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Biomarkers for Underreported Alcohol Use

USE OF BIOMARKERS TO DETECT ALCOHOL USE

Patients who are not forthcoming about their alcohol history jeopardize our ability to provide the best possible clinical care. Many instruments such as the CAGE rely only on patients self record. Likely, we have several biomarkers to assist us, how and when to use which test. Welcome to The Clinicians Roundtable. I am Dr. Lesley Lundt and with me today is Dr. David Spiegel. Dr. Spiegel is an associate professor of Clinical Psychiatry and Behavioral Sciences and Director of the Consult Liaison Service at Eastern Virginia Medical School.

DR. LESLEY LUNDT:

Welcome to ReachMD, Dr. Spiegel.

DR. DAVID SPEIGEL:

Thank you, Dr. Lundt. It is a pleasure to be here.

DR. LESLEY LUNDT:

Dr. Spiegel, why is it important for us to know how to use biomarkers to detect alcohol use?

DR. DAVID SPEIGEL:

Well, Dr. Lundt, I think it's from two perspectives, I feel it's important. First, from a psychiatric perspective, I feel that there are two acute psychiatric emergencies that psychiatrists often confirm - the first would be lethality such as suicidality or homicidality, but the second would be alcohol withdrawal with the possible complications to delirium tremens or DTs. By recognizing who is at risk for alcohol withdrawal or DTs, we can prevent it by treating with the appropriate medications, i.e., benzodiazepines and thus prevent the possible significant mortality of up to 20%, but, in terms of regular primary care physicians, 10% to 25% of patients underreport their alcohol use. So as physicians I think we need to be aware that about after four to six weeks of heavy drinking, they substantially increase their risk for alcohol withdrawal and most important like I said can lead to DTs, which would be a complication in the medical part of hospice.

DR. LESLEY LUNDT:

Makes sense, so you don't necessarily go along with, I believe, you just double whatever the patient says as far as how much they are drinking?

DR. DAVID SPEIGEL:

Well, you can't do that and I often find that patients definitely underreport, but I would like to think that even if they are saying that they are doubling from two to four from four to eight, it takes about four to six solid weeks of drinking before the risk occurs and so these alcohol biomarkers, one thing good about them is that they don't lie. You may have false positive, false negative, but they definitely don't lie and that's I think is a little better objective way of assessing alcohol misuse.

DR. LESLEY LUNDT:

Okay. Let's start up with blood alcohol level. We all know about that, but is it only helpful if the patient is acutely intoxicated?

DR. DAVID SPEIGEL:

Yeah, as a rule I think that's the only time they are helpful and certainly within 24 hours with what alcohol is going to lead us into a false insecurity, i.e., it is going to read a false negative with respect to risk of alcohol withdrawal and unfortunately I see that many times where in the emergency room or on the medical surgical service, a blood alcohol is the only assessment for alcohol misuse ordered and once it comes back negative, there is no other screening for this.

DR. LESLEY LUNDT:

Yeah, makes sense. What is the half-life of alcohol?

DR. DAVID SPEIGEL:

Alcohol has about a four-hour half-life and about an elimination rate of 7 g per hour, which then is equal to about one standard drink per hour. An example of a standard drink could be 12 ounces of beer, 5 ounces of wine, or nice shot of hard liquor. Therefore, by the time they do reach the emergency room,

may not even be getting an accurate assessment of what their blood alcohol is because they will have time in transport to have blood alcohol being lowered.

DR. LESLEY LUNDT:

Right, by the time they actually get their blood drawn who knows how long it's been. Now, another marker we have used for decades is the MCV. When is macrocytosis useful in this context?

DR. DAVID SPEIGEL:

Well, macrocytosis or mean corpuscular volume is actually helpful as it does elevate after about six weeks of alcohol misuse. So, in that respect if someone is a chronic drinker that value will rise.

DR. LESLEY LUNDT:

And, is the cutoff still a 100?

DR. DAVID SPEIGEL:

Yeah. At this point, we still use 100 femtoliters as the cutoff value for macrocytosis, but I will tell you that there are experts in the field who think that once you have an MCV greater than 90 fl that there is a cause for concern, especially in the appropriate clinical setting where alcohol is suspected.

DR. LESLEY LUNDT:

And also even 90, okay.

DR. DAVID SPEIGEL:

There are some people who believe that as high as 90 or as low as 90s.

DR. LESLEY LUNDT:

As low as 90s, yeah. How long does it stay elevated if the patient does manage to stop drinking?

