Airing Pain Programme 125: Opioid-Induced Constipation

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Looking at the side effects of opioids for chronic pain management

While opioids are seen as an effective treatment method for acute pain, there is an increasing debate on the efficacy of opioids when treating chronic pain conditions. One of the most common side effects of long-term opioid usage is constipation. Conditions like irritable bowel syndrome are more common in people who are living with chronic pain conditions, so better understanding of the connection between opioids and constipation is key for medical professionals currently working with chronic pain patients.

Following on from **Airing Pain** *123, this edition sees Paul Evans speaks to Dr Maria Eugenicos, who is a gastroenterologist at the University of Edinburgh. Dr Eugenicos starts by outlining the different conditions that are treated at her gastro-intestinal clinic and how these conditions can present. Dr Eugenicos then discusses the prevalence of opioid-induced constipation in clinical patients and how shifting treatment methods and properly educating patients on their conditions can help to improve their standard of living.*

Issues covered in this programme include: Opioids, abdominal pain, amitriptyline, bowels, constipation, side effects, fatigue, fibromyalgia, IBS: irritable bowel syndrome, neuromodulators, painkillers, pelvic pain, stomach pain, stool and tricyclic antidepressants.

Paul Evans: This is ***Airing Pain***, a programme brought to you by Pain Concern, the UK charity providing information and support for those of us living with pain, and for those who care for us. I'm Paul Evans, and this edition of ***Airing Pain*** has been funded by Kyowa Kirin. In a recent edition of ***Airing Pain*** – that is number 123, which is still available to download, we looked at issues around the use and overuse of opioid-based medications for the management of chronic pain. One of the contributors in that programme was Dr Cathy Stannard, an internationally recognised expert on aspects of pain management, and particularly opioid therapy. I'll just remind you something she said in that programme.

Cathy Stannard: Do you think the medicines are making much difference? And there is a dawning realisation that it's just like taking Smarties. [That's] something that we commonly hear. We know that patients are fearful of reducing because of course, if your pain is bad, and you're on medicines, what if it's worse [off medicines]? It's very difficult, and it depends on the individual's perceptions and so on. But we do have evidence from a huge number of patient reports that, freed from the many burdensome side effects, people feel much more alert, able to engage with their families and engage themselves in strategies which help manage their pain. So we know that most of the medicines that we prescribe for pain which actually stop the way that nerves talk to other nerves do have side effects which make people sleepy, sedated, giddy and so on. And all those things make it very difficult to start trying to manage people's lives to try and mitigate the effects of long term pain.

Evans: That was Dr Cathy Stannard, reminding us from an earlier edition of ***Airing Pain*** of some of the issues and side effects experienced by those prescribed opioid-based medications for the management of their chronic pain. Well, in this edition of ***Airing Pain***, I want to look at another side effect that's – judging by the volume of calls Pain Concern's helpline received – is of particular concern to those using opioid-based medications for the management of their chronic pain, and that is constipation.

Maria Eugenicos: 27% of the constipated patients may relate their constipation to medications. In my last clinical audit, I found that approximately 30% of the patients who present with constipation would be on opioid treatments for [a] chronic pain condition.

Evans: This is Dr Maria Eugenicos. And as we recorded this interview during the Covid-19 crisis – socially distanced, of course, via a video conference line – there are references to the crisis in 2020. So Dr Eugenicos asked is a clinician gastroenterologist and senior lecturer at the University of Edinburgh and Edinburgh's Western General Hospital. She specialises in functional gut disorders.

Eugenicos: Constipation is defined by several criteria that may include difficult, painful defecation, incomplete bowel-emptying, decreased frequency of emptying [and] manual manoeuvres. And by definition for functional constipation, this should be the diagnosis if there is insufficient criteria to make a diagnosis of irritable bowel syndrome, as in functional constipation. And usually, when we *do* diagnose constipation, people do not present with loose stools, but with hard, lumpy stools, and may present with loose stools only in the presence of laxatives, if they have been using laxatives probably [due to] their symptoms.

Evans: One question we have to ask is, what does regular mean? What [are] regular bowel movements?

Eugenicos: If I were to reverse the question, I suppose, I would say, 'Is it abnormal to have less than one bowel movement per day?' And that perhaps is not necessarily the case, in that when [we] have done a study questioning healthy controls, then their frequency of bowel movements varied from three times per week to six times per week. So just frequency does not define constipation. But if the decreased frequency is associated with several other criteria already mentioned, like straining, difficult emptying, painful emptying, then perhaps this allows you to make the diagnosis of constipation. If you compare that with patients with constipation, the majority of patients with constipation would admit to frequency [of] less than once per week. That's the majority of patients – about 60% of these patients. About 20% of patients would say once a week, [and] maybe 5% would say twice a week.

So yes, the majority of patients with constipation would have decreased bowel [movement] frequency. The patients with constipation are a great healthcare burden, in that, in previous studies, 80% of the patients attended community nurses requesting treatment for their constipation. So if we track admissions to hospital, where perhaps the primary endpoint, if you like, would be constipation, then it amounts to 70,000,000 in recent studies. The consultant or GP consultations with regard to treatment for constipation management may amount up to 30,000,000 per year, so it's not a dismissive cost. And furthermore, patients who may suffer from constipation may call more often absent from their work – absenteeism is quite high.

