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Diving into the Details of Bile Acids, Lipids, and Nucleotides in Psoriatic Arthritis

Dr. Turck:
Welcome to *Clinician's Roundtable* and ReachMD. I'm your host, Dr. Charles Turck, and joining me today to discuss the article, titled "Dysregulation of Bile Acids, Lipids, and Nucleotides in Psoriatic Arthritis Revealed by Unbiased Profiling of Serum Metabolites," is corresponding author Dr. Ananta Paine. He's a Principal Investigator and Research Assistant Professor at the University of Rochester Medical Center in Rochester, New York.

Dr. Paine, welcome to the program.

Dr. Paine:
Thank you, Dr. Turck.

Dr. Turck:
Before we dive into the details of your study, Dr. Paine, what was previously known about the link between psoriatic arthritis and bile acids, lipids, and nucleotides?

Dr. Paine:
Initially, not much. It has been noted in psoriasis patients, obesity is quite common, but rather than any direct connection it has been always seen as a coincidence. So this was a first, this kind of investigation, to really figure out if there is any underlying differences between the patient who develops psoriasis but never convert to psoriatic arthritis. And we wanted to find what might actually trigger the conversion from psoriasis to psoriatic arthritis. So this was, we believe, one of these first studies where we had also the patient monitored longitudinally, so in that sense also this is quite unique. I'm sure there will be much more known, and further studies will be done during the coming years.

Dr. Turck:
So was it a little bit more like there really wasn't any research in this area before and what you decided to do was follow serial labs to see if you could find a connection?

Dr. Paine:
Yeah. We actually wanted to also find the biomarkers because one of the biggest challenges for psoriatic arthritis that delayed diagnosis results into permanent damage. And diagnosis is not easy because there are not much known about any established biomarker, which can predict which psoriasis patient will develop psoriatic arthritis over the years, so because of the delayed diagnosis, permanent joint damage actually happening to this patient, so we wanted to find out if we can identify any gene protein or metabolic biomarker so that we can use those to predict which patient especially came with psoriasis but have the higher chances to develop arthritis. So that is the rationale we established.

And we have been collecting in Rochester. We have more than 500 patients in our cohort. Many of the patients come as psoriatic arthritis to begin with, but some of them also come as psoriasis patient, and we actually have been monitoring them for more than five to 10 years. And some of these patients who came as psoriasis patients eventually converted to psoriatic arthritis, so now we have a unique opportunity to compare those patients who did not convert during this time with those patients who converted to psoriatic arthritis. So basically, can we differentiate this patient based on certain gene protein and metabolic biomarker? And especially in our earlier studies, which we have not published, we have done transcriptomic studies and noted some of the changes in the genes related to metabolism, so we had the hunch that there might be something we can note in the metabolites. So we have, actually, further

analyzed the metabolic metabolites in the serum of this patient.

Dr. Turck:
Is there anything else you could tell us about how the study was designed or a little bit more about the patient sample you examined?

Dr. Paine:
Sure. So we had selected around 71 patients or subjects. Out of them, 16 were healthy control. Then we had 21 psoriasis patients who came as psoriasis and stayed as psoriasis after more than four to five years. And then we had 13 unique patients who came as psoriasis patients but eventually developed arthritis. So we actually compared this one with the ones who did not convert, and in addition, we also had another additional 21 patients who actually was diagnosed with psoriatic arthritis to begin with. So we had this for population, and especially for the patient who converted, we also had the samples from before and after the psoriasis onset. So altogether, we actually analyzed all these patients. We also had some controls for arthritis and osteoarthritis, but for these studies we actually rather focused on comparing the patient who actually did not develop the arthritis and who developed arthritis.

Dr. Turck:
For those of you who are just tuning in, you're listening to *Clinician's Roundtable* on ReachMD. I'm Dr. Charles Turck, and I'm speaking with Dr. Ananta Paine about his research on the dysregulation of bile acids, lipids, and nucleotides and psoriatic arthritis.

And now that we have some insights into how you conducted your study, I was wondering if you would share some of its key results.

