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Neonatal Stroke: More Common Than We Know?

### NEONATAL STROKE

Stroke has been increasingly recognized in children in recent years. Neonatal stroke in particular occurs at a much higher rate than in older children. What are the risk factors of neonatal stroke, how is it diagnosed, and what are the recommendations for managing stroke in newborns.

You are listening to ReachMD XM 157, the channel for medical professionals. Welcome to the clinicians roundtable. I am your host, Dr. Jennifer Shu, practicing general pediatrician and author. My guest is Dr. E. Steve Roach, Professor of Pediatrics and Neurology at the Ohio State University College of Medicine and Chief of Neurology at Nationwide Children's Hospital in Columbus, Ohio.

#### DR. JENNIFER SHU:

Welcome Dr. Roach. Dr. Roach you are the lead author of a New American Heart Association scientific statement on managing stroke in infants and children. What was the impetus for publishing this statement now?

#### DR. E. STEVE ROACH

In recent years we have come to realize that this is a major problem and we have gotten away from this idea that stroke just simply does not occur in children and the reason for doing this paper at this point is that we believe that there is a considerable gap between those obviously who study the topic in detail and know the topic and those people who are out there on a day-to-day basis who are then faced with having to take care of these children. So, the impetus for the paper is to try to narrow that gap so that we can put everything down in one place by a group of people who reach a consensus on how to diagnose, how to manage these children, and make it available to anyone who needs it.

#### DR. JENNIFER SHU:

In your paper you mentioned that a large proportion of stroke in children actually occurred in newborns. How do you define newborn or neonatal or perinatal stroke?

#### DR. E. STEVE ROACH

You see it is defined differently in different places, but we basically define neonatal the same as everyone else and this concept of perinatal stroke comes from the recognition that some of these strokes actually occur prior birth and the need therefore to expand our horizon just a little bit. We have good evidence that some strokes occur before birth and in fact some of the children who are born a bit early the stroke may be the cause for precipitating the early delivery as opposed to say the delivery itself causing the stroke.

**DR. JENNIFER SHU:**

Now for the neonatal stroke, would your definition then be in the first 28 days of life or 7 days, how is that defined?

**DR. E. STEVE ROACH**

I tell you it is 28. We argued that point, but I think it is 28 that is what we settled down on the paper.

**DR. JENNIFER SHU:**

Now, let's talk a little bit more about neonatal stroke, how common is it?

**DR. E. STEVE ROACH**

It is much, much more common than we once would have thought. Current evidence suggests that it occurs about once in 4000 live births.

**DR. JENNIFER SHU:**

And would you say that most of those would be of ischemic type or hemorrhagic.

**DR. E. STEVE ROACH**

Mostly ischemic.

**DR. JENNIFER SHU:**

All right.

What kind of risk factors might you see in a neonatal stroke?

**DR. E. STEVE ROACH**

A lot of the children have no identifiable risk factors, and of those who do, there is evidence now that children and their mother's who have some intrinsic coagulopathy have an increased risk of stroke. There is evidence that inflammation of the placenta increases the risk of stroke. Congenital heart disease of course we have long recognized this as a risk of stroke and that is certainly true also in neonates, so those are the main things – coagulopathy, amnionitis, congenital heart disease, and when you start seeing those things in combination, the risk of stroke goes up even further, but a lot of the children still have no identifiable risk.

**DR. JENNIFER SHU:**

Now what if there is some birth trauma without any coagulopathy, is that a risk factor?

**DR. E. STEVE ROACH**

Almost certainly overrated. Most of these children have no difference in their risk factors, normal or traumatic birth than anyone else and it is true, however, that sometimes the stroke gets blamed on the delivery, but there is actually relatively little evidence for that in most children. I am sure there are exceptions, but most of these kids are born just like everyone else and are recognized a few hours after birth when they start having a seizure, but they really do not have a consistent history of birth trauma.

**DR. JENNIFER SHU:**

Are there any medications that the mother might get or the newborn might get or any drugs of abuse that might increase the risk of neonatal stroke?

**DR. E. STEVE ROACH**

Probably, there is not great empiric evidence as to how often that happens, but certainly there are case reports of children having stroke after their mothers took cocaine or other stimulants. There are reports of babies having hemorrhagic tendency in response to mothers taking certain anticonvulsant drugs such as phenytoin or phenobarbital and of course we have been talking about ischemic stroke and of course major hemorrhagic tendency would predispose to hemorrhagic stroke, but certainly there is precedent for drugs taken by mother causing a stroke in babies.

**DR. JENNIFER SHU:**

You mentioned that seizures in the first few hours of life might be one presentation, is that the most common presentation?

**DR. E. STEVE ROACH**

It is. Absolutely.

**DR. JENNIFER SHU:**

Other ways that a stroke might present in the newborn period.

**DR. E. STEVE ROACH**

Sure. Occasionally you will see babies who are just lethargic and not as responsive as usual, do not want to feed as well as usual and that prompts some kind of evaluation and we find the stroke that way. Sometimes we find a stroke actually later even though we think it occurred in the neonatal period. The typical scenario there is a family who bring in a 6- to 8-month-old child and they have noticed that the right arm is not used as much or as consistently or as well as the left arm or something of that sort or that child is slow to develop or whatever and then occasionally even later still as a 3, 4, or 5-year-old child they will come in with epileptic seizures and the evaluation for the seizures will find what is clearly an old prior stroke that when we added all up we conclude this probably occurred during the neonatal period, but I would think the majority of the kids will show up with seizures in the neonatal period.

