Phototherapy for Psoriasis in the Age of Biologics

Joel M. Gelfand, MD, MSCE, FAAD, interviewed by Kari Lyn Martin, MD, FAAD

KARI LYN MARTIN, MD, FAAD: Hello, everybody, and welcome to *Dialogues in Dermatology*. This is Kari Martin. I'm an Associate Professor of Dermatology and Child Health at the University of Missouri, in Columbia, Missouri. I'm sitting down today with Dr. Joel Gelfand, who is a Professor of Dermatology and Epidemiology at the University of Pennsylvania's Perelman School of Medicine. He's also Vice Chair of Clinical Research, Medical Director of the Dermatology Clinical Studies Unit, and Director of the Psoriasis and Phototherapy Treatment Center there.—

--He is a nationally and internationally recognized expert in psoriasis, clinical epidemiology, drug safety, and clinical trials. The overarching goal of his research in clinical practice is to improve psoriasis patient outcomes in the skin and joints, while lowering the risk of diabetes, cardiovascular disease, and mortality. And today, we're going to be chatting about Phototherapy for Psoriasis in the Age of Biologics. And he tells me he is quite active on Twitter, so if you need all the current, up-to-date info on Twitter, you can follow him at @JoelGelfand for the most up-to-date info. Did I get that Twitter handle right?

JOEL M. GELFAND, MD, MSCE, FAAD: You were close, @DrJoelGelfand.

KARI LYN MARTIN, MD, FAAD: @DrJoelGelfand, perfect. Can you start out by telling our listeners kind of what got you interested in psoriasis, how you started down this path, and what about phototherapy has kind of gained your interest here?

JOEL M. GELFAND, MD, MSCE, FAAD: So phototherapy has interested me for a long time, going back to medical school. So I went to medical school at Harvard and I got interested in dermatology a little bit late in the game. And took some time off and did some research and knew I was interested in doing clinical research as part of my career. At a time, one of the big

controversies in dermatology was whether or not ultraviolet light would activate HIV in people with HIV disease. Because there were studies in mice showing it similar to herpetic infections that ultraviolet light could activate and stimulate the promoter for HIV and in theory increase viral replication.—

--So in the mid-‘90s when I was a medical student, this was a big area of controversy in the field of dermatology. And patients with HIV often frequently need ultraviolet phototherapy for a variety of HIV-related dermatitic disorders, including prurigo nodularis and things of that nature, eosinophilic pustular folliculitis, things we don’t see so much these days now that we have HAART therapy. And so I ended up designing a study with a woman named Mary Klotman, who was head of ID at Mount Sinai in those days and took a year off to do research in New York. And also Mark Lebwohl was an early mentor of mine at Mount Sinai, where we looked prospectively at about 18 patients with HIV and AIDS who were getting phototherapy for a variety of different indications: psoriasis, prurigo nodularis, eosinophilic pustular folliculitis, things of that nature.—

--And followed their PCR levels of HIV in the blood in a sort of serial way at different time points after each treatment. And showed in this cohort of patients that their viral levels remained rock stable, they didn’t really change whatsoever. And that was a really important study at the time, because there were some other studies suggesting well, maybe phototherapy was causing problems. Their T-cell counts went down or people would get phototherapy and say die of an opportunistic infection. Those studies were probably just related to the natural history of disease.—

--Patients had very advanced AIDS and the phototherapy was just sort of coincident with that. And to this day now, that study has sort of been one of the landmark studies in demonstrating the safety of phototherapy in people with HIV or AIDS. And it’s now still routinely used in the

setting of people with HIV, based on that data. So phototherapy, photobiology are really important and interesting parts of our specialty. And to this day, I still find it extremely gratifying to treat people with phototherapy who are appropriate candidates for this modality.

KARI LYN MARTIN, MD, FAAD: With the onslaught of all these amazing biologic medicines for psoriasis, how has the use of phototherapy in your practice changed?

