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(866) 423-7849

Expanding the Spectrum of Immunoglobulin Therapy

EXPANDING SPECTRUM OF IMMUNOGLOBULIN THERAPY

You are listening to ReachMD XM 160, The Channel for Medical Professionals. Welcome to Hot Topics in Allergy presented by the American College of Allergy, Asthma, and Immunology.

Your host is Dr. Todd A. Mahr, Director of Pediatric Allergy/Immunology at Gundersen Lutheran Medical Center in La Crosse, Wisconsin.

What developments have there been in immunoglobulin therapy and what are latest usage for the therapy. Joining us to discuss expanding spectrum of immunoglobulin therapy is Dr. Stanley Fineman, Clinical associate professor in the Department of Pediatrics at Emory University School of Medicine.

DR. TODD A. MAHR:

Welcome, Dr. Fineman.

DR. STANLEY FINEMAN:

Thank you.

DR. TODD A. MAHR:

So when we talk about immunoglobulin therapy or IGIV, a lot of us are familiar with it, but may be as providers don't use it regularly, what can immunoglobulin therapy be used to treat?

DR. STANLEY FINEMAN:

Well, immunoglobulin therapy has been around for a long time and currently we use it mostly for primary immunodeficiencies; particularly the ones we see in our office are the common variable, which is the humeral deficiency. It is also used for other indications including some dermatologic diseases and some autoimmune conditions and interestingly they are doing some work, experimenting with it for certain neurologic conditions and even infections like toxic shock. I think for the purposes of your listeners, just a little historical background, it was started to be used back in the 50s and you know it has been given mainly for things like infections for sometime and after Dr. Rosen described a humoral immunity deficiency, it's been used to supplement the patients who have humoral immunity deficiency. These are patients who have difficulty making specific antibodies, so they usually present with recurrent infections and when we check their quantitative serum immunoglobulins, they have low levels of IgG and then when we do specific antibodies and give them a vaccine, they don't produce the specific immunity that would in most normal people would be resulted in an immune response.

DR. TODD A. MAHR:

So they need to have then supplemental immunoglobulin because they are producing their own sufficient quantity or of the quality that would be needed to help them fight infections.

DR. STANLEY FINEMAN:

That's correct. So we would use it particularly in the patients that I see usually have low quantitative values and this helps to supplement. When it became an IV preparation, I think back in the 70s and 80s, this was a big advance because prior to that they had to only use it intramuscularly. So we have been using it for 20 plus years now with an intravenous preparation and interestingly recently there has been a subcutaneous preparation, which seems to have some advantage over the IV preparation. The main advantage is the fact that IV immunoglobulin usually has a half life of about 30 days, and so when we give the patients the immunoglobulin by IV, we sometimes on an intermittent basis check the trough levels. You know, we get another total IgG level 30 days after they receive the infusion. The nice thing about the subcutaneous injection, those are given on a weekly basis and in fact can be self-administered once the patient is taught how to do it. The peaks and troughs of the level of total gamma globulin seems to be more stable when you give it on subcutaneous basis. So it is more of a steady state.

DR. TODD A. MAHR:

So rather than the IV being given about every 30 days and having this huge spike of immunoglobulin, then tapering off, by subcutaneous giving weekly, it kind of smooths things out a little bit and you have been using this having some success with this in your practice?

DR. STANLEY FINEMAN:

Yeah. We've had patients who have been on the IV for years really like this subcutaneous preparation and in fact one of our patients this past week got rid of her port, you know the IV port that they

frequently have to have put in so that they can get intravenous access. So, of course, it's always a risk for potential infection with any port or anything like that, so it's, I think a superior way to do it you know for certain patients I think that can tolerate it.

DR. TODD A. MAHR:

Great, and so that's actually the newest thing in immunoglobulin replacement therapy would be subcutaneous. Have there been other issues with the IV gamma globulins treatment that you've had in the past decade or so.