If you have just joined us, you are listening to the clinicians' roundtable on ReachMD XM 157. I am your host, Dr. Jennifer Shu. Our guest is Dr. E. Steve Roach, Professor of Pediatrics and Neurology at the Ohio State University College of Medicine and Chief of Neurology at Nationwide Children's Hospital in Columbus, Ohio. We are discussing neonatal stroke.

**DR. JENNIFER SHU:**

Let's talk a little bit about the diagnosis in neonatal stroke. How do you look for it, to diagnose it?

**DR. E. STEVE ROACH**

In terms of confirming with a test given that you are dealing with neonates, probably the first thing that is done in most nurseries would be a cranial ultrasound and you can identify the lesion, but often times it is not as clear as to the nature of the lesion as it will be if you do a CT scan or MRI scan, but the first step of course is suspecting the diagnosis, but then in terms of confirming the diagnosis, usually the first test is an ultrasound and then almost always you have to follow that up then with a CT or a MRI scan.

**DR. JENNIFER SHU:**

Are there any places where an MRA or MRV with CT angiogram might be useful?

**DR. E. STEVE ROACH**

We have not got a lot of experience yet in babies with CT angiograms and of course then one increasing concern is trying to limit the amount of radiation. We do with some regularity to MRA/MRV in these children and we did not talk about venous thrombosis, but certainly babies have an increased risk of that as well. So, some of those babies will present with seizures, some of them with different things, but we do MRVs in babies with some regularity, but in terms of just the standard ischemic stroke typically not an MRV, sometimes an MRA though.

**DR. JENNIFER SHU:**

Now this is such a tight time here in the immediate perinatal period and then plus 28 days of life, is it possible to tell the age of the stroke on ultrasound or CT or MRI.

**DR. E. STEVE ROACH**

Not ultrasound to my knowledge. CT occasionally if you add the CT contrast sometimes you will see contrast enhancement of the stroke and we have recognized that that phenomenon does not usually occur for a couple of days, so for example if you have a newborn who begins having seizures at 8 hours of life and you do the CT then you already have contrast enhancement of the abnormality, you can assume that stroke is considerably older than 8 hours and probably couple of days, and given that hypothetical scenario, what that means is that stroke occurred before the delivery. Similarly, there are some MRI parameters that someone who deals with MRI all the time can often give you at least an estimate about how old the stroke is, but not usually with ultrasound.

**DR. JENNIFER SHU:**

When you are saying stroke in such a young age, what is the prognosis, the outcome, any residual effects. Is it better to get stroke as an infant or is it better to get stroke later on in life?

**DR. E. STEVE ROACH**

If you are going to assume the same size of abnormality and so on, it is arguably better to get it early than later because there is enough plasticity of the brain that to some extent anyway you can actually learn test that would have been done by that part of the brain with other parts of the brain. The biggest example of that probably is language. A baby who has a stroke in what would eventually become the language area typically will learn to talk, now their vocabulary may not be as rich as it would have been or they may have word finding difficulties or whatever, but almost always they learn to talk whereas the same abnormality in a 10- or 15-year-old or of course in an adult, you might or might not then regain language function once you developed it so. There is a limit to the plasticity notion, though it is the old idea that if you are a baby you have almost unlimited potential to recover from a stroke or other injury. This simply is true. I mean if you have a large lesion or multiple abnormalities, there is going to be a price to pay for that, so what if you are talking about a small abnormality, the chances of a good functional recovery is pretty good whether you are talking about a neonate or an older child, but it is probably better in the neonate.

**DR. JENNIFER SHU:**

Would you expect any recurrence of the stroke to happen or chronic seizure disorder anything like that?

**DR. E. STEVE ROACH**

Most of the babies do not have another stroke. It depends a bit on why they have the stroke to begin with and certainly if they have congenital heart disease that has not been fixed that would represent an ongoing stroke risk for additional strokes. The average typical neonate with the stroke who probably had it for reasons that we cannot identify almost never do have a second stroke in those kids. In that sense, the prognosis is excellent. The second part of your question about seizures, while most of these kids present because they had a seizure in the neonatal period or even in the nursery, it is relatively unusual for that to persist as epilepsy. I think the current

estimate of the neonates who have a stroke probably about 15% of them eventually will develop chronic epilepsy, most of the time the seizures are just in response to the acute injury and those seizures almost always go away, but then about 15% of the time, those children will resume having seizures later.

**DR. JENNIFER SHU:**

Let's talk a little bit about the management of acute stroke. Obviously, there is supportive care such as oxygen and fluids, but what about any type of thrombolytic or other pharmacologic therapy, is that indicated in newborns?

**DR. E. STEVE ROACH**

Well the problem is we have no data. Certainly, the thrombolytic agents are not approved in the United States for children of any age let alone neonates and we basically in this paper wrestled with that issue a great deal and decided that the appropriate place to use thrombolytic agents in a child or particularly in a neonate was in the setting of a clinical trial. We are recommending that they not be used in neonates except in a very controlled setting like that. We do not know if the risk is the same. Part of the problem of course is how do you ascertain when the stroke occurred. Even in adults, the usual recommendation is do not use a thrombolytic for an ischemic stroke after about 3 hours because the rate of hemorrhage goes way up. Well, if we are dealing with a 10-hour-old baby whose stroke might have occurred even before they are born, obviously we have a problem and that is aside from just the fact that you know there are so few times it has actually been used. So, we are discouraging thrombolytics, although it would be appropriate to do more research on it.

**DR. JENNIFER SHU:**

I would like to thank our guest, Dr. E. Steve Roach. We have been discussing neonatal stroke. I am Dr. Jennifer Shu.

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