Findings and Implications

Rates of lipid and liver function abnormalities may be higher than estimated. What does that mean for clinicians and patients?

By Dina Anderson, MD

When the popular press publicizes findings regarding a well-known therapy, physicians often find themselves re-examining their patient care habits and launching patient education counter-offensives. So a recent study¹ reporting more laboratory findings regarding lipid and liver abnormalities than expected among acne patients treated with isotretinoin means that we as clinicians must be prepared to properly monitor patients, provide education, and address any specific concerns they may have regarding these study findings.

What's New? What Isn't?

It is a widespread practice for physicians to monitor blood counts, lipid levels, and transaminase levels of patients undergoing therapy with isotretinoin with baseline labs and

additional tests at intervals throughout therapy. However, no set schedule for monitoring has been established. While some standards have been proposed,² other researchers have argued that only limited lab monitoring—other than pregnancy testing in females—is necessary for most patients.³ Interestingly, though the new iPledge program educational materials mention possible effects of isotretinoin on liver function and lipid levels, the program does neither require nor provides recommendations for routine monitoring of blood counts, lipid levels, or liver function.

The challenge for clinicians has been lack of large studies investigating the rates of new lipid abnormalities, hematologic changes, and transaminase increases in a large population of acne patients treated with isotretinoin to help determine the proper role and

frequency of monitoring. The two studies noted above included only 907 and 141 patients respectively. The recent report by Zane et al., based on a retrospective analysis of a significantly larger cohort of 13,772 patients aged 13 to 50 treated between March 1995 and September 2002, may offer clinically-relevant clues.¹

Like previous researchers, the current team found that new abnormalities in hematologic parameters among isotretinoin-treated patients were uncommon. However, the team found “substantial increases in the cumulative incidence of abnormalities...in serum lipid and transaminase levels” during isotretinoin treatment versus baseline. The reported cumulative incidence of new abnormalities in patients with normal values at baseline was 44 percent for triglyceride level, 31 percent for total cholesterol level, and 11 percent for transaminase level.

These rates are higher than those suggested by previous research (only 1.5 percent of 907 patients had significantly elevated serum triglyceride levels in one study²) and probably higher than many clinicians suspected. But the headlines in the popular media, describing “worse liver, cholesterol” did not tell patients or medical professionals the whole story.

For the majority of cases, lab levels returned to normal ranges once therapy was withdrawn. The authors state that “moderate to severe abnormalities in lipid and transaminase levels were

Clarification

Please note that Solodyn (Medicis) — discussed in last month's column (vol. 3, no. 9, p. 20-22) — is indicated for the management of inflammatory lesions of non-nodular moderate to severe acne vulgaris. Studies demonstrate a significant *decrease* in inflammatory lesions among patients treated with the novel minocycline formulation compared to controls. Due to an error, last month's column stated that the therapy increased inflammatory lesions. Once-daily Solodyn is available in 45mg, 90mg, and 135mg tablets. Recommended dose is 1mg/kg daily.



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generally transient and reversible,” and, “elevations in transaminase level are generally mild.” They also note that their investigation did not quantify other potential influences on liver function, such as other drugs, alcohol consumption, or hepatic comorbidities.


Implications

In light of news reports, some patients will inevitably question the safety of isotretinoin relative to liver function, lipid levels, and blood counts. Assure patients that dermatologists have long known about these possible effects and are prepared to monitor them. Explain that while the rates of abnormalities may be “higher than previously estimated,” the study provides no new evidence that patients are at significant risk for long-term adverse effects from isotretinoin therapy. The current study does not measure rates of clinical complications, and to my knowledge there are no new reports of increased rates of clinical complications, such as

hepatotoxicity, leucopenia, and thrombocytopenia associated with isotretinoin therapy. Presumably, more consistent lab monitoring would actually prevent development of such complications. Note that anecdotally, abnormalities are said to occur between six and eight weeks from start of therapy and always resolve with withdrawal of therapy. However, I have seen high triglyceride levels appear as late as the last month of therapy.

Reassure patients by letting them know of your familiarity with isotretinoin, Share any personal experience of dealing with laboratory abnormalities or lack thereof in your own practice. Advise patients that the typical approach to management is to lower the isotretinoin dose rather and recheck levels rather than simply withdrawal treatment.

Regarding monitoring strategies, the authors note that monitoring of

white blood cell counts, hemoglobin levels, and platelet counts during isotretinoin therapy may be of little benefit absent clinical suspicion of an abnormality. However, regular monitoring of serum lipids and transaminase levels in most other patients may be wise. Note that normal baseline values of serum lipids and transaminase levels do not seem to provide prognostic benefit. Normal baseline scores did not preclude the development of new abnormalities during isotretinoin treatment in the study cohort. 

1. Zane LT, Leyden WA, Marqueling AL, Manos MM. A Population-Based Analysis of Laboratory Abnormalities During Isotretinoin Therapy for Acne Vulgaris. *Arch Dermatol.* 2006;142:1016-1022.

2. Alcalay J, Landau M, Zucker A. Analysis of laboratory data in acne patients treated with isotretinoin: is there really a need to perform routine laboratory tests? *J Dermatolog Treat.* 2001 Mar;12(1):9-12.

3. Altman RS, Altman LJ, Altman JS. A proposed set of new guidelines for routine blood tests during isotretinoin therapy for acne vulgaris. *Dermatology.* 2002;204(3):232-5.

New In Your Practice

Feel So Young. PCA Advanced Skin Care Systems recently unveiled its new pHaze 41 Creamy Cleanser, a new facial cleansing solution for aging skin. pHaze 41 Creamy Cleanser is formulated with natural cleansing agents and anti-inflammatory extracts to remove dirt, oil, and makeup without stripping the skin of moisture or disrupting its pH balance, PCA says. pHaze 41 Creamy Cleanser also contains rose hip oil, credited with hydrating the skin, helping diminish wrinkles, and restoring natural tone and color.



Bald No More? Scientists have been searching for an effective way of treating baldness, and recently at the University of Manchester in London, researchers may have made a breakthrough. The research team claims to have discovered a protein code that instructs cells to sprout hair. Thus, by sending the code to more cells than usual, scientists bred mice with more fur, which is something scientists say could be replicated in humans.

Say Yes to Salex. For patients with keratosis pilaris, Salex (6% salicylic acid, Coria Laboratories, Ltd.) Lotion, which incorporates a multivesicular emulsion delivery system, has shown to be an effective treatment. According to data presented at Academy '06 and reported by Coria, Salex was found to produce superior results and was better tolerated than tretinoin 0.025% cream or ammonium lactate 12% lotion in patients with keratosis pilaris on the face or arms. The comparative study found that treatment with Salex lotion resulted in significant improvement in 71 percent of the patients after eight weeks, as compared to only 33 percent of patients treated with tretinoin and 21 percent treated with ammonium lactate lotion.