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Delivery of an ICH Care Bundle: Illustrative Case

Announcer:
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Dr. Parry-Jones:
So I'll just go through a case briefly to highlight how we take this approach with a specific patient and also some of the uncertainties that can creep in.

So this is a fairly typical case, a 61-year-old man with no pre-stroke disability, type 2 diabetes, hypertension, a previous TIA, and atrial fibrillation. He's been anticoagulated with apixaban. And he's found with right-sided weakness and drowsiness at 9 a.m., and brought into hospital, which is an hour prior to you seeing him. He's got a GCS of 12, right-sided neglect and hemiplegia, and an NIHSS score of 21, which is a moderate to severe stroke. And he's very hypertensive.

So this scan shows you the appearances when he arrives in hospital. So there's a deep bleed with intraventricular extension, there's a suggestion of some early hydrocephalus, and you can see evidence of small vessel disease, which is likely the underlying etiology of his bleed. And we've calculated the volume for years, 20 mL, using the ABC/2.

And then it gets a little bit more difficult because he's unaccompanied, and when he took his last apixaban dose is not known. So he can't tell you. You call the patient's son, he tells you that he lives alone, looks after his own medication. No one's seen him since 11 o'clock the day before, which is happens quite commonly with stroke patients, you often get this kind of story. He seems to have slept in his bed, got up and got dressed, it sort of makes you wonder whether he might have been okay when he first woke up. But the son says he has quite poor compliance and he'd recently been given a blister pack to try and help with that. But that wasn't brought in to hospital, so you don't know if he's taken it. Some lab results have come back, so you know he's got normal renal function, his estimated GFR is over 90. So it's now 11 a.m., and first thing is you're unsure when his stroke began. So it could be 2 hours ago, it could have been 24 hours ago.

So what actually happened in this case was there was a call to hematology, they advise to give PCC which was done. We don't have andexanet alfa currently available in the UK. And BP lowering was commenced shortly afterwards. He was discussed with neurosurgery because of his signs of hydrocephalus. And because of his GCS, was transferred to high-dependency unit, had an arterial line for blood pressure management, and went back to his local hospital later.

So just to highlight a couple of the areas of uncertainty here. So we didn't know when he last took an anticoagulant. So how would that matter? So this is a pharmacokinetic curve showing you rivaroxaban and apixaban. If you just focus on the yellow and the red, that's apixaban. So if he had taken it as prescribed, then the levels in his blood would have been around 120, as you can see from these lines here. If he'd missed the morning dose, it would have been about 50, so much lower. And if he actually hadn't taken it for 2 days, then it'd be almost 0, it'd be down to 10. So we've got this considerable band of uncertainty as to how anticoagulated this patient is. And we're often left with dealing with this and don't know what to do.

Two other areas that are important to think about is what's this gentleman's risk of the hematoma expanding. And 2 key factors are time from onset and the volume. So we have the volume, we know that that's 20 mL, and you can see from this curve here from a statistical model, in an anticoagulated patients, so probably underestimated a bit, it's around 25%, his risk of hematoma expansion. If we look at time, he could be 2 to 24 hours here, so there's a wide band, but still it's quite high, regardless. So still, it's going up to about 25%. So you might argue in this case, that actually the risk is quite high. If he bleeds again, then he's going to get a lot worse, so therefore, he was treated.

So just to summarize, approximately 10 to 20% of ICHs occur on anticoagulants. Delays increase the risk of expansion, so you need to decide really quickly whether or not you're going to treat these patients, you need to get on with it. Two key times to consider in thinking about that was when was the last anticoagulant taken? And what was the time since ICH onset? And then a couple of other key patient factors are how big is the hemorrhage? And also do they have a very poor prognosis before you're thinking about it? Is this a case that needs to be palliated and isn't going to improve with the reversal?

So thank you.

Dr. Gibler:
Excellent. Dr. Parry-Jones, that was well done. Do we have questions?

Dr. Mockel:
Yeah. Thank you very much. I love your approach using care bundles. And what is the role of the emergency physicians in developing these panels? And what barriers do you experience to implement it?

Dr. Parry-Jones:
Well, I think in my experience, there's a lot of variety in terms of who looks after these patients. So at our center, they're met at the door by the stroke team. We get support from the emergency physicians if they're very unwell and need critical care input. And we also work with the emergency care team in terms of thinking about anticoagulant reversal, because obviously this is only one group of patients that need it. So for example, when we brought PCC into the emergency department, we did that in tandem with the emergency medicine team to make sure that it was improving care for all of their patients as well.

Dr. Body:
Yeah, Adrian, thanks very much. There was a recent trial published, INTERACT3, in July. I was wondering if you could say a few words on that and how it has changed your perspective on bundling of care?

Dr. Parry-Jones:
Yeah, so INTERACT3 has added quite high-level evidence for care bundles in intracerebral hemorrhage. So it was a cluster randomized trial, it was around 8,000 patients in 144 hospitals in 9 low- to middle-income countries and 1 high-income country. So what they found in INTERACT3 was implementing a care bundle was associated with reduction in deaths and a reduction in disability at 6 months. And the care bundle is very similar to the one I described to you. So it involves anticoagulant reversal and blood pressure lowering, but it also included control of glucose and control of temperature over the first 7 days. So it certainly lends a much higher level evidence to this approach.

Dr. Gibler:
It's very interesting in the UK because of the NICE committee, and if you could explain to people what that is. Actually andexanet alfa, is indicated for GI bleeding, where it's not currently for ICH. Can you talk about ANNEXA-I as it relates to its being published here in the next month or so?

Dr. Parry-Jones:
Yeah.

Dr. Gibler:
And how that could potentially impact the NICE rules, if you would?

Dr. Parry-Jones:
Yeah. Okay. So those of you not familiar with it, NICE is a organization in the UK that looks at the value for money for healthcare interventions and makes recommendations across the National Health Service. So there's often a threshold

around value for money that they look at. And I think when andexanet alfa was looked at initially, it was felt there was some uncertainty around that. I think with the ANNEXA-I trial being published and being presented, that should change things. So it's, as you've heard on the previous talk, it's been stopped due to meeting its efficacy outcome. So if it's better at reducing hematoma expansion, then it's quite likely that it's going to improve outcomes and deliver better value of money from what we're currently doing now, which is giving PCC to

these patients.

Dr. Gibler:
Excellent. I wanted to ask a question, how many of you all work in environments that are not academic medical centers or big hospitals? You work more in rural, smaller hospitals? How does that wrap into your care bundles? Because I, you know, for this to work, obviously, if you, and Dr. Sehgal will talk about that as relates to GI bleeding, how does that work in care bundling for ICH?

Dr. Parry-Jones:
Well, I can talk about experience in my region. So stroke care is centralized so that suspected stroke patients go to 1 of 3 hospitals, and we have 9 emergency departments in the region. What we've agreed as a region is that if a patient presents to another hospital that's not a stroke center, and that they're anticoagulated with suspected stroke symptoms, they should have their scan there. If the scan confirms hemorrhage, then the anticoagulant is reversed. Then they're transferred to the stroke unit for further care. So we deliver the blood pressure lowering, consideration of neurosurgery, etc., when they get there. But our view was that placing these patients in an ambulance when they are extremely high risk of the hematoma expanding is not the right thing to do and that you should be reversing as quickly as possible to maximize the benefit.

Dr. Gibler:
Excellent. Dr. Parry-Jones, thank you very much. We very much appreciate your making the trip for this meeting.

Announcer:
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