Palliative Care Chat Episode 6
Dr. Kathryn Walker and Dr. Lynn McPherson
Speed Dating Tips – Part 2

Dr. Lynn McPherson: Hello, this is Dr. Lynn McPherson. Welcome to Palliative Care Chat, the podcast brought to you by the online Master of Science and graduate certificate program at the University of Maryland. I'm super excited to be joined by Dr. Kathryn Walker, who is the senior clinical and scientific director of palliative care with MedStar Health and an associate professor at the University of Maryland School of Pharmacy. How are you today, Ms. Kat?

Dr. Kathryn Walker: I'm doing well. What about you? I'm happy to be here.

Dr. Lynn McPherson: If I was any better, I would be twins I think. Kat and I for three or four or five years have done speed dating with the pharmacy ladies. Last month we had one part of our podcast. Today we're going to continue with the second half.

The first tip I'd like to talk about is, I think sometimes when we treat chronic disorders in end of life care, maybe we don't have to go for the gold. I think sometimes good enough is good enough. When we look at diabetes, certainly for someone who is not with a serious illness at the end of the road, we want to target type-blood sugar control if type is appropriate for that patient. But often in end of life care we want to loosen the reins a little bit and sometimes a twice a day NPH insulin may be just as good as a once a day long-acting.

I wanted to point out that Walmart has their own brand of insulin called, ReliOn, for regular NPH and 70/30 NPH regular. It's about $25 a vial versus about a 140 a vial for Humulin or Novolin RN or 70/30. Then when you look at the long acting insulin, they're anywhere from 250 to 500 dollars a vial. That is a lot of money.

So my point is-

Dr. Kathryn Walker: That's a lot.

Dr. Lynn McPherson: It's an awful lot. Since CMF expects us to pretty much pay for all the drugs now I wanted to point this out. For example, when we have someone who's getting Dexamethasone once a day and it causes symptomatic hyperglycemia, the time course profile of that hyperglycemia is entirely consistent with one dose of NPH. So this would be a much more cost-effective way to handle that, or if you need some basal insulin using NPH twice a day instead of the long-acting once a day. That's a nice tip I think.

Another website that I found that I thought was pretty informative is, Diabetes Medication Education. It's http://diabetesed.net. It's a lovely website. They've

got some little pocket cards to educate people about diabetes. They also have an app called CDE coach app. That's a nice application as well.

Speaking of diabetes, so many of our patients have diabetic neuropathy and they often turn to using a coanalgesic such as gabapentin, which is probably the number one coanalgesic used in the world. But gabapentin has been a naughty kitten. We are seeing the abuse and misuse of gabapentin rising, particularly in people with a history of substance abuse. We know that gabapentin abuse is noted in almost 2% of the population. Still, when you look at opiate abuses the prevalence is anywhere from 3 to 6% so it's not out of the ballpark.

Almost 12 thousand reports that gabapentin [inaudible 00:03:10] abuse identified from 2004 to 2015, with over 75% of them just in the past three years of that timeframe. And substance abuse and psychiatric comorbidities are mis-factors. Of course pregabalin has been abused also. Again, if a family member tells you, "The dog ate the morphine," or, "The dog ate the gabapentin," number one, "I want to see the dead dog to make sure that we're telling me true here."

But I think we are hearing now people abusing gabapentin and pregabalin. So something else to keep an eye out for.

Dr. Kathryn Walker: I think so too. I think a lot of times the reports on those are that people were administering higher than recommended doses which means they would need more frequent refills, so another red flag that would go up for looking into this a little further and similar risk factors to other agents that they would have used. I think it's something to keep on our radar for sure. So a good tip.

This is a quick one but a good one. I'm always surprised, actually ... I'm like, "I'm never surprised." I'm always surprised that ... How I work in a hospital setting and we very much under-utilize Intensols. I think sometime our little joke here is, "Whoa, that's intense." It's an Intensol. But in hospitals it can be difficult to get access to these medications because it requires special preparation from the pharmacist and it's not an easy thing to throw in a Pyxis machine and pull out for every patient. They have to do pre-loaded, pre-filled and they're concentrated solutions.