JOEL M. GELFAND, MD, MSCE, FAAD: It's interesting. I think for me, I may be a little bit of an outlier, but it's actually ended up increasing my use of phototherapy. The reason being is that more and more patients now are aware that we have things to offer them to treat their psoriasis and so more people are coming in for treatment. And then if you give the patient the various options available to them based on their skin disease presentation, the locations that are involved, their underlying health issues, many patients still are kind of reluctant to take systemic therapies.—

--They want to avoid medicines for their disease. They don't want to take pills by mouth or injectable biologics, even though these things are pretty safe and well tolerated and work pretty well. And so for many patients, phototherapy is a very patient-centered way of treating their disease. And I'm always amazed by how challenging it would be for us as clinicians to predict how people will do. Because I've had some people with phototherapy who do so incredibly well and they're in remission for years after that phototherapy.—

--Granted, that's sort of a minority of patients, it's not the usual experience. But it always makes me think about these patients who I say, "Alright, we're going to choose a biologic for you. And I know this is going to cost the health system tens of thousands of dollars per year." And most of those people will stay on those treatments for decades. So I think as clinicians, we need to take a step back and remember that we're dealing with a chronic disease here. And that if we're going to jump to a biologic as a first treatment for all patients and not at least offer people an

option of phototherapy for those who are inclined to pursue it, that we may be treating a lot of people who don't necessarily need long term treatment with a biologic.—

--We're conveying them to a longterm treatment when maybe they don't need it. And then, of course, as a person who practices at a referral center for psoriasis, I have tons of patients who have tried multiple biologics. Maybe they do well, they lose response, they keep having to cycle through treatment, that's not a good situation for those patients, either. And so oftentimes, using phototherapy as an adjuvant to our existing therapeutic armamentarium could be very helpful for our patients.—

--Someone has been on biologic number three or four at this point, adding phototherapy when they're starting to lose response to try and maintain their ability to stay on that treatment, their biologic, it's often an advantageous thing to do for our patients. And then finally, some people have very hard variants of psoriasis to treat. The palmoplantar plaque or pustular variant of psoriasis, particularly the pustular variant, is notoriously difficult to manage. There's some data that biologics help for it, maybe apremilast helps for it, but the reality is that they don't nearly have the kind of benefit with palmoplantar pustular disease as they do for the standard, garden variety plaque psoriasis.—

--And so having access to things like topical PUVAs is an extremely valuable modality. And we use a lot of topical PUVA for patients with palmoplantar disease, as well.

KARI LYN MARTIN, MD, FAAD: Are there any other specific types of patients that phototherapy kind of jumps to the front of your list of treatments? Or are there any specific patient scenarios where you find it most helpful?

JOEL M. GELFAND, MD, MSCE, FAAD: Well, certainly guttate psoriasis is a classic example where we really should think about phototherapy, because most of those patients will go back

into remission on their own if we don't do anything, but we want to hasten that remission quickly if we can. It's not pleasant for our patients to have small spots of psoriasis all over their body. And that's another example where a short course of phototherapy is highly effective for guttate psoriasis, likely to put them in remission and certainly much more inexpensive to the healthcare system than say doing a biologic, for example.—

--Now, one of the biggest challenges of phototherapy for our patients, or two of the biggest challenges, one is the inconvenience. One has to be lucky to see a dermatologist who actually offers phototherapy. Ninety percent of the counties in the U.S. do not have a dermatologist that offers phototherapy. There's a lot of coverage in this country where people don't have access to phototherapy. And then the second issue is that even if you're fortunate enough to have access to phototherapy, peoples' lives are just so incredibly busy these days.—

--Even some of my patients who work in my health system, who are in the same buildings for phototherapy, like they can't find ten minutes during the day to come down and get a quick treatment of light, that's how busy we've gotten. And so because of this, we've been working on a study funded by the Patient-Centered Outcomes Research Institute, or PCORI, doing a pragmatic trial with a goal sample size of 1,050 patients, of comparing home phototherapy to office phototherapy. Which we know home phototherapy seems to work pretty well for psoriasis, it's been established that way in Europe, for example.—

