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How to Monitor and Manage Patients on Antipsychotics

ANTIPSYCHOTICS AND HOW TO MONITOR AND MANAGE THEM

Two out of the 10 biggest sellers in the Unites States Pharmacopeia last year were anti-psychotic medications. What do we need to know about these meds, should non-psychiatrists be prescribing them routinely.

You're listening to ReachMD XM 157, The Channel for Medical Professionals. Welcome to the Clinician's Roundtable.

I am Dr. Leslie Lundt, your host, and with me today is Dr. Stephen Stahl. Dr. Stahl is the Adjunct Professor of Psychiatry at the University of California in San Diego. He is an internationally recognized clinician, researcher, and teacher in psychopharmacology and the author of more than 350 articles and chapters. His latest book is the third edition of Stahl's Essential Psychopharmacology.

DR. LUNDT:

Welcome to ReachMD, Dr. Stahl.

DR. STAHL:

Hi, Dr. Lundt, how are you doing?

DR. LUNDT:

Not bad! There is a lot about antipsychotics in the news today, Dr. Stahl, and my first question is should non-psychiatrists even be prescribing these medicines as liberally as they seemed to be?

DR. STAHL:

This is a topic of great controversy today. I believe that any well informed prescriber can give these medications, but the secret is not necessarily being primary care physician so much is being well informed. They are expensive drugs and there are drugs with risks. If they are given out in a cavalier way, and particularly if they are given off label, then it's probably not such a good thing; however, they





can be used prudently and we certainly can leverage the psychiatry community by having non-psychiatrists prescribe them.

DR. LUNDT:

Let's back up and talk about some of the basic pharmacology of these drugs, we talk about the conventional antipsychotics like Haldol and Thorazine and then the atypical antipsychotics like olanzapine and several others. What makes an atypical antipsychotic atypical?

DR. STAHL:

Well, that's very good question. Some people would say it's their pharmacology, some would say it's their price, as they are very expensive. The definition of atypical comes from the idea that you could have antipsychotic actions without having extrapyramidal side effects. That is really what atypical means and it turns out that when you have a blocker of the D2 receptor for dopamine, the dopamine D2 receptor, you have at least a conventional antipsychotic because that will help psychosis. However, if you add a serotonin to an antagonist to the atypical, you can get 'hey, may be have your cake and eat it too.' What I mean by that is the D2 properties will allow you to have antipsychotic action just like in a conventional antipsychotic, but for pharmacological reasons the serotonin 2A antagonist properties take away or at least mitigate the extrapyramidal side effects, so there is your atypical, something that causes antipsychotic action without extrapyramidal side effects.

DR. LUNDT:

But doesn't having your cake translate into significant weight gains?

DR. STAHL:

Wow! That was a good one, Leslie, wow! You know, in the old days, I am an old guy, you know, and I was at Stanford in the 70s, and I had a Tardive Dyskinesia Clinic. Now, people are walking around with no tardive dyskinesia from EPS or extrapyramidal symptoms, but they are walking around 300 pounds, what's happened? Well, the world, of course, has changed and for a while we thought that's all that's happened, there are too many McDonald's and bad diets and certainly patients who take antipsychotics that live in North America have the same problems that we all have with our weight, and if you are a schizophrenic, it turns out that the chances of getting diabetes and gaining weight is even higher just because you are schizophrenic, but that's a smokescreen that kept us from recognizing as fast as we probably should have recognized that these drugs can cause problems with weight that have nothing to do with eating too much McDonald's or having the gene for schizophrenia. They have only to do with the fact that certain drugs cause changes in metabolics. Some of that is pure weight gain because <_____> and your appetite goes up, but it turns out it is even more complicated than that and has a lot more to do with things like insulin resistance, which can change with these drugs.

DR. LUNDT:

So is that what you mean when you talk about the metabolic highway in your book?

DR. STAHL:

Actually, the metabolic highway, the first on ramp is weight gain and weight gain, of course, leads eventually to obesity and then obesity





on this highway leads to insulin resistance, which leads to stress on your pancreatic beta cells, which then can lead to prediabetes, which then can lead to diabetes, which then, of course, is a risk for having heart attacks and death. So the metabolic highway starts with obesity and ends with death. What we thought was that you got on this highway only at the obesity on ramp and that the drugs gave you the <_____> ate too much, it got too heavy, and then you propelled yourself down the highway, but what is very interesting is that these drugs can have you enter the highway at the level of changing triglycerides. In other words, you can have dyslipidemia without any weight gain. If you gain weight, you are going to have dyslipidemia. If you lose weight, you'll actually improve that, there is no question about that, but there are people that have changes in lipids very much faster than their weight changes. It's as though these drugs, in some people, with some drugs, can immediately change insulin, such that you have insulin resistance shortly after taking them, and if insulin resistance persists, this will lead to diabetes and cardiovascular events.

DR. LUNDT:

Can we do anything to stop all this?