I think it's something to continue to work on. In our hospital we've struck a bargain with the pharmacy that we would try to reserve this for patients being discharged or that didn't have IV access to be able to use it. But I'm always thinking of this as something to avoid that next IV line being placed when one blows or having to do a subcutaneous infusion. Remember, it's not just your Oxycodone and your morphine 20 milligrams per mil, there's also Alprazolam, Dex comes at one per one. Diazepam, Lorazepam, methadone, our favorite, 10 milligrams per mil, and Prednisone.

I think there's a lot of options and lot of times when patients can't swallow, people automatically think, "We need a line. We need to give them something else." But if you prop their body up 30 degrees you can put up to a milliliter and a half in their buckle cavity. And we know that the more lipophilic medications get absorbed better directly into the bloodstream, but even if they're not that lipophilic and they end up trickling down, it's the same as a PO absorption would be and that's okay with us, right?

Dr. Lynn McPherson: Absolutely. It always kills me when I hear about a patient in our in-patient hospice unit and they've been in the unit for a few days, they were having a pain crisis. They get them stabilized on an IV infusion and then the team will say, "We want to send him home today, what do we do now?" "Why didn't you think of starting them on the methadone or the morphine Intensol a couple of days ago to get him stabilized before you send them home?" So I think this is a great alternative to IVs. Particularly at home.

Dr. Kathryn Walker: Absolutely. That's why we got a little bit upstream in the hospital setting because if you can show families that it's working and show them how it's being done in the hospital, it leads to a much better transition. And you know we're all about good transitions in care.

Dr. Lynn McPherson: Absolutely. Switching gears a little bit. You have heart disease and your knees hurt. What's that all about? We have been waiting and waiting and waiting breathlessly for the results of the precision trial which is where they compare the cardiovascular safety of Celecoxib, which is a COX-2 selective inhibitor, with Ibuprofen and Naproxen, which of course are non-selective inhibitors. There are almost 25 thousand patients in this study with osteoarthritis which was 90% of them, or RA 10%, and established cardiovascular disease or at an increased risk of developing cardiovascular disease.

They were randomized to receive either Celecoxib, a hundred milligrams twice a day. Ibuprofen 600 three times a day, or Naproxen 375 twice a day. The mean treatment duration was almost two years so 20 months, and the means follow-up was almost three years. 34.1 months. About half these patients were taking low-dose aspirin at base time. The primary outcome they were looking at was cardiovascular death including hemorrhagic, non-fatal MI, or non-fatal CVA.

Now what's interesting is almost 70% of patients stopped the study-drug during the study, and 27.4% stopped it during the follow-up. So this is a very difficult trial to do so they had to unroll huge numbers, just get numbers at the end so they could do data analysis. They did break it down by intend to treat, and then people who were on treatment all the way to the bitter end.

What they found was, looking at this primary outcome, looking all the way to the end, Celecoxib was 1.7% of people achieved at primary outcome which was cardiovascular death and a non-fatal heart attack or stroke. Ibuprofen was 1.9% and Naproxen was 1.8%. The risk of [inaudible 00:08:20] was significantly lower

with Celecoxib than either of the non-selective ones and the risk of [inaudible 00:08:26] was significantly lower with Celecoxib than Ibuprofen, but Celecoxib was not significantly less than naproxen.

This is an interesting finding because the naproxen people petitioned the FDA to be able to put in their labeling and marketing that they were nonsteroidal with the lowest risk of heart disease. But now this study, which was a non-inferiority study, has shown that Celecoxib was non-inferior with regards to the heart attack and the stroke.

Now, the study was heavily criticized. Of course, this is a very difficult study to pull of with all these patients. One of the criticisms was the dose of Celecoxib was limited to 200 a day where we know a lot of people are taking 200 milligrams twice a day. So these are lower than doses that have been previously associated with cardiovascular toxicity. Interestingly, the Ibuprofen and Naproxen doses, they were not allowed to be increased. We also know that Ibuprofen and Naproxen, but not Celecoxib, inhibit Aspirin binding to the plate like COX-1, so the cardio-protective effects of aspirin may have been blunted in the patients who were getting the non-selective, nonsteroidal.