DR. DAVID SPEIGEL:

Generally speaking, about two to three months, the MCV will stay elevated, but one thing in each count is that the sensitivity of the increased MCV ranges between 20% to 70% and with the specificity in the mid 60s. So, again there are other things, as we know, that elevate an MCV. So, we cannot rely on that solely as a test, but, I will tell that it's not unusual that's the only alcohol biomarker if you would that is ordered on the chart by the time I do a consultation.

DR. LESLEY LUNDT:

Yeah, and that's surprising, that's what we are all trained with, right?

DR. DAVID SPEIGEL:

Yeah and you should be at least more surprised when we talk about or we ever going to get a liver function test, how rarely that's ordered initially.

DR. LESLEY LUNDT:

Well, let's do it. Let's move onto liver function tests, which are most reliable as a biomarker for alcohol use.

DR. DAVID SPEIGEL:

But there are generally, four that are in, well I should say four that are in used and three in common practice. Three familiar to most people I think would be the AST, which is aspartate aminotransferase; the ALT, which is alanine aminotransferase; and the GGT, which is gamma-glutamyltransferase. But the fourth one, which is the old one and actually has an FDA indication for alcohol misuse is CDT or carbohydrate-deficient transferrin.

DR. LESLEY LUNDT:

And when that most of us don't order?

DR. DAVID SPEIGEL:

Well, now most of us don't order including my hospital because it is expensive. It's expensive and unfortunately, few institutes of ones the tertiary care centers will have access to CDT, but, the good news is, there is good news, that with the combination of liver function tests, we can get a pretty reliable assessment of whether or not a person in risk for withdrawal. So, for instance if you combine the AST to ALT ratio and that's greater than 2:1, we have about 70% sensitivity of picking up alcohol misuse and even better you have 92% to 100% specificity for alcoholic induced liver disease. What that means is the AST/ALT ratio is less than 2:1, it's pretty good chance they are not going to go into withdrawal; however, I will take it once that further, if you have a ratio of greater than 3:1, then that's almost diagnostic for alcohol misuse unless proven otherwise.

DR. LESLEY LUNDT:

So, AST to ALT ratio greater than 3, you are in trouble?

DR. DAVID SPEIGEL:

AST, well the patient in trouble, you and me are fine. So, the patient in trouble, we need to treat them right away.

DR. LESLEY LUNDT:

Right, now, I always thought that GGT was the best.

DR. DAVID SPEIGEL:

GGT is very good actually, I think GGT is actually better than the AST to ALT ratio and I think it's much more common to use the GGT as an assessment than this ratio, but I think we were taught in medical school that GGT is the best test. Only recently has the AST to ALT ratio been taught in medical students to assess alcohol misuse.

DR. LESLEY LUNDT:

So, how about the GGT? How long does it stay elevated after one stops drinking?

DR. DAVID SPEIGEL:

For about two to six weeks that will remain elevated after the alcohol cessation, but instantly it takes about two to four weeks to become elevated upon heavy alcohol usage. When I mean heavy alcohol usage, I mean about daily alcohol usage greater or equal to six drinks per day and again what we call six drinks, usually 12 ounces of beer, 5 ounces of wine, or the shot glass.

DR. LESLEY LUNDT:

So, if the patient says, "Oh well, I just partied last night and that's why my blood test is abnormal today, but usually I don't drink." Should we believe them or not?

DR. DAVID SPEIGEL:

Well, again I think in the context of this, there is nothing such raise in the GGT and I'll be the first to admit that bile disease can raise GGT, other alcohol disease can raise GGT, but in the appropriate clinical setting, where there is nothing else present other than an elevated GGT and again elevate is going to put you somewhere in the vicinity of greater than 60 then as a result, I would kind of not take their assessment as being accurate.

DR. LESLEY LUNDT:

If you are just joining us, you are listening to the Clinicians Roundtable on ReachMD, the channel for medical professionals. I am Dr. Lesley Lundt, your host, and with me today is Dr. David Speigel from the Eastern Virginia Medical School. We are discussing how to decide, which blood test to perform to determine alcohol misuse.

DR. LESLEY LUNDT:

David, which of all these tests is the more sensitive for heavy drinking?

DR. DAVID SPEIGEL:

Well, Lesley while we get to it that is the one test we haven't talked about which is the carbohydrate deficient transferrin as that has a sensitivity of up to 90% of picking up heavy alcohol misuse and a specificity of about 85%.

DR. LESLEY LUNDT:

Now, you mentioned that it was expensive. How much we were talking here?

DR. DAVID SPEIGEL:

I think we are told about \$20 per assay to check this out where basic liver function tests and GGT are in the dollar ranges. So, it's definitely more expensive and I am using it on as many patients that come into our hospital with alcohol misuse, you are probably talking about a lot more money.

