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Extraesophageal GERD: Fact or Fiction?

You are listening to ReachMD, The Channel For Medical Professionals. Welcome to GI Insights where we cover the latest clinical issues, trends, and technologies in gastroenterological practice. GI Insights is brought to you by AGA Institute and sponsored by Takeda Pharmaceuticals North America. Your host for GI Insights is Professor of Medicine at University of Illinois, Chicago Dr. Jay Goldstein. Dr. Goldstein has served as an independent contractor, consultant, and is a member on the speaker's bureau for Takeda Pharmaceuticals North America Incorporated. He has also been the recipient of funding for research grants and educational grants from Takeda Pharmaceuticals North America Incorporated. A great deal of information has come in to the press, press and medical literature regarding the extraesophageal manifestations of GERD. This is commonly referred to and discussed in symposia meetings and in medical discussion. Joining us to discuss extraesophageal GERD fact or fiction is Dr. John Inadomi Dean M. Craig endowed chair in gastrointestinal medicine at the University of California in San Francisco.

**DR. JAY GOLDSTEIN:**

Welcome John.

**DR. JOHN INADOMI:**

Thanks so much Jay, glad to be here.

**DR. JAY GOLDSTEIN:**

What is GERD and what constitutes extraesophageal manifestations of GERD?

**DR. JOHN INADOMI:**

Well there is a recent AGA summary that actually defined GERD for us which is quite convenient and it is a condition which develops when the reflux of stomach contents causes troublesome symptoms or complications. Now this is a rather lengthy definition, but it basically reflects the fact that we want to define GERD based on patient symptoms and not specifically physiology.

**DR. JAY GOLDSTEIN:**

Well that makes sense. So if that's the case for GERD what is the extraesophageal manifestations of GERD or what is that disease state?

**DR. JOHN INADOMI:**

Well certainly the typical esophageal GERD symptoms are heartburn and acid regurgitation, but there is a variety of symptoms and possibly diseases that are caused by this particular process that affects the lungs, the teeth, the larynx, and a variety of other things and that's what encompasses extraesophageal GERD.

**DR. JAY GOLDSTEIN:**

Do you have to have GERD with heartburn before you can develop extraesophageal manifestations, do they run hand in hand. What is the actual link between these?

**DR. JOHN INADOMI:**

Well you know, its an interesting point you bring up Jay. We are sure that these things are associated mainly based on epidemiological evidence showing that let's say people with reflux actually do have more of these symptoms and also people who have these extraesophageal symptoms actually do have more reflux disease. So there clearly is an association, but the tightness of this association isn't as great as we once thought.

**DR. JAY GOLDSTEIN:**

Well what are some of the symptoms that patients would actually come in with if they were manifesting extraesophageal manifestations?

**DR. JOHN INADOMI:**

Well there is a variety, I will give you a list of them. One is chest pain which can really mimic cardiac disease. There is a variety of lung symptoms such as chronic cough or asthma or any kind of reactive airway disease. There is laryngeal types of symptoms, either sore throat or hoarseness, maybe even dental caries.

**DR. JAY GOLDSTEIN:**

I have a fair number of referrals myself from our ENT colleagues. Many times they send to me patients with hoarseness or chronic cough or one of these other type symptoms. In the absence of typical heartburn, should I really be scoping them, looking at them, evaluating them, treating them empirically, are they likely really to have extraesophageal manifestations of GERD?

**DR. JOHN INADOMI:**

Well this is a great topic Jay and in fact we do have this recent AGA guideline upon which we can draw some of the evidence. In terms of your specific question, patient actually lacks symptoms of either heartburn or acid regurgitation. Its actually very unlikely that this

extraesophageal symptoms can be attributed to GERD with the one exception of chest pain.

**DR. JAY GOLDSTEIN:**

So its unlikely that they are going to do it, have these symptoms. Many times they have been placed on proton-pump inhibitors and have failed, does that support your position?

