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Progressing Towards Post-ERCP Pancreatitis Prevention

Dr. Buch:

Welcome to *GI Insights* on ReachMD. I'm your host, Dr. Peter Buch, and joining us today to discuss strategies for preventing post-ERCP pancreatitis is Dr. Prabhleen Chahal. Dr. Chahal is the Program Director for the Advanced Endoscopy Fellowship in the Department of Gastroenterology at Cleveland Clinic.

Welcome to the program, Dr. Chahal.

Dr. Chahal:

Thank you so much, Dr. Buch, for having me.

Dr. Buch:

So let's jump right in, Dr. Chahal. What are the patient-related, procedure-related, and operator-related risk factors for developing post-ERCP pancreatitis?

Dr. Chahal:

We are starting off with an excellent question, and of course, dealing with post-ERCP pancreatitis, which is the most dreaded complication of this procedure. As we know, the incidence, it varies anywhere from four to 10 percent in what we call as average risk patient population, but this risk can go as high as up to 15 percent in those whom we considered high risk for developing post-ERCP pancreatitis. And you have so astutely categorized them into patient-related, procedure-related risk factors, so this is how we like to look at it. When we look at the patient-related risk factors, we are looking at somebody young, female—by young, I mean less than 50 years of age—somebody who has had a history of prior pancreatitis, history of recurrent pancreatitis, somebody who is carrying around the diagnosis of possible Sphincter of Oddi dysfunction. So those are the patients that we are careful about because studies have shown they carry high risk for developing post-ERCP pancreatitis.

Now the procedure-related risk factors include multiple or repeated cannulations of pancreatic duct, either inadvertent most of the time, or sometimes we are working on the pancreatic duct for pancreatic stricture management; inadvertent contrast injections into the pancreatic duct—by that I mean extensive contrast injection, what we call as acinarization, where you're able to see the side branches, so there's a significant contrast injection—any heat that gets delivered to the pancreatic sphincter like when we are doing pancreatic sphincterotomy; difficult cannulation—by that I mean we have spent multiple attempts trying to get into the bile duct, but we are repeatedly getting into the pancreatic duct—or failed cannulation attempts lasting more than six minutes as per the definition, leading to what we call as a precut sphincterotomy technique. The precut itself, studies have shown it's not an independent risk factor. I think it's all the prolonged effort that precedes the difficult cannulation precut sphincterotomy that increases the risk of post-ERCP pancreatitis.

And then, of course, the operator. I think there are a lot of studies that have shown it's important to have proper training while doing this procedure. ASGE recommends one year of training with a minimum of 200 ERCPs under the belt. If we look at our partners across the pond, ESGE recommends 300 procedures, and somebody who graduates with more than 80 percent success rate in cannulating the bile duct. So I think the competence of the operator is also critical in leading to safe and successful execution of this procedure.

Dr. Buch:

Thank you. And just a word for our primary care listeners. Is there such a thing as a diagnostic ERCP?

Dr. Chahal:

Again, excellent question. I think this is where it's very important that we look very closely at the indication of this procedure because this is not a risk-free procedure. So this is not a diagnostic procedure. I think in an era where we have excellent noninvasive imaging, like MRI, the technology has improved so much where it's important to get the noninvasive imaging first. And if there's still doubt, consider endoscopic ultrasound before embarking on ERCP. ERCP is only for therapeutic purposes.

Dr. Buch:

Perfect. Well stated. So when utilizing prophylactic NSAIDs, is the timing before or after the ERCP important?

Dr. Chahal:

Let me start by saying, before or after timing is critical to some extent yes, but I would say if it was yes and no, always go for yes. I would rather give an NSAID if you remember during the procedure, even immediately after concluding the procedure, so do give rectal nonsteroids instead of not giving it at all.

But what does the data show? And what does the Society guidelines tell us? I think ASGE doesn't outline outrightly specify whether before or after. They say periprocedurally. But if you look at ESGE, they categorically state before ERCP. And the reason behind that might be it takes about 30 minutes to have a peak plasma concentration after rectal nonsteroidal administration, so it's good to have that on board, especially if you think that the patient might be higher risk for developing post-ERCP pancreatitis.

And there is data that also support giving the rectal nonsteroidals before the procedure. There were multiple studies, and then the largest 2,600 single head-to-head study that looked at randomly assigning nonsteroidal before or after the ERCP, and they found that the risk of post-ERCP pancreatitis was higher in the cohort that received rectal nonsteroidal after the procedure.

Dr. Buch:

Thank you very much for the information. Is there an increased risk of post-sphincterotomy bleeding when utilizing prophylactic NSAIDs?

Dr. Chahal:

I think again excellent question. But we can be all rest assured, there is no data to support increased risk of post-sphincterotomy bleeding if we use nonsteroidals. I think we have a lot of studies looking at that, including several meta-analyses. So if there is no contraindication to nonsteroidal—by that I mean sometimes some patients can have history of anaphylaxis from nonsteroidal or history of Stevens-Johnson syndrome or pregnant, women more than 30 weeks out in their pregnancy—so you should consider avoiding NSAIDs in them, but bleeding is not a risk factor and should not prevent us from using this.

Dr. Buch:

And, Dr. Chahal, when are pancreatic duct stents important to prevent post-ERCP pancreatitis? And should they be long or short?

Dr. Chahal:

So pancreatic stent, I think they are the cornerstone in preventing post-ERCP pancreatitis. Again, these are several studies, multiple RCTs, multiple systematic review meta-analyses. This is endorsed by both ASGE and ESGE. And I think the mechanism behind that is because when we are performing ERCP, anything that creates trauma to the pancreatic sphincter or pancreatic orifice, either by heat when we are using sphincterotomy or mechanical when we are doing balloon sphincteroplasty or hydrostatic when we are injecting a lot of contrast in there, or sometimes infection—so all these factors that affect the outflow of the pancreatic secretions or create edema at the pancreatic orifice can increase the risk. So that's the postulated mechanism of post-ERCP pancreatitis. So by placing the stent across the pancreatic sphincter, we are alleviating those factors, we are maintaining the flow of the pancreatic secretions, and this is how we think that pancreatic stents help.