--But there's not large U.S. scale studies, especially in people who are diverse skin types that we have in the U.S. And so this study is designed to have fairly equal representation based on people with darker skin types, like skin type 5 or 6, where you may need longer treatment times, higher dosages to penetrate the darker skin, to treat the psoriasis. Or people with fairer skin, skin type 1 or 2, who maybe they might burn more with home phototherapy, maybe it's not calibrated as accurately as we do in the office.—

--And so this study is ongoing. We already have several hundred people enrolled in a trial. We have about 30 sites across the country, dermatologists working on this study. And our hope is through the work that we've done with engaging with the National Psoriasis Foundation and payers across the country that if the study shows that home phototherapy works about as well as office-based phototherapy, that payers will make it much more available to their patients. The goal will be that a dermatologist would write a script and get it covered without what today is currently a real challenge.—

--Interestingly enough, it's always on Medicare. Medicare covers home phototherapy, it's very good coverage for home phototherapy. For most regular payers, home phototherapy is called a durable medical device. And that's a different rider of insurance. And so for an insurance company, oftentimes the durable medical goods side is happy to say, "Yeah, let the pharmaceutical side pay $80,000 a year for that biologic, we don't want to shell out the $3,000 for the phototherapy machine." So there's all of these misaligned incentives.—

--And hopefully this study, by bringing stakeholders together, because we have a number of payers involved in design and analysis of the study, hopefully that will change the standard of care in a way that will be better for our patients and for our colleagues out there.

KARI LYN MARTIN, MD, FAAD: That would be fantastic, for sure. I think it's nice to bring to light kind of phototherapy again, as a good reminder to all of our listeners to not forget about it, and that it really has a place today still.

JOEL M. GELFAND, MD, MSCE, FAAD: Absolutely. I think one thing I want to make sure people know about it is that we published a paper in *JAAD* about two years ago now, comparing skin outcomes and quality of life outcomes in people getting phototherapy compared to placebo and compared to adalimumab, a TNF-inhibitor. This was not really the primary purpose of the study, this was a study about cardiovascular biomarkers, if you will. But surprisingly, and what

was really a population of people who really needed systemic agents, because the study was designed that once you were after week 12 and don't with placebo, you would get adalimumab for a year.—

--So these are people who have had nail disease or scalp or genital disease, not necessarily the kind of people who might pick phototherapy. They actually had similar PASI 75 response rates between adalimumab and phototherapy. And actually what was really surprising to us is that for a lot of the patient-reported outcomes, people with phototherapy did better than people on adalimumab, which is pretty surprising actually. In fact, they were more likely to have better overall health improvement on the EQ-5D, a measure of generic health.—

--They were more likely to experience a reduction in pain, which is a fascinating finding because we know from other work done by Steve Feldman and other colleagues in dermatology that phototherapy, it must increase endorphins in people. There can be sort of this addictive quality to say tanning, for example. And so it was really interesting to me to see that you had better relief in pain with phototherapy than with a TNF-inhibitor, which is obviously a very effective drug in treating arthritis and usually reduce those types of pains, and that's what's going on.—

--The other thing also may be the fact that our patients really benefit a lot from the care they get from our staff. A skilled phototherapist who is checking in on our patient on a regular basis, I think that relationship is really a powerful one that really makes a big difference in healing. So it's hard to know if all this is the effect of ultraviolet light therapy, maybe some of it is the clinical benefit of being seen by our staff, and I think that's important to keep in mind for our colleagues.

KARI LYN MARTIN, MD, FAAD: To kind of wrap things up, what would you say are one or two key takeaway points for our listeners that you'd like them to remember about phototherapy?