The conclusion was ... The researchers state that Celecoxib is non-inferior to Ibuprofen and Naproxen from a cardiovascular perspective, although others refute this to say, "You really can't make that conclusion because Celecoxib, this dose was too low to support that conclusion."

I think it's a very interesting study and to be certain, it's one that won't be repeated. At least it's, I think, partially put some of our fears to rest.

Dr. Kathryn Walker: For sure. That's a complex tip you had there.

Dr. Lynn McPherson: I know.

Dr. Kathryn Walker: That's a tough one. These are a couple of quick ones. My last tip was about Intensols so I think maybe I'm passionate this session about non-oral dosage formulations-

Dr. Lynn McPherson: I think you are.

Dr. Kathryn Walker: ... or what else can we use here? But this one is about using levetiracetam subcutaneously. I think when you think about this, the conversion is one to one and the manufacturer's German and said that it should be diluted in at least a hundred milliliters of D5 or other [inaudible 00:10:38] and administered twice a day over 15 minutes.

There's a couple other studies out there that looked at different ways to administer it but either way there's a couple good references about using it

subcutaneous. I think this is something that we don't always think of doing and would be a good trick to keep in the back pocket.

A couple of the other studies, one looked at continuous infusion as well. So that's something that they administer [inaudible 00:11:05] over 24 hours and had good success with it.

The other SubQ option out there is SubQ methadone. I think this is one that we think of, "We use methadone a lot." Don't always think of SubQ dosing and using half of the oral dose would be the dosing conversion you'd use. It's been reported intermittent and continuous infusion but some of the things you see in the literature ... That there's a risk of irritation. People have done all kinds of things to mitigate these risks. They've looked at frequently changing the infusion sites, flushing the site with normal saline, limiting the doses to 30 milligrams or so, and some people have been adding Dex or [inaudible 00:11:47] to the infusion to prevent the irritation and whatnot.

There's conflicting things because there's also studies not using a lot of these mitigating factors and saying that they had good success. Either way I think for short-term use there is data to support using that methadone ... This might be a good option. Although for most of our practice I think you can [inaudible 00:12:13] is still probably ideal considering the volumes and doses that most of our patients need are very low.

The other one that I think is useful and we work a lot within our health system with, as many people do with advanced heart failure population, often we're thinking about when the oral, the diuretics are not useful and they're not getting the diuresis that we were hoping for, that using subcutaneous Lasix is an option. The concentration is 10 milligrams per mil so if you need a large volume it can be a little bit of a challenge. But a great tip if you want to keep that patient and do it in a home setting. That's an option.

We're on a podcast right now so you cannot do this, but the pictures of the dogs that we had, you have to come see it in-person I think. Absolutely.

Dr. Lynn McPherson: It's very cute.

Dr. Kathryn Walker: What kinds of dogs are those too? Look at them. One is a bulldog maybe? What is that? A bulldog?

Dr. Lynn McPherson: Bulldog and maybe a greyhound or something. [crosstalk 00:13:19]

Dr. Kathryn Walker: [crosstalk 00:13:20] it's a magical thing right after Lasix dose.

Dr. Lynn McPherson: I wish I could lose weight like that. I think my favorite Lasix tip is, oral Lasix, taking it on an empty stomach doubles the bio-availability. How many people

don't know that that take it after breakfast for example and then they wonder why it doesn't work.

Dr. Kathryn Walker: Maybe that needs to be another tip of taking things with food. It's amazing how many people you talk to that say, "I take all my meds with breakfast. I don't want to upset my stomach." Even for medications that are not possible to upset your stomach. But for Lasix, that'd be a bad idea.

Dr. Lynn McPherson: That's right. It would be like a day without sunshine if you got up but did not get an email from some source saying another horrible thing associated with the proton-pump inhibitors. It is among the most widely prescribed drugs worldwide and in the U.S. and side effects for anywhere from four months to two years of treatment include things like: atrophic gastritis, carcinoma, [inaudible 00:14:17], fractures, hypomagnesemia, interstitial nephritis, and B12 deficiency.

