Clinical Chemistry

Diagnostic Accuracy of Plasma Glial Fibrillary Acidic Protein for Differentiating Intracerebral Hemorrhage and Cerebral Ischemia in Patients with Symptoms of Acute Stroke

Bob Barrett: This is the podcast from '*Clinical Chemistry*'. I am Bob Barrett. When a patient is presenting with acute stroke symptoms, there is little time to determine the origins without a scan from large imaging devices like MRI. A test that could be performed prior to hospitalization could assist emergency medical technicians in alerting the hospital that a patient is presenting with either an ischemic stroke or an intracerebral hemorrhage and thus speed up the administration of proper treatment.

Dr. Christian Foerch of the Department of Neurology at the Goethe University in Frankfurt, Germany and colleagues published in the January 2012 issue of '*Clinical Chemistry*' a study of a potential biomarker that may determine if a patient is having an intracerebral hemorrhage.

In their study, Dr. Foerch and his team found that analysis of the biomarker Glial Fibrillary Acidic Protein can make this determination making future point-of-care assays possible. Dr. Foerch is our guest in this podcast. Doctor, what are the major achievements of biomarker research in stroke so far?

Dr. Christian Foerch: Within the last three to four decades I would say many groups went into biomarker research for stroke, but most of the groups stay focused on the ischemic side of the story because if you know most early CT scans and they're inconclusive if the patient has an ischemic stroke. And so of course their research was first focused on identifying biomarkers for ischemic stroke. But unfortunately, so far no biomarker was identified that has an high enough diagnostic accuracy for being useful in the clinical routine.

And the most promising research was done by groups that addressed a panel of biomarkers derived from the ischemic cascade. But, when they did prospective studies, they showed that this is rather easy for the biomarkers to differentiate between strokes and controls, but it's very difficult to distinguish between stroke patients and mimics, and this is actually the reason why so far no biomarker made it into the clinical routine.

Bob Barrett: Tell us doctor what is GFAP?

Dr. Christian Foerch: GFAP, this is Glial Fibrillary Acidic Protein. That's an Intermediate Filament Protein with a molecular weight of about 50-55 kilodalton. It's highly brain-specific. We can find it in astrocytes, and it's a cytoskeletal protein of the astrocytes, which is responsible for cell structure and processes formation. It's not actively secreted from the astrocytes into the intracellular space, but is rather released in case of cellular destruction and structural disintegration of the cells.

Bob Barrett: This is released differently into the blood stream from intracerebral hemorrhage and ischemic stroke. Why is that?

Dr. Christian Foerch: Yeah, that's true. We assume that an instance of a hemorrhage actually, we have a very rapid destruction of the brain tissue due to the rapidly expanding hematoma and this leads to an immediate cellular disintegration of the astrocytes and release of GFAP into serum.

But, in ischemic stroke the necrosis, or signs of necrosis do not occur before 6-12 hours after symptom onset, and so in ischemic stroke, GFAP is released much more delayed and this is actually the case that we have different kinetics of cellular destruction between intracerebral hemorrhage and ischemic stroke and this leads to a different release pattern of GFAP into serum.

Bob Barrett: Let's talk now about the BE FAST Study. What was the main finding of that study?

Dr. Christian Foerch: Yeah, we had about 15 centers in Germany and Switzerland who recruited patients for the BE FAST Study. We included acute stroke patients within 4.5 hours after symptom onset, and all of them had to have a rather severe type of stroke, hemiparesis and at least one cortical sign.

We took blood at hospital at mission and we measured GFAP with a newly developed immunoluminometric ELISA assay, and actually, the main finding of the BE FAST Study was that most of the ischemic stroke patients did not have any measurable GFAPs in their serum. That means when we consider our pathophysiological hypothesis, it's not yet released in this early phase of ischemic stroke.

But, the vast majority of patients with intracerebral hemorrhage, they had clearly elevated GFAP values because the protein was already released due to the very rapid cellular destruction in case of the expanding intracerebral hemorrhage.

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And actually, we also found that this pattern of different release of GFAP was also true for those patients who were included very, very early within the first 60 minutes after symptom onset and we also found that there was a strong correlation between intracerebral hemorrhage volume and the GFAP plasma values.

At the end we had about a sensitivity of 85%, and the specificity of about 96% for differentiating intracerebral hemorrhage and ischemic stroke.

Bob Barrett: So doctor, what might be the clinical implications of these findings?

Dr. Christian Foerch: The main implication might be that in the future, we may be able to develop a GFAP point-of-care test, and we may use this test already in the paramedics, in the pre-hospital phase of acute stroke care where the paramedics might be able to differentiate that our patients with some acute stroke symptom has intracerebral hemorrhage, or has ischemic stroke, and this of course may help to save time in the critical early hours of stroke. This may lead to an optimized triage of acute stroke patients, to stroke units or to hospitals with neurosurgery facilities.

This may also help to identify patients with an acute intracerebral hemorrhage, and if we think of ongoing studies like the INTERACT Trial, we may in the future reduce the blood pressure in patients of intracerebral hemorrhage very rapidly even in the paramedics in the pre-hospital phase in order to limit hematoma expansion and to improve functional outcome of those patients, and we may also, if we have an acute ICH patient who is on warfarin anticoagulation, we may also be able to rapidly reverse the anticoagulation in the pre-hospital phase if we have some positive GFAP result.

So to my point-of-view, these are actually the most impending points that maybe achieved with the GFAP test. It's rather difficult to think that a thrombolysis in ischemic stroke maybe performed based on a GFAP measurement because at this phase, we actually need to be 100% sure that hemorrhage is ruled out before we start thrombolysis in ischemic stroke. And based on our data, of course, this biomarker is not able to perform this as a 100% security.

Bob Barrett: Dr. Christian Foerch is from the Department of Neurology at the Goethe University in Frankfurt, Germany. He has been our guest in this podcast from *'Clinical Chemistry'*. I am Bob Barrett. Thanks for listening!

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