DR. LESLEY LUNDT:

So, what's the best as we have been talking about a kind of acute abuse? What is the best test to determine if the patient has relapse so they have been sober and now they just started drinking again?

DR. DAVID SPEIGEL:

Another super question, Dr. Lundt and let me tell you how this will work. Okay, the CDT will take only about one to two weeks to elevate with greater than five standard drinks. So, as a result, say a patient has been abstinent for two months or three months from alcohol and then they only start drinking one week. Afterwards, the CDT is going to pick this up with possibly within one week and as a result the relapse sensitivity for CDT is high as 76%. You want to compare that to a GGT or the other LFTs what we are talking about again possibly anywhere up to four to six weeks of heavy drinking. So, well that may be a better test, the liver function test and GGT may be a better test to pick up risk for alcohol withdrawal in terms of actual relapse sensitivity, the CDT is going to be the most efficient test.

DR. LESLEY LUNDT:

Now, do we need a patient's consent to order these labs?

DR. DAVID SPEIGEL:

Actually, the only thing I would say is as much as a physician needs a patient consent to order a CBC or routine LFTs, which is generally by patient signing in and they come and give you that consent, that's the same level that you go into need to get any of these test orders.

DR. LESLEY LUNDT:

So, just like any other lab test for anything.

DR. DAVID SPEIGEL:

Yeah, exactly, that's my point. There is no special consent, nothing to sign. There will be just work them up.

DR. LESLEY LUNDT:

Okay, it seems to me if you are working in an ER or Urgent Care kind of setting, you can probably get this on everybody, wouldn't you?

DR. DAVID SPEIGEL:

I do. I mean, when somebody keep in mind i am an psychiatrist, so I mean alcohol and drug abuse are part of my daily living and so as a result anytime I see someone in the ER, I am in the ER here at Eastern Virginia Medical School about three times a week, the physician will only draw blood alcohol and a urine drug screen and without ordering the GGT, the AST, or ALT because we don't have access to the CDT. They are missing a potential risk of the person developing withdrawal in the ER setting.

DR. LESLEY LUNDT:

Hmm, absolutely.

DR. DAVID SPEIGEL:

And certainly I have been known to begin alcohol detox in the ER setting to prevent what you don't want to happen the worst complication of DTs.

DR. LESLEY LUNDT:

Right, and you know any of us that have worked in the emergency room knows that even after you

decide to admit them, it usually takes several hours to make that happen, so if you can start it earlier makes sense.

DR. DAVID SPEIGEL:

Absolutely and even a patients are going to leave ER, safe is to admit them, not going to be admitted for whatever reason. It's not uncommon in the good old days in the 80s and the 90s, we used to stop people add-on "as epoxide or Librium" and so it's not unusual for me to give a patient 75 mg or 100 mg of Librium if they are at some type of risk, but having started showing symptoms yet and just tell them that when they start feeling the symptoms of nausea, vomiting, headache, tachycardia, etc., that they should come back to the ER as soon as possible.

DR. LESLEY LUNDT:

Any resources to help our physician listeners whom what to review this material?

DR. DAVID SPEIGEL:

Yes, actually as I mentioned early I think I have a great article that might help clinicians very much, part of the reason I say it's a great article because I was the lead author. The article is to currentpsychiatry.com so it is a one word currentpsychiatry.com. It's in the September 2008 issue, volume 7, no. 9 and the article is entitled, it's a catchy title because they came up with it "I am sober doc really," best biomarkers for underreported alcohol use and so by the part of the article, I had three other co-authors who I would like to mention now, <_____> who is a resident physician as well as Francis Gill who is resident physician and Diana Reddick who is a third year medical student here at the Eastern Virginia Medical School.

DR. LESLEY LUNDT:

Well, it's something certainly that no matter what our specialty is that we come and contact with more than we probably wish we did. So, I think everybody should read this material.

DR. DAVID SPEIGEL:

Thank you, I appreciate it. They enjoy it.

DR. LESLEY LUNDT:

Thanks so much for being on our show today.

DR. DAVID SPEIGEL:

It is a pleasure. Thank you again, I appreciate your time.

We have been speaking with Dr. David Speigel from Eastern Virginia Medical School about the pros and cons of different biomarkers to detect underreported alcohol use. I am Dr. Lesley Lundt. You are listening to ReachMD, the Channel for Medical Professionals. Please visit our website at www.reachmd.com, which features our entire library through on-demand pod casts or you can call us toll free with your comments and suggestions at 888-639-6157. Thank you for listening.

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