Here's another one. A nationwide observational study looking at pre-clinical studies showed that PPIs reduced the production of nitric-oxide leading to endofilio dysfunction, and now it's been linked to cardiovascular disease. So their study showed a dose-related increase for ischemic [inaudible 00:14:40] for all four of the proton-pump inhibitors studied, but no increased risk for the H2 blockers.

Their conclusion was, "Regard these results as preliminary but this study adds to the evidence questioning the cardiovascular safety of the PPIs." Then this next ... I have a slide here said, "Shoot me in my lower left lobe." This is a study from the University of Finland from 2005 to '11 with 65 thousand patients looking at the risk of pneumonia in Alzheimer's patients and comparing it with the use of donepezil, oral rivastigmine, transdermal rivastigmine, and galantamine, and memantine.

Memantine, the hazard ratio was 1.6 for developing pneumonia as opposed to donepezil. Rivastigmine transdermal patch was 1.15 and oral rivastigmine and galantamine were not associated with an increase risk.

So, just worried about the side-effects of drugs. The PPIs I think, my big take home message there is, let's make sure the patient really does need it. We see patients in the hospital who get on a PPI for prevention of stress-ulcer, then they get switched from IV to oral, and then they get sent home on oral and we're seeing this accumulating body of evidence about adverse effects associated with PPIs. Again, we could talk for three days about, "When should we stop the drugs for Alzheimer's disease once someone, at least in my practice, is hospice appropriate? I believe those medications don't bring a lot to the table. And we do know that Alzheimer's patients have a very high prevalence of pneumonia, so yet another compelling reason to re-think those medications.

Do you agree with that one Dr. Walker?

Dr. Kathryn Walker: I definitely do. I think that PPIs are one, on medication reconciliation on discharge, I think get overlooked all of the time. They're seen as a low-risk medication and I think it's something we should back up on the radar for sure.

Dr. Lynn McPherson: Absolutely. I like that Canadian website, deprescribing.org, they've got that-

Dr. Kathryn Walker: That's a good one.

Dr. Lynn McPherson: ... very nice flow sheet for several drugs. Hyperglycemic drugs and Benzodiazepines. They've got a very nice one on the appropriate prescribing of PPIs. So deprescribing.org. Wonderful website.

Dr. Kathryn Walker: The PPI one's very clear. We can print it out and wallpaper the hospital with it.

Dr. Lynn McPherson: Love it.

Dr. Kathryn Walker: I think this is our last tip here tonight.

Dr. Lynn McPherson: I think it is.

Dr. Kathryn Walker: It's about symptomatic bradycardia. Most people believe when you use these eye drops for glaucoma that it has this topical effect and it's not absorbed but actually, fun fact, 80% of it is actually systemically absorbed. It avoids first pass metabolism so you really have to be careful. Although it will give you lower concentration, say with Timolol than an oral beta-blocker, it can still induce cardiovascular side effects, all of the same type of side effects that you would see and I think you really have to be careful. So this is another one can be totally overlooked on medication reconciliation.

A lot of times patients forget to tell you they're on eye drops. It's not seen as a medication but definitely something that can come into an effect for our patients. Something to keep on our radar, especially in our older adults that are very sensitive to that or that have underlying cardiovascular diabetes.

Dr. Lynn McPherson: I'm the worst offender. When I look at a patient's medication regiment, I kind of blow off all the opthalmics. I guess I shouldn't be doing that, should I?

Dr. Kathryn Walker: No, look a little closer at those.

Dr. Lynn McPherson: I think I should. I'm getting a little [inaudible 00:18:14] just thinking about it.

Dr. Kathryn Walker: We all need to get out our magnifying glass and take a look at those meds that slip through the holes.

Dr. Lynn McPherson: Absolutely. I would like to thank my guest, Dr. Kat Walker in joining me in doing a re-cap of some of our speed dating tips. And I would like to thank you for

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