Evans: So how much of a problem is opioid related constipation?

Eugenicos: Now, the opioid related constipation, it is sometimes hard to define, because in a recent study that we performed, we found that patients may be started on opioids without prior inquiring about their symptoms. What we know [is] that 27% of the constipated patients may relate their constipation to medications. Now, opioids are not the only medication that may cause constipation, but it's the most common medication that [is] prescribed and does cause [constipation]. So it's not a negligible amount either. Only 46% of patients with constipation may present with a primary, the rest of them are on secondary. So when we have tried to identify how many of the patients develop constipation, once they have started opioids, it was difficult to define because we did not have that information. For those patients

that we had the information – it was about 34% [who] may not have had any symptoms whatsoever, and may develop constipation, following opioids.

From anecdotal evidence, though, we know that if we do not treat the constipation, if we do not address that, and people continue to be opioids, then they may develop opioid induced constipation further down the line. And this is what sometimes may perhaps affect the patient's judgement to say, 'But I have been on opioids and they didn't [cause] the symptoms in the beginning, [but] now I've developed the symptoms.' It could be cumulative effect, because the patient may start on a low dose of the opioids, and then they may increase the dose and then may develop further symptoms.

Evans: How do you address that with a patient coming to you saying, 'I have constipation, and I'm on opioids', and they've already made that link between them – whether it's a correct link or not? How do you address it?

Eugenicos: That may vary depending on the cause of why the patient was started on the opioids in the first place. Education of patients is very important in these cases. So we try to explain to the patient that the opioids in the treatment of pain perhaps are most successful for the acute pain situation. Yes, we do offer opioid treatment for patients who have got cancer pain, but for chronic conditions, perhaps it's better to try other neuromodulators rather than go directly to the opioid, for the particular reason that constipation itself may cause pain. So we may be aggravating the 'syndrome' – if you like, in inverted commas – of pain, because we're trying to address one type of pain by replacing [it] with something else. I would go through their lifestyle [and] try to address lifestyle measures, and we address their diet [and] their liquid intake. I advocate water – hot water regimes, [as well as] regulating the bowel habits. Trying to make the bowel habits predictable is very important. Exercising, physical activity, the position on the toilet to facilitate relaxation of the pelvic floor, avoiding straining – all of these play a role [in managing constipation] and we try to identify those.

Once a patient though, has been referred to my clinic, which is [specifically] a tertiary referral clinic, almost always they would have been tried on other medications. So, we do not only address the lifestyle measures, we would address what medications they have, what doses have they had [of] these medicines. And we are addressing this with the simple laxatives – osmotic laxatives, which is the first choice of treatment, or other similar laxatives if they have had something like that. And if they have not been responding to these, then we would go on to prescribing specialist medications to contract the opioid effect on the bowel motility.

[There is] a new opiate receptor antagonist that we have got available, which can be prescribed orally, and the patient can take it at home.

Evans: Now, I guess you're seeing people who are coming to you because they are unwell. Constipation is a problem to them. What would you suggest people do if they know they're going to be prescribed opioids, to prevent this from the very start.

Eugenicos: We try and educate the patients, in that patients who are on chronic opioid treatment may develop hypersensitivity, visceral hypersensitivity, which is the case in patients who have got IBS, and in particular, in this group of patients, IBS constipation. So if I treat their pain with something that, in the long run, may make their body debilitated to address pain, then perhaps I'm not addressing the question correctly. So what I try and do usually – I would appreciate [that] the patient is in pain, [and] the patient may *need* to be treated. So I would usually advocate neuromodulators, and the neuromodulators of choice – and these are the medicines that they would be prescribed usually, as a first choice in the pain clinics, especially pain clinics – is tricyclic antidepressants in small doses, either amitriptyline if it's tolerated or nortriptyline. Nortriptyline has got less sedative effect. And [we] only take the opioid over and above for an acute situation [that it] would work better [in]. Sometimes the patients are prescribed mild opioids when patients present with abdominal pain and they are really trying to control their symptoms and that may lead to constipation. And then we're dealing with a mixed type of disorder, which sometimes is harder to treat.

Evans: You mentioned IBS, irritable bowel syndrome. Explain what that is.

Eugenicos: The irritable bowel syndrome is a syndrome characterised by abdominal pain, which is associated with altered bowel habits. So it may relate either to diarrhoea [and] the presence of abdominal pain, or constipation [and] the presence of abdominal pain. We would make the diagnosis if the symptoms have been present for at least three months prior to the presentation. So it has to be a continuous type of effect. Anybody may develop abdominal pain. When [someone has] altered bowel habits, it doesn't mean that [they] have IBS. But if this is persistent presentation over a period of time, then it would make the diagnosis of IBS. People who may have had chronic constipation for years may develop IBS, when especially each time they have got altered bowel habits, this relates to abdominal pain. And we do warn them that sometimes it can fluctuate. The recent Rome IV criteria have defined that discomfort is not part of the IBS as a syndrome. It has to be pain. And the reason for that is that anybody with constipation may have discomfort, when they become bloated, when the

bowel distends with faecal loading, etc. But [when] the pain is present, it's characteristic of the IBS, irritable bowel syndrome.