DR. STAHL:

There are a few things, one is monitoring. Even though some of the drugs, clozapine and olanzapine might be examples, cause dyslipidemia and obesity more than the others, they don't always cause it. I have patients in my practice; I think two of them on clozapine that are as thin as a rail. They are lucky. May be pharmacogenomics some day will likely tell us who they are, but trial and errors is all that we have today. So it doesn't mean that you have to avoid all patients taking drugs that have high risk of this. It just means you have to monitor and what is monitoring, it's not just taking your weight. It's getting triglycerides, fasting triglycerides. You know, one of the things that happen is that it takes weeks, may be even months, to be sure you're getting weight gain. If someone comes in with a 4-pound weight gain, I am not sure I can tell it, you know, somebody can see this in my clothes, it's my menstrual period or whatever, but by the time you gain 40 pounds, boy, I can even tell with my eyes, too late. However, if you get fasting triglycerides you can see that changing before your weight changes and it can go up, you know, in 10, 20, to even 40 points and you can do that within days to weeks after starting a medicine that is going to do that. Well, if somebody is taking olanzapine and their triglycerides go up, party is over. If somebody takes olanzapine and the triglycerides don't go up, may be they are one of those lucky ones. So you have to monitor, and there is also low-risk drugs and drugs in the middle. The lowest risk drugs are aripiprazole and the _> with the drugs like risperidone and clothiapine in the middle, it doesn't really matter. The thing is that this all came up with the atypicals including your conversation that as a psychopharmacologist the listener should be thinking about doing this to any psychotropic drugs. Have you ever seen the patient gaining weight on Depakote, valproic acid, on lithium, on certain antidepressants? The idea is that one should be monitoring weight, body mass index, which is just, you know, how tall the person is and there is charts that will help you convert it, and at least fasting triglycerides. If someone is already a diabetic, of course, you have to measure glucose and you have to make sure they are not a diabetic by measuring the fasting glucose at least once, but long before somebody has a fasting glucose problem and long before they have gained 40 pounds and become obese, we want to know whether they are going to get dyslipidemia and eventually become a diabetic and so forth. Almost make a joke out of this, I think that one of the psychiatric vital signs is fasting triglycerides, no matter what drug you are on.

DR. LUNDT:

If you're new to our channel, you're listening to the Clinician's Roundtable on ReachMD XM 157, The Channel for Medical Professionals. I am Dr. Leslie Lundt, your host, and with me today is Dr. Stephen Stahl. We are discussing antipsychotics and how to monitor and manage them.

Dr. Stahl how soon after starting one of these medications should we get a fasting triglyceride?





DR. STAHL:

Realistically, I would say every month. I think you need a fasting triglyceride before you start, but I see most patients monthly, and I think that when you're adding a drug, subtracting a drug or changing the dose of the drug, you should be getting these monthly. Now if somebody is unstable and you know that they have or haven't changed their triglycerides and of course you're measuring weight as if this is a long time along with it, you know, once you're stable, may be you only have to do it once a year, but I think the idea is when you start a high-risk drug, monitor weight, BMI, and triglycerides monthly.

DR. LUNDT:

Now, back to anything we can do to prevent the antipsychotic induced weight gain, so monitoring clearly, what if they are gaining weight, you just have to stop the drug or can reduce something else?

DR. STAHL:

Theoretically, you could change lifestyle. You really think you're going to get patients to stop smoking and start exercising and restrict calories enough to lose 40 or 100 pounds, it's not impossible, it's just unlikely. You can't change your grandmother. May be some of us would like to change a few of our parents, but you know, we've got the genes that we've got. You can't change your risk factors. So what you really can do, I think, is one thing for sure and the second thing possibly; the sure thing is you can switch to another drug and the class, particularly a low risk one. The other thing you can do is possibly some experimental ideas of new diabetes drugs added on, metformin, but even some things like pramlintide, which is an injectable peptide, these drugs, which have been out on the market for treatment of diabetes can also mitigation of the dyslipidemia and weight gain in patients on antipsychotics. Now, I am saying this is again widely off label because it's still in investigation. So, it's not ready for prime-time and can't be endorsed, but this is where the field is moving. Some people try, you know, the usual appetite suppressants. Topiramate can do that and some people Topamax. There is a zonisamide, which is Zonegran; it's another anticonvulsant that can make some people lose weight. These are not highly effective. There is an old fashioned appetite suppressants. They have their own problems, side effects and efficacy. I think that the actual thing is to switch drugs is probably the most potent and if you can't do that, I believe, you can try to get people to have lifestyle changes, but I've had a couple of people in my practice, I've actually tried some of the diabetes drugs on.

DR. LUNDT:

And what kind of results?

DR. STAHL:

Pretty good actually. I've got a specific lady who basically is a bipolar who tried essentially everything that was out there and she consistently got better on olanzapine and nothing else and consistently gained 40 pounds and so we put her on pramlintide, which is an injectable peptide. It's actually something that changes your appetites and your sense of satiety and she either had a choice of being bipolar or obese, couldn't have been not bipolar and not obese, so, so far it's early days, it's hard to tell. I have tried metformin a few times with moderate results. Usually, it's hard to make olanzapine or clozapine have that kind of weight gain mitigated, but drugs with a little more moderate signal such as risperidone or clothiapine might be better to use. There is some techniques on, but that's just my own anecdote and it's early days.





DR. LUNDT:

And certainly groups such as the Mood Disorders Group in Toronto, Dr. Roger McIntyre, they are looking closely at these sorts of treatment.

DR. STAHL:

Yes, there is a big push to try to find a solution for this. You know, I believe that it is probable that these antipsychotic drugs find some yet unknown receptor probably and skeletal muscle or fat or liver to change insulin resistance almost immediately and if we knew what that was, and I don't think that that will be a secret forever, we can then engineer the new antipsychotics to not have that binding property, but until then it's going to be pretty hit and miss.

DR. LUNDT:

Well, thank you for educating us on this today, Dr. Stahl.

DR. STAHL:

My pleasure.

DR. LUNDT:

We've been speaking with psychopharmacology expert, Dr. Stephen Stahl, about what's new in antipsychotics and the importance of monitoring the patients closely.

I am Dr. Leslie Lundt, you've been listening to the Clinician's Roundtable on ReachMD XM 157, The Channel for Medical Professionals.

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