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Advantages of Bloodless Medicine

Announcer:

You're listening to ReachMD, the Channel for Medical Professionals. Welcome to Medical Breakthroughs from Penn Medicine, with your host, Northwestern University internist, Dr. Lee Freedman.

Dr. Freedman:

Patients may choose bloodless medicine for medical or ethical reasons. How safe and effective are bloodless procedures compared to more traditional approaches? Joining us to discuss bloodless stem cell transplant is Dr. Patricia Ford, clinical associate professor of medicine, medical director of the Center for Bloodless Medicine and Surgery, and director of the peripheral stem cell program at Penn Medicine. Thanks for being with us, Dr. Ford.

Dr. Ford:

Thank you. My pleasure to share this information with you.

Dr. Freedman:

Well, I'm excited to hear about this. And perhaps we could start right at the beginning. What is bloodless medicine? And what is the history of this?

Dr. Ford:

Well, the history really dates back to the care of the Jehovah Witnesses. And they're certainly a population that based on religious convictions will not allow the transfusion of certain blood products. So caring for Jehovah Witnesses, doctors were kind of then forced or challenged, I should say, to think about some alternatives that might be appropriate to allow them to go through any type of medical illness or any type of surgical procedure, simply doing it exactly the same without the use of blood products. So the history really was based on care of the Jehovah Witnesses.

But as time went on, we've learned that there may be as many as 30% of blood transfusions in the United States that are given that may be unnecessary. So we really feel that some of these alternatives we use and some very simple strategies we'll go into would help all of our patients, if not eliminate, certainly reduce unnecessary transfusions.

Dr. Freedman:

Very interesting. So this is kind of a term that applies to transfusion medicine, and would be applicable in oncology situations, hematology, I imagined perioperative type of circumstances. Is that correct?

Dr. Ford:

You're absolutely right. And we've kind of expanded it now to using more of the terminology of best patient blood management so that it really gives the connotation that you can use this in every patient. And we're really hoping to promote best usage of blood products.

Dr. Freedman:

And obviously, you mentioned the Jehovah's Witnesses. Are there other patients who choose this approach for particular reasons?

Dr. Ford:

Maybe not totally eliminate blood transfusion, but reduce their risk of infections or other complications by looking at some of the alternatives. So there are some patients that absolutely will never take a blood transfusion, even if it's deemed life threatening, but there's many other patients who are much more educated and want to look at some of the alternatives that could reduce their exposure to blood products.

Dr. Freedman:

Do we have things for all elements of the blood packed cells, white cells, platelets? What are our options here?

Dr. Ford:

Well, a lot of our blood transfusions are done in the surgical patients, so I'll start there with that patient population. And what we were finding for our elective procedures is that many of our patients going in for the more common procedures, which have a large blood loss potential are orthopedic patients, some cardiovascular patients, so they're some oncologic patients, those are the big ones. And what we're finding is a large number of this patient population is older, coming in anemic having some anemia, renal insufficiency, or anemic chronic disease.

For women, it's a little different. The big procedures done there are hysterectomies and some women Cesarean sections where you can lose a large amount of blood. And those women coming in anemic are very different. They're mostly iron deficient.

So one thing we found is trying to identify early those patients for elective procedures that have anemia, that we might be able to correct ahead of time. So a very important strategy is identifying preoperative anemia, and diagnosing it and, if possible, correcting it before entering into surgery because one of the biggest risk factors for needing a perioperative transfusion is your preop hemoglobin.

Dr. Freedman:

I should probably remember this, but what is the time frame that you need if you're going to be giving someone iron to see a meaningful increase in their hemoglobin and hematocrit?

Dr. Ford:

You can start to see an increase in reticulocytes and even the hemoglobin in about 3 to 5 days. On average, what I'm finding is that we can increase the hemoglobin about 1 gram per week. So we tend to have a target in our mind. For instance, if you're going into surgery, you'd like to have a normal hemoglobin, which is around 12 for women, a little higher for men, so we want to at least target a normal hemoglobin going in. So if someone has a hemoglobin of 9 – 9, I know that I may need 3 weeks to hit my target of 12 by giving intravenous iron or sometimes erythropoietic-stimulating agents.

Dr. Freedman:

So this is certainly something that can be employed, as you said, preoperatively and have a meaningful response.

Dr. Ford:

Absolutely. And that's a very simple strategy and just I think a re-education of the surgeons and the referring physicians to really, just like they prepare their patients for surgery by evaluating cardio and pulmonary function, to really look at the blood work and make sure you're not sending an anemic patient into a large blood loss potential surgery.

Dr. Freedman:

And are there products that help with either white cells or with platelets or clotting factors?