DR. STANLEY FINEMAN:

Yeah, the biggest problem that we have was the IV gamma globulin is reactions and this generally relates to the rate of infusion and with a newer preparations we really don't see quite as much of a problem with that. There has been some concerns with patients who have a low or absent IgA levels; the immunoglobulins, of course, we have IgG, IgM, and IgA are the main 3 immunoglobulins that we measure and some patients have a low IgG and a low IgA and in fact hypogammaglobulinemia A is the most common of the immune deficiencies and normally if it is just IgA deficiency, we usually do not have to do any kind of replacement. In fact, typical IV gamma globulin preparations do not have a very significant amount of IgA when they do the fractionation and the preparation of it, but there are some preparations out there that have really reduced the amount of IgA in them you know almost completely and so that tends to reduce the risk for potential reactions for patients who have low IgA, although in my experience it really hasn't been that much of a problem, and I think the concern or the potential theoretical risk of reactions to IgA is really not panned out in anyway in my experience.

DR. TODD A. MAHR:

So you talked at the beginning a little bit about where it's being used and alluded to some of the disease states and some of the specific places where IV gamma globulin or even now subcutaneous is

used, where do you see it being used the most?

DR. STANLEY FINEMAN:

Mostly, we use in our practice as replacement therapy for patients who have low IgG's with poor antibody production. These are patients with common variable hypogammaglobulinemia and so that's where we use it the most. Now it's interesting there have been some reports of patients receiving it for certain off-label type uses; in terms I guess since they're off-label, it's just been that it's relatively newly proven for some of these things such as Kawasaki disease, which kids have gotten and has been, I guess, for little probably 20 years now. It's not really off-label, it's really indicated for those patients with Kawasaki disease. Interestingly, I have also recently heard that some people using it for myasthenia gravis. This has been for sometime as well and patients who are resistant to typical therapy, this seems to help with that. In other neurologic diseases, they have used it for Guillain-Barre and in fact there was a study recently using it in Alzheimer's because it seems to have antibodies to the beta-amyloid, and the beta-amyloid is what causes some of the problems in Alzheimer's and so these are trials and they are certainly not, really wouldn't be using them for an indication. These are really experimental trials. In fact, for the dose that we would need to use, it really wouldn't even be enough gamma globulin around to use it for patients with Alzheimer's at this time, but it's just sort of an interesting phenomenon that IGIV does have antibodies even to the beta-amyloid. So I thought that was a kind of an interesting finding.

DR. TODD A. MAHR:

If you are just tuning in, you are listening to hot topics in allergy on ReachMD, The Channel for Medical Professionals. I am your host, Dr. Todd Mahr, and joining me to discuss expanding spectrum of immunoglobulin therapy is Dr. Stanley Fineman, clinical associate professor in the Department of Pediatrics at Emory University School of Medicine.

So, you were discussing a little bit about kind of the expanding role like any therapy we have, I think people always will kind of think about what about in this area and in more novel areas, but, I think you

did mention something about having enough immunoglobulin. I know there have I think been some shortages, have you experienced that; do you have any insight into immunoglobulin supply?

DR. STANLEY FINEMAN:

Well, that's a big concern because the source of immunoglobulin is really from the general blood supply and we get them from general blood plus commercial plasma donation centers and so they are really all manufactured from plasma and here in the United States they are all from US plasma donors that are screened and there is really no risk for viral transmission problems, so it's a safe preparation and because it's a source from pooled human donors, it's only a finite amount, it's not something you can manufacture in a lab.

DR. TODD A. MAHR:

So there is definitely some shortage as I think that have occurred from basically production issues and things like that. You are using at majority in your practice as an allergist/immunologist for immune deficiencies. I think you mentioned a little bit in some of the other areas that it's been experimented, and I guess experimentation would be the word, it's been trailed in some of these other unique areas, and Alzheimer's is interesting, and from what you've heard, is it showing some success in some of these other areas.