JOEL M. GELFAND, MD, MSCE, FAAD: The key point is that phototherapy is a critical modality we need to have available to us in clinical practice. Despite all the advances in management of psoriasis, there's still plenty of people with this chronic disease who will benefit from phototherapy. Patients who would rather not take a pharmacological treatment for their disease, patients with guttate psoriasis, patients who are doing well with their systemic agents but not completely clear and need additional adjuvant therapy, particularly their joints are well controlled and you don't want to start mixing things around.—

--Patients with severe underlying comorbidities who may not be able to go on a systemic agent, for whatever reason. As well as different variants, like palmoplantar pustulosis, which currently our systemic agents really don't do great in that setting. So lots of opportunities for us as medical dermatologists to use this tried and true modality to bring a lot of relief to our patients.

KARI LYN MARTIN, MD, FAAD: Thank you so much for catching us all up and giving us some insight into your practice and how you find it most helpful.

JOEL M. GELFAND, MD, MSCE, FAAD: My pleasure.

KARI LYN MARTIN, MD, FAAD: Well, thank you so much for joining us today on *Dialogues in Dermatology*. Again in closing, this is Dr. Kari Martin, interviewing Dr. Joel Gelfand from the University of Pennsylvania's Perelman School of Medicine.

Commentary

Ian M. Ferguson, MD with Todd Schlesinger, MD, FAAD (ed.)

Phototherapy for psoriasis includes Broad Band- ultraviolet B (UVB), Narrow Band-UVB, excimer light or laser, and psoralen plus ultraviolet A or UVA (oral or topical), the combination is also known as PUVA. Phototherapy has been shown to moderate inflammatory skin disease through induction of apoptosis, modification of the cytokine milieu, and immunosuppression[1]. In this podcast of Dialogues in Dermatology, Dr. Kari Martin joins Dr. Joel Gelfand, Director of the Psoriasis and Phototherapy Treatment Center at the University of Pennsylvania's Perelman School of Medicine, to discuss the role of this quote "tried and true" modality in the age of biologics.

Dr. Gelfand notes an uptick in patients pursuing evaluation and treatment for psoriasis as the success of biologics has alerted more patients to the reality of effective treatments their disease. Many of these patients are reluctant to start systemic therapies and choose instead to pursue phototherapy if it is offered as a management option. Phototherapy may also help patients with severe underlying comorbidities who may not be able to go on a systemic agent.

Many patients do exceptionally well on phototherapy. For example, phototherapy can hasten remission in most cases of guttate psoriasis. Even for those patients who are potential candidates for systemic therapies, starting biologics without first establishing whether phototherapy would be sufficient commits the patient and healthcare system to potentially decades of excessive costs.

Many patients' psoriasis is difficult to treat regardless of the modality, and in some cases, phototherapy can provide a useful adjunct. Palmoplantar and pustular variants are notoriously treatment resistant, less responsive to biologics, and may benefit from phototherapies such as topical PUVA. Often patients have tried multiple biologics without durable relief, therefore introducing phototherapy when a chosen biologic may be losing its effectiveness can maintain its benefit. Likewise for patients with psoriatic arthritis who have good control of joint disease on a given biologic, phototherapy can contribute to further clearing their skin.

Phototherapy appears to have intangible benefits over biologics as well, which are not necessarily captured in objective scores. In one study comparing phototherapy to adalimumab, despite similar PASI 75 response rates, phototherapy showed greater improvement on the EQ-5D (a widely used measure of generic health status), notably leading to greater reductions in pain[2]. Dr. Gelfand highlights that endorphins released during phototherapy and the nurturing relationships with phototherapy staff may contribute to the relief patients experience.

Unfortunately, phototherapy uptake is limited by access and inconvenience. The vast majority of U.S. counties do not have a dermatologist who offers phototherapy[3]. Even where phototherapy is available, patients may be too busy to schedule the recommended frequency of sessions. European studies have demonstrated the efficacy of home phototherapy compared to in-office phototherapy[4]. Cost-analysis studies show a greater up-front cost for home phototherapy; however, after 3 months, total costs from in-office phototherapy were 5 times greater[5]. Studies are underway to evaluate home therapy across diverse skin types in the U.S. which could lead to increased payer coverage of these devices.

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