Dr. Ford:

So for the clotting factors, some simple things I've found to avoid any excess bleeding is to make sure that people have adequate vitamins, especially vitamin K, which you know, is one of the most important in terms of the coagulation cascade in proteins. But very importantly, what we found is that nowadays people are really taking an awful lot of alternative supplements, whether it's vitamins, or fish oil, or ginkgo. And what we do is we have a little education process. Everyone knows before surgery to avoid aspirin and maybe you have to come off your Plavix and some of your other antiplatelet drugs to avoid bleeding. But what they may not ask is, one, alcohol use. And you have to be very careful to specify this includes all alcoholic beverages and you want to have them stop alcohol 7 to 10 days before the surgery because that also interferes with platelet function, as do some of these supplements, fish oil, ginkgo, etc. So we go through everything with them. And we strongly recommend they come off all unnecessary medications. Certainly, all supplements, all alcohol 7 to 10 days ahead to make sure you're entering with healthy platelets and lessen your chance of bleeding.

Dr. Freedman:

Very smart, simple things to do that I can see would really make a big difference.

Dr. Ford:

Very simple. And in the hospitalized patient just to give another very simple strategy. What we find in hospitalized patients, they can literally lose anywhere from 300 to 400 milliliters, even on a general medical floor with repetitive blood draws. So if you think about the hospitalized patients, getting daily blood draws, the first thing that happens when the sun comes up is in goes the phlebotomy team, they draw off a lot of blood, and in a very stable medical patient or any patient, you may not need to check a CBC and chemistry without an abnormality or change every single day. That can save an awful lot of iatrogenic blood loss. And the phlebotomy teams will often say

they overdraw into the tubes, because they know it's not infrequent that later on the house staff will call asked for additional testing to be added on and they don't want to come back to re-stick the person.

So what we find is we really had to educate our phlebotomy team to draw off very small volumes, just what you need. It may only be 1 to 2 milliliters instead of a 10-milliliter tube. And then re-educate our house staff to not order unnecessary testing. Frequently, I see routine CBC and chemistry and they're normal every single day on a patient that's in for a medical issue or on the day of discharge. There you go. Blood has been ordered again on the day of discharge.

Dr. Freedman:

If you're just tuning in, you're listening to Medical Breakthroughs from Penn Medicine on ReachMD, the Channel for Medical Professionals. I'm your host, Dr. Lee Freedman, and joining me is Dr. Patricia Ford, clinical associate professor of medicine, medical director of the Center for Bloodless Medicine and Surgery, and director of the Peripheral Stem Cell Program at Penn Medicine. Dr. Ford, those are all excellent points, very practical. Tell us a little bit about this interesting thing of blood the stem cell transplant.

Dr. Ford:

I'm a general hematologist/oncologist and I also direct an autologous stem cell transplant unit. And what I found as I was caring for Jehovah Witnesses and becoming more adept at some of the alternatives and how to deal with profound anemia and thrombocytopenia, I was faced with the challenge of having a Jehovah Witness who had a relapsed lymphoma in our practice a number of years ago. And really at that point, no one had felt comfortable performing an autologous transplant because of the inability to provide red cell and platelet transfusions during their 2- to 3-week period of pancytopenia after the high-dose chemotherapy.

So at that point, I felt very comfortable in dealing with low blood counts. And I really said I have enough strategies that I think someone can survive this by just doing some of the simple strategies already discussed, preparing these patients entering into transplant by getting their hemoglobin up as high as I possibly can, limiting the unnecessary blood volume draws, using some of the hemostatic agents in lieu of platelet transfusion. So normally in a transplant patient, once the platelet count is under 10,000, we would normally give a single-donor platelet transfusion. In a Jehovah Witness, we cannot do that; that's one of the prohibitive products. So then what I do once the platelet count starts getting low as I try to enhance hemostasis by utilizing simple things like vitamin K, aminocaproic acid, which is an anti-fibrinolytic. And I've actually found in the 100 patients that we've transplanted, I've had only one major bleeding complication in these profound thrombocytopenic patients by the simple use of other hemostatic agents.

Dr. Freedman:

That's incredible. And I know our blood supply is relatively safe. But have you applied this in patients who are non-Jehovah Witnesses?

Dr. Ford:

I have. And I'm at the point right now and those patients who will accept transfusions that were only transfusing about 1 out of 3 of our transplant patients. And prior to my gaining some expertise in this, I was transfusing upwards to 90% of patients going through transplant. So a pretty profound reduction in the non-bloodless patients, also which I think is a good thing if they're unnecessary transfusions.

Dr. Freedman:

And do you just have a lower threshold in these non-Jehovah Witness patients for red cell transfusions?