DR. STANLEY FINEMAN:

Yeah, that's why they thought it showed some promise, but I think that what we are going to find is that now that they realize that the effect is probably the fact that the antibodies to the beta-amyloid is what is the IGIV is supplying. So if somehow or other now they can go the next step and sort of make some specific antibodies to beta-amyloids and that would be a little bit better. I mean, we have seen that in other conditions like in pediatrics, I am trying to think now, you know, years ago they used to use gamma globulin even for things like measles, now of course we have a vaccine, so, you know, I think it

just shows the first stage, it just shows that some of these patients need a better immune response and once we can figure out how to give them that immune response then that's a future therapy.

DR. TODD A. MAHR:

So from the standpoint of use of immunoglobulin, are there guidelines or parameters for the general provider, an allergist to follow.

DR. STANLEY FINEMAN:

Yes, the allergy community has published the use of intravenous immunoglobulin for human diseases. This is a practice parameter that was published in the Journal of Allergy and Clinical Immunology in 2006 and is still current and accurate. It's well documented and I would refer our listeners to that document. This is Journal of Allergy and Clinical Immunology and it's the practice parameter that was published in the April 2006 issue.

DR. TODD A. MAHR:

So this is from the joint task force on practice parameters of the American College of Allergy, Asthma, and Immunology and the American Academy of Allergy, Asthma, and Immunology.

DR. STANLEY FINEMAN:

Correct, and this was of review really from the members of the Primary Immunodeficiency Committee, which is really mostly from the academy, although the college I think reviewed it as well.

DR. TODD A. MAHR:

Okay, so that sets down the where, the when, the how from the standpoint of use of IGIV in your clinical practice.

DR. STANLEY FINEMAN:

Correct.

DR. TODD A. MAHR:

All right. When you've used it in your office, you had mentioned basically having the number of patients on it. Do you need to pretreat generally for most patients on IGIV?

DR. STANLEY FINEMAN:

I do. Do you think we just use antihistamines; sometimes we will use H1 and H2 antagonists. On occasion, I have had patients who may need a dose of steroid, but usually we just need an H1 and H2 prior to the infusion.

DR. TODD A. MAHR:

You have somebody present to you who may have deficiency of their immune system, how would you work that patient up?

DR. STANLEY FINEMAN:

Mainly they present with recurrent infections and when patients have recurrent infections, then you have to be on the look out or at least consider what's causing that and certainly immune deficiencies frequently do. The first thing we usually get is a quantitative immunoglobulin. This is a total quantitative IgG, IgA, and IgM level and then if the IgG level is low, then we will order specific antibodies and the specific antibodies we order are usually the tetanus antibody, diphtheria antibody, and the pneumococcal antibodies. There is a series of stereotypes that we get with the pneumococcus. Now if those are low then we will give the vaccine and recheck that specific antibody level 4 weeks later and if there is a response then that shows the patient has a good immunoglobulin response and if does not have a response, then they might be a candidate for supplemental immunoglobulin like an IGIV preparation or the subcutaneous and then treat them that way.

DR. TODD A. MAHR:

So you are look quantitatively and then qualitatively at the immune response for that patient.

DR. STANLEY FINEMAN:

That's correct.

DR. TODD A. MAHR:

And it's not something you can necessary do on one visit. What you are saying is you have to actually do that initial blood draw after a good history and physical and then potentially see them back and then potentially even vaccinate them and have them blood drawn again?

DR. STANLEY FINEMAN:

That's correct.

DR. TODD A. MAHR:

I would like to thank my guest from Emory University School of Medicine, Dr. Stanley Fineman. Dr. Fineman, thank you for being our guest this week on Hot Topics in Allergy.

DR. STANLEY FINEMAN:

Thank you, Todd.

You've been listening to Hot Topics in Allergy on ReachMD XM 160. This show has been presented by the American College of Allergy, Asthma, and Immunology. For more information on the ACAAI, please visit www.acaai.org. For more information about this or any other show, please visit www.reachmd.com which now features on-demand pod casts. Thank you for listening.