Dr. Paine:
Sure. So we have conducted this study with any preconceived notion which particular group of metabolites we'll identify or we'll see difference. However, when we analyze, we actually noted that especially the level of multiple bile acids from primary bile acid, as well as secondary bile acid were lower in the serum of patients who developed arthritis, and these levels were lower even before the onset of arthritis. Apart from that, we also noted difference in terms of butyrate and guanine. Now what actually is very interesting, especially with these few metabolites or group of metabolites I mentioned about first, the bile acid actually gets synthesized in the liver, and then the primary bile acid, which gets synthesized in the liver, gets converted in the gut by microbes. So these differences in terms of primary and secondary metabolites, which are bile acid in this case, suggest either there are some dysfunction of liver in the patient who developed arthritis or it might be also the difference in terms of microbes, which are present in this group of patient, so it might be possible that both these regions actually contributing to these observed changes. And the butyrate level is also interesting because it has been known to be a metabolite, which is very important for gut permeability, and also gut health. So lower butyrate levels also goes indicating there might be some gut microbial dysfunction or leaky gut symptoms in this patient. Again, we have not really looked into this in the follow-up studies, and it will need further investigation. And apart from that we also noted in the changes in the level of multiple lipid metabolites. Those also will need further studies.

Dr. Turck:
So is it too early to begin to apply these findings to patient care to patients with psoriatic arthritis? And you mentioned further research. I was wondering what else needs to be done.

Dr. Paine:
Actually, it's interesting. I have noted one study, which is not really a research study but it was an opinion article published long time back by one clinician who had treated patient with bile acids, especially psoriasis. Again, so this is too early to say but it seems there might be some observational studies indicate this treatment might be possible, but again, this is too early to say. It will need further investigation. Our study more focused on identifying those differences. But what will be the implication? We can postulate certain things, but we need to follow up with further studies to really make any concrete conclusion. But overall, I am very optimistic that there might be some possibilities where we can change diet or supplement with certain metabolites and thereby can treat these patient or at least prevent the onset of arthritis. But again, as I suggested, these are too early to say, and in science we cannot say anything with confidence unless we have done the study.

But this is also an opportunity where maybe patient-reported observations or outcome studies might be important or we need systemic clinical trial, but the challenges will be to find the money. And it probably has to be nonprofit organization or governmental organization because this intervention, I am not sure if it will be commercialized by any pharma companies, so chances of getting funding to do those big clinical trials will be not impossible but need the support from nonprofit organization and also government organization.

And one thing I would like to mention, this study was only possible because of the generous support of National Psoriasis Foundation. Again, I believe we have found some very interesting thing. Our study actually indicates there might be even more exciting and interesting things, which need further investigations.

Dr. Turck:

So before we conclude, Dr. Paine, are there any final thoughts you would like to share with our audience today?

Dr. Paine:
Sure. What I mentioned is just the tip of the iceberg. One example, actually I'll mention, we have noted the patient, especially after the onset of arthritis, they have lower glutamine level and also some other metabolites. I just again want to emphasize some of these metabolites can be changed with supplementation. And again, that indicates that we need to go into deeper and further see if there can be any interventional studies with any changes in the food habit.

So, again, this is just the beginning of this field. Our study clearly emphasizes and shows that there might be metabolic dysfunction as a potential cause for this onset of arthritis in psoriatic arthritis patient, and patients need to be very careful about their gut health also. So together, our studies suggest the patient should not only be focusing on the treatment but also should focus on their food and exercise and other possible avenues.

Dr. Turck:
Well, on that note, I want to thank my guest, Dr. Ananta Paine, for sharing his research and insights on serum metabolites in psoriatic arthritis.

Dr. Paine, thanks so much for joining me today.

Dr. Paine:
Thank you very much.

Dr. Turck:
For ReachMD, I'm Dr. Charles Turck. To access this and other episodes in our series, visit *Clinician's Roundtable* on ReachMD.com where you can Be Part of the Knowledge. Thanks for listening.