Dr. Ford:

That is an absolute fourth strategy that is very simple, and we call it tolerance of anemia to really not transfuse someone based on a number. So I know even for myself, I was, uh, trained in transplant anytime the hemoglobin was under 8 to give 2 units of blood. So the two mistakes there I've learned was number one, not every person with a hemoglobin under 8 is clinically in need of a blood transfusion. Red cells are designed to provide tissue oxygenation not to be used as volume. So we keep our patients very euvolemic, we keep them on oxygen. And we decide when we feel they need a blood transfusion. And for some of these, they may have hemoglobin 6 or 5 before there's any signs of tachycardia or some sign telling us that we need to give a transfusion. We also don't need to give 2 units. So again, it was just one thing I was trained to give 2 units. Whenever you need to transfuse, give 2, right?

Dr. Freedman:

Right.

Dr. Ford:

If you need to give it, you must need 2. And we find that that's unnecessary. So we will give 1 unit of red cells and then reassess. Do we clinically have a reason to administer a second unit?

So two very simple things rapidly reduced the amount of transfusions I was giving. Not transfusing on any basic number, and then giving

1 unit instead of 2.

Dr. Freedman:

And you mentioned the tachycardia. Are there other specific clinical things you look for that would indicate, 'Hey, now's the time to give that unit of packed cells?'

Dr. Ford:

Right, all the things we learned in terms of assessing tissue oxygenation, because as you know, there's not a good correlation necessarily between the pulse ox and what how you're actually oxygenating tissues. So looking at the things we were taught so well as medical students, kind of going back on your clinical skills, assessing mentation, looking at urine output, and of course, looking at blood pressure and tachycardia, and the patient's symptomatic complaints potentially of dyspnea, whether it's on exertion or just at rest. We also keep them monitored. So we have a continuous cardiac monitoring going also, so that we're not missing maybe some asymptomatic arrhythmias or some other signs there.

Dr. Freedman:

Prognostically, I imagine there's no big difference down the road for people who have a bloodless stem cell transplant versus traditional?

Dr. Ford:

Well, there's no difference in terms of their response to their tumor, the efficacy of the transplant, because they all get the same dose of drugs. So they're not attenuated. They all get high-dose chemotherapy, as would be recommended for any relapsed lymphoma or multiple myeloma patients. So they're all getting the same standard treatment. And so as expected, you would imagine that their response rates, their survival, disease-free survival would be the same. And it is.

The difference with the Jehovah Witness patient population, and I am very upfront with them is, I would say, in general in the United States, right now, the safety of an auto transplant should be around 1 maybe 2%, in most centers, mortality directly related to transplant. And what we find is that our mortality is slightly higher in our 100 patients, we've actually had 4 deaths. So there is a slight increased risk of mortality with this patient population. But the alternative for many of these patients, this is their only curative potential.

Dr. Freedman:

Sure.

Dr. Ford:

Or maybe their best potential. So they find this slight increased risk acceptable.

Dr. Freedman:

Is there any difference in terms of complication rate or hospital stay infection or other things?

Dr. Ford:

We've seen no difference. And we've actually looked at this. So we've evaluated infectious complications, and it actually was somewhat lower. And one thing that has been noted with blood transfusions in other patient populations, there's a leading article that was out in the *New England Journal* just a couple of years ago from Dr. Colleen Koch on her cardiac patients, looking at older versus newer blood products being given, and she did find a difference.

So it seems like, A, patients who are transfused, have an increased infectious risk. We think it may be part of the whole immunosuppressive aspect of getting this product, because if you think about it, these are live cells, so it is an organ transplant at some level. These are live cells. And even though we try to look to reduce our blood products, you do get some contaminating donor leukocytes, which are live and viable, and account for things other than infectious risk and red cell products, that accounts for your transfusion-related acute lung injury potentially, and we think may also alter the recipient's immune system and make them somewhat more acceptable to infections. So we have also seen in this population, a slight decrease in infectious complications.

In terms of cardiac complications, we have had an increased risk, and they were all manageable. And what I mean by that, there was a little bit more hypotension requiring more fluid and more cardiac monitoring, but we've had no significant events such as thrombosis or myocardial infarction. So it's been mostly a little bit more need to monitor them carefully in terms of volume and cardiac monitoring, and assessment of arrhythmias. We've had a couple increased incidence of arrhythmias.

Dr. Freedman:

I very much want to thank Dr. Patricia Ford, who has outlined for us Bloodless Medicine. Dr. Ford, thank you very much for being our guest this week on Medical Breakthroughs from Penn Medicine. And as always, thank you for listening.

Dr. Ford:

Oh, my pleasure. Thank you.

Announcer:

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