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Exploring Experimental Medicine Studies, the Risk of Thrombosis, & the Impacts of Hypoglycemia

Dr. Anderson:
You're listening to *Diabetes Discourse* on ReachMD. I'm Dr. John Anderson and on this program, we're going to hear from Dr. Simon Heller, a Professor of Clinical Diabetes at the University of Sheffield, and honorary consultant physician with the NHS Foundation Trust in the United Kingdom. Here's Dr. Heller now talking about what we know about the role of severe hypoglycemia in major cardiovascular events in diabetic patients.

Dr. Heller:
So the first important thing to say is that these studies, which have shown the effects of increased risk of thrombosis are, of course, experimental medicine studies and they're designed to look for mechanistic reasons why that might happen. But of course, they can't prove that hypoglycemia can do that. So, if you said to me, well how long do these effects go on for? Studies we've done where we've lowered the glucose to fairly modest levels, to around 45, 50 mg/dL, which is around 2.5 to 3 mM/L. We clamp the glucose by giving people an insulin infusion and giving them a glucose infusion to lower them and then we make those measurements. And we did this with people with type 2 diabetes and then we brought them back a week later and we continued to discover that they still had increased inflammation in their body, and their platelets remained more likely to clot for at least a week. Now, we don't know whether it goes on for longer, that hypothesis is it probably goes away, but of course, what might be happening is repeated episodes of not severe hypoglycemia because these are, we can't clearly make people unconscious or induce severe hypoglycemia in the lab, that would be unethical. So, these glucose levels may accumulate, and therefore in somebody we mustn't forget that people with diabetes are already at increased risk, this might accumulate and then precipitate, an acute myocardial infarction or possibly, a stroke. So, that's the hypothesis.

We can't do a randomized control trial, clearly. But we know, for example, that smoking can cause lung cancer. There's never been a trial randomizing people one to the other, but people have looked at, the epidemiology and come to the conclusion that there are things which might be proof, or very strong suggestion that this is hypoglycemia. So, in smoking, we know that if you smoke more, you're more likely to get lung cancer. And so that's important. Importantly, the smoking comes before somebody gets lung cancer, so these are just examples of what epidemiologists do to try and prove it. And then, if we look at hypoglycemia, there'd been a number of studies where people have shown that increased risk or rates of hypoglycemia are more likely to have an adverse cardiovascular event. And number of studies, not all, have shown that the hypoglycemia comes before the increased risk. So, that's an example of evidence which has accumulated over the last ten, twenty years to say, you know, I think there is something in this but it's almost certainly multi-factorial.

And one of the things we must also remember that some people have said, well, it may not be the hypoglycemia, which is responsible for the death. If you're very old and frail, you're much more likely to get hypoglycemia when you're treated and maybe you're more likely to die. We call that confounding by association. It shows that it's not a causal, it's an association. And in my view, it's probably a bit of both, but nevertheless, either way you cut it, hypoglycemia is obviously not a good thing.

Dr. John Anderson:
That was Professor Simon Heller talking about what we know about the role of severe hypoglycemia in major cardiovascular events in diabetic patients. For ReachMD, I'm Dr. John Anderson. To revisit any part of this discussion and to access other episodes in this series, visit ReachMD.com/Diabetes-Discourse, where you can Be Part of the Knowledge. Thanks for listening.