Now the question is short versus long, and this is again, when we look at the Society guidelines, ASGE does not categorically recommend stent length, but if we look at the ESGE guideline, they do state that short five French pancreatic stent without internal flap is superior than longer three French pancreatic stent. And I also had the honor of leading the randomized controlled trial, and this is exactly what we found. When we're using pancreatic stent, prefer the one without internal flap but one with external flap or a pigtail so they don't migrate inside. Why short? Because I think you want the stent to remain in the head of the pancreas. You don't want them to be pushing against the genu. And then the three French stent, the longer, I think it takes a little bit more manipulation to get the stents across. And then the spontaneous dislodgement rate of longer stent is also less than the shorter five French, which means that patients will need to come back for a repeat endoscopy for stent removal, which again, is not a cost-

effective procedure.

Dr. Buch:

For those just tuning in, you're listening to *GI Insights* on ReachMD. I'm Dr. Peter Buch, and I'm speaking with Dr. Chahal about preventing post-ERCP pancreatitis.

And continuing our discussion, please explain the role of aggressive hydration in preventing post-ERCP pancreatitis and with the latest information, not too aggressive hydration.

Dr. Chahal:

Yes. So this is the third pillar in preventing post-ERCP pancreatitis. And I think in the last decade we have seen tremendous progress in this particular area, and we have gained a lot of knowledge starting from what type of fluid we should be using, and the studies have shown lactated Ringer is superior—again, endorsed by ASGE and ESGE. And we can discuss for whatever information we have why LR is superior than a normal saline. And then more recently, we have significant data and multiple RCTs, recent WATERFALL study that was published, which clearly shows hydration is paramount in order to reduce the risk of post-ERCP pancreatitis.

So when we talk about hydration, both Societies, they recommend aggressive hydration, which by aggressive they mean you start lactated Ringer three milliliters per kilogram per hour during the RCP; then you give them 20 milliliters per kilogram bolus after the procedure; and then you continue at three milliliters per kilogram per hour rate for about eight hours; but that means that patient will need to be hospitalized overnight to get that kind of a hydration. So obviously, this is probably not a practical solution for everybody, but in patients who we think they have high risk for developing post-ERCP pancreatitis, we should seriously consider the hydration.

Now the question is, can we do this aggressive hydration in all the patients? Well, the answer to that is no because we have to be mindful about the underlying comorbidities and decide on how much hydration that we can provide in the periprocedural area. In my personal practice, based on the patient comorbidity, I can do anywhere from 1.5 to up to three liters. And of course, based on the risk factor for the patient, you determine whether it's safer to admit them overnight and continue hydration than discharging them home.

There are several studies, which have shown that the aggressive, they led to lower rates of post-ERCP pancreatitis. The adverse events were comparable, but then again there was some concern of overhydration or fluid over-related complications in several RCTs despite excluding the patients who we think were at increased risk for complications. So be cautious and mindful on the cohort that we discussed about the aggressive hydration.

Dr. Buch:

I'm going to give you the opportunity of just briefly telling us why we should be using lactated Ringer's as opposed to normal saline.

Dr. Chahal:

I think the reason people think that lactated Ringer outperforms than normal saline in preventing post-ERCP pancreatitis is because of a slightly higher pH, and thus reducing the risk of metabolic acidosis. Second is lactated Ringer itself has been shown to have an anti-inflammatory component to this, which reduces. So when pancreatitis happens, substances like nonsteroidals that act as an antagonist to phospholipase A2 or prevent the proinflammatory cascade, that's how that reduces the risk of post-ERCP pancreatitis, and LR seems to exert some sort of an effect, anti-inflammatory effect as well.

Dr. Buch:

Thank you. So if you can just share with us any new data with regard to employing both NSAIDs and pancreatic duct stents to reduce the risk of pancreatitis after an ERCP.

Dr. Chahal:

Yes. I'm glad you asked that question, Dr. Buch, because just hot off the press a week ago we saw a publication of this landmark study in *Lancet* journal. This was a randomized noninferiority trial where they randomized close to 2,000 patients. One group was assigned to just indomethacin alone, and then the second group was assigned to indomethacin and the pancreatic stent. So what they found in the result was that the group that received combination—that is indomethacin and prophylactic pancreatic stent—they had a lower incidence of post-ERCP pancreatitis, and they found that the cohort that was deemed to be high risk for developing post-ERCP pancreatitis benefited the most by getting both rectal NSAIDs and pancreatic stent. So if you, during ERCP, get into the pancreatic duct, I would highly recommend leaving a pancreatic stent in. Even if you get a wire

in there once or even if you inject it there once, once the PD is cannulated or injected, always err on the side of the leaving the pancreatic stent. And I think this also comes from the data that out of all the patients who could have benefited from pancreatic stent, only 10 percent of them end up getting stent, so I think we clearly are underutilizing this safety net.

Dr. Buch:

This was an excellent review of preventing post-ERCP pancreatitis, and I want to thank my guest, Dr. Chahal, for sharing her insights. Dr. Chahal, thanks so very much for joining us today.

Dr. Chahal:

Thank you so much for having me.

Dr. Buch:

For ReachMD, I'm Dr. Peter Buch. To access this and other episodes in this series, visit reachmd.com/GIInsights, where you can Be Part of the Knowledge. Thanks for listening, and looking forward to learning with you next time.