**DR. JOHN INADOMI:**

There is a lot of evidence and a lot of studies trying to look at therapies for GERD and whether or not these can actually reduce symptoms of extraesophageal GERD and the one symptom state that is actually pretty well established as being responsive to GERD therapy is the noncardiac chest pain. We call it now the reflux chest pain syndrome and in that entity certainly it appears that use of double dose PPIs can alleviate the symptoms of chest pain in several randomized trials. The problem is that in other symptoms we talked about, there are very little in the way of good studies or studies that will illustrate any kind of benefit with acid reduction therapy unless those patients have concomitant esophageal reflux symptoms such as heartburn or regurgitation.

**DR. JAY GOLDSTEIN:**

Well lets go to that entity of chest pain that you are describing. They come into your office and they are basically complaining of it as chest pain, do you evaluate them, do you, you know, assuming that its nonexertional chest pain and low risk for cardiac event. Do you go ahead and put them straight on double-dose PPIs and empiric therapy, or what do you do?

**DR. JOHN INADOMI:**

Well the short answer is yes Jay. I think that the one thing we do have to keep in mind and you have alluded to this is that this can be indistinguishable from cardiac chest pain. So the first thing you really do is to ensure that whoever has referred them to you has adequately ruled out atherosclerotic disease and that the symptoms are not actually cardiac in origin. Once that happens, I agree with you that first therapy or the first step in management is an empiric trial of double-dose proton-pump inhibitors mainly because of fact that the various studies have shown in this particular patient group that a substantial number of these people can have alleviation of their symptoms and this is before other diagnostic tests embarked upon.

**DR. JAY GOLDSTEIN:**

Double-dose being your first choice. You don't go to single dose.

**DR. JOHN INADOMI:**

Well the main reason is because the fact that we are using this as a trial. It is almost a diagnostic test and there actually are several studies using a PPI test as its actually called as a way of diagnosing whether or not chest pain is in fact of GERD etiology and the reason why we use double dose is because if we use single dose and it didn't respond perhaps we would need to go up to a double dose and that's the reason why we kind of start them off with the highest reasonable dose possible and then of course if you once your symptoms are controlled, then we can try to back down if they are able to.

**DR. JAY GOLDSTEIN:**

What should our listeners be telling their patients if they start them on double dose, how soon should they expect a response and what kind of trial length do you give these patients?

**DR. JOHN INADOMI:**

Well the usual recommendation is for 2 months and the reason for this is because unlike typical reflux symptoms such as heartburn, it often takes a prolonged period of time for these extraesophageal symptoms to respond to acid reduction therapy. For that reasons, it's a prolonged empiric trial for 2 months. Once the end of that 2 months comes up, you know there is fewer data to show to clearly guide what we do. Most people who say that their symptoms are relieved on double-dose PPI, then we could try stepping down and then use the minimal dose necessary to achieve our therapeutic goal which in this case is symptom control.

**DR. JAY GOLDSTEIN:**

If you are just tuning in, you are listening to GI Insights on ReachMD Radio on XM160, The Channel For Medical Professionals. I am your host, Dr. Jay Goldstein, and joining me to discuss extraesophageal manifestations of GERD, fact or fiction is Dr. John Inadomi Dean M. Craig endowed chair in gastrointestinal medicine at the University of California in San Francisco.

Well John lets turn our attention to more traditional ENT findings because we as gastroenterologist often interact with these individuals. Many times they will send me patients or send our colleagues patients after they have failed sometimes double dose or single dose trial of PPIs or non-chest pain type symptoms such as hoarseness or cough. What should we be doing with these patients, generally they've already looked down their throat and have seen some "redness" in their laryngeal area. What do we do with those patients?

**DR. JOHN INADOMI:**

A practical matter Jay is that we see these people all the time, but we also have to realize that in addition to reflux, there is a variety of other etiologies for this kind of redness in the vocal cords including things like postnasal drip, overuse of the voice, there is also neuropathies that occur and are being more and more revealed in the literature. I think overall thought that most of the data and the experts include in the guidelines will agree that in the absence of concomitant heartburn or acid regurgitation, it is very unlikely that empiric therapy with PPIs will alleviate the symptoms associated with laryngitis or symptoms of laryngitis and generally the guidelines would not recommend undergoing any type of empiric therapy for these individuals.

**DR. JAY GOLDSTEIN:**

Well these are the patients who have tried empiric therapy, do you go ahead if they failed, if you think that this is in the realm of possibility, do you do endoscopy on these patients. Do you do pH studies on these patients, 24-hour pH studies. Do you do motility studies looking for other causes. Do you purse it or do you really stick to your guns?

**DR. JOHN INADOMI:**

Again this is an excellent question mainly because there is a guideline that is out that actually does kind of support a fact where we would sit back and just do base our management on empirical data, but from a practical matter I have to say that I would actually perform the ambulatory esophageal pH monitoring and the reason for that is because it is a much more sensitive test than endoscopy for detecting reflux disease. Keep in mind that is not a perfect test, but certainly if there is evidence of abnormal esophageal acid exposure, then I think therapy is indicated in that case.

**DR. JAY GOLDSTEIN:**

I am kind of glad you said that because that's what I would do to, the question I have for you now is, do you do it on the PPI or off the PPI?

**DR. JOHN INADOMI:**

This is another great question. If you have ask experts from actually around the world, you will get a mixed response and there is a variety of rationale, certainly if you do it off PPI what you are looking for is whether or not the patient does in fact have baseline abnormal acid exposure given the diagnosis of GERD. You do it while on PPI what you are really doing is trying to figure out whether that residual symptoms despite PPI are actually due to excess of acid. The general recommendation at this point, however, is to perform the ambulatory pH test off of PPI and again that's just to ensure that what you are doing with is a patient who does have baseline abnormal acid exposure or at least again the have physiology set up for gastroesophageal reflux disease.

**DR. JAY GOLDSTEIN:**

When you go to talk to your ENT colleagues and they really are pushing this issue, what do you tell them about the redness means that they see, why don't we expand on that?

**DR. JOHN INADOMI:**

I think we have to go back and say that there is a variety of causes of this redness and reflux certainly can be one of them, but it is not the only one and I think that we have to at some point realize that after empiric PPI trials and after ambulatory esophageal pH measurements, there is very little to be gained by doing more testing and I specifically mean upper endoscopy or lets say even motility studies and again that's in the absence of a traditional esophageal reflux symptoms such as heartburn or acid regurgitation. Now certainly there could be an element of benefit from reassurance, but from most of the clinical trials that have been published, there really isn't much of a rationale for pursuing additional diagnostic testing beyond that.

**DR. JAY GOLDSTEIN:**

What else do you tell your patients beyond a trial of PPIs and appropriate use, what guidelines do you tell your patients or your referring physicians that may help them better treat patients with reflux and reflux-like symptoms?

**DR. JOHN INADOMI:**

Well you know I think that again we are facing a lot of problems with the fact that GERD doesn't have a perfect diagnostic test. It is

really difficult to define a gold standard for GERD, having said that, most of this is symptom driven, so I think we can be pretty well assured that as long as we control symptoms that we are doing the right thing to our patient. You know this is not a talk about Barrett's esophagus and esophageal carcinoma, we could spend another hour on that, but barring that issue again I think that symptom relief is the main goal of therapy. So besides that I talk to my PCPs and my patients that you know once we have a patient relieved on symptoms to try to step down to the lowest dose that's effective for managing their symptoms and also that if the symptoms continue, once the empiric trial fails and perhaps after doing esophageal ambulatory measurement if those are all normal, then reassurance and try to look for other etiologies of these symptoms because it is very unlikely that these will be reflux in origin.

**DR. JAY GOLDSTEIN:**

What in your opinion is the most common cause of PPI failure in acid-related disorders?

**DR. JOHN INADOMI:**

The issue with PPIs is they are very good drugs and especially a double dose PPI. Once you are on double-dose PPI it is very unlikely that residual symptoms are due to acid reflux.

**DR. JAY GOLDSTEIN:**

I'd like to thank my guest from the University of California in San Francisco Dr. John Inadomi. Dr. Inadomi thank you very much for being our guest on this week's GI Insights.

**DR. JOHN INADOMI:**

Thanks a lot Jay.

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