Evans: You said constipation *or* diarrhoea. I've talked to some people who have both.

Eugenicos: When you make a diagnosis of IBS constipation, the patient presents with hard, lumpy stool. And we define that through our consistency, the bowel movement consistency, because this may reflect more accurately the pathophysiology of the syndrome. But these people may have loose stools, but it should be less than 25% of the time. Now, the patients who present with IBS diarrhoea would have abdominal pain and would have looser, watery stools, they could have harder stools, but it should be less than – again – 25% of the time. Now [though], if people present with alternate bowel habits – [as in] constipation alternates with diarrhoea – and this may happen more than 25% of the time, then we are dealing with mixed type IBS. And we have got… there are subtypes that, at times, present with constipation, at times they present with diarrhoea, and they can fluctuate. So it's four types. And again, the reason for the differentiation of these four types is because the bowel [movement] consistency would be different. And that reflects different pathophysiology. And as a result, it would mean different types of treatment for these people.

Evans: And the reason why I'm asking about IBS is because IBS, irritable bowel syndrome, does seem to go hand in hand with some chronic pain conditions, like fibromyalgia [and] like other conditions, and in some cases, pharmaceutical treatments are the same. They seem to be working on the same systems, am I right?

Eugenicos: Yes, the pain control for fibromyalgia, for example, or for IBS is neuromodulation. For all the chronic pain syndromes like this, [the treatment] would be neuromodulation. We have come across, more often, patients who may have IBS, and may present with fibromyalgia, or other chronic conditions. We do not really know whether this is because it's a very common condition, or whether there is a causative effect, or whether pharmaceutical treatment to address one condition may lead to another. It is a very complex and interrelated situation. But in my clinic, I get quite a few patients with IBS who have resistant symptoms, quite a few of them would have fibromyalgia, quite a few of them may have Ehlers-Danlos syndrome, and other conditions.

Evans: Now one of the reasons we're doing this edition of ***Airing Pain*** is because of the number of people who phoned up our helpline about it. But also, because of the controversies over using opioids for the management of chronic pain. Do you get people

who come to see you with chronic pain conditions, who are heavily reliant on opioids and have constipation?

Eugenicos: Yes, in my last clinical audit, I found that approximately 30% of the patients who present with constipation would be on opioid treatment for a chronic pain condition. So it's quite a high proportion of the constipation patients. Whether these people are referred to my clinic because their primary care professionals or physicians would like us to [advise] these people on specialist treatment or whether [it's] because they are not familiar with a specialist treatment, and the first and second lines of laxative treatment have failed, it is difficult to know.

But yes, I do have a cohort of patients [who] present to my clinic with this problem. A young man – he's forty-two years old and was referred to my clinic because his symptoms of constipation and pain were not responding [to treatment]. He had a diagnosis of IBS, [which was] constipation-made, and one of my colleagues, a gastroenterologist asked me to see him. I saw him last July, he was a very switched-on patient. So I took him through the pathophysiology of the IBS syndrome [and] of the constipation and explained to him the long term effect of somebody being on the opioids to control the pain, and offered him the modern way of addressing chronic pain through neuromodulators. And when I explained to him that although I'm trying to treat [his pain] – although it was not me who initiated the opioids – but I said to him, 'I'm your physician, I'm trying to treat your pain, and I'm giving you opioids because they *do* control the pain. But I have to tell you that in the long run, our studies show that you may develop a hypersensitivity, so I'm giving you opioids to treat the pain, [and they] may make you more hypersensitive to pain and they may not be addressing the pain control at all. He was so motivated, that he went home, studied the information leaflets I gave him on how to gradually reduce and come off the opioids, [and] he managed within three months' time to stop the opioids. And [he] had a review [with] my colleague who saw him in the first instance, in November – which makes it four months down the line – and declared that, 'I followed Dr Eugenicos' advice, I'm off the opioids now, my bowels are back to normal. I do not have much pain, very little pain at all. So I'm feeling much happier.' So you might say, 'Oh, maybe this anecdotal, maybe it is different.' But there is a follow-on story, in that we ran into the [Covid-19] situation. And the patient became quite stressed and quite anxious about his job about this and that, like most people nowadays with the lockdown. And I reviewed him in my specialist clinic only a month ago. And the symptoms, were back to square one. So I was so disappointed. So I said to him, 'What happened?' And he said to me, 'I don't

know what happened.' And when I took the history of medications and stuff, he was back on opioids. But I said to him, 'Do you remember when you stopped the opioids, you went and saw so-and-so who wrote to me to say, "Thank you so much, because you managed to advise my patient, and he's now free of symptoms."?'

He couldn't remember it, of course, because he went into the situation, had developed pain – perhaps because of stress, because of anxiety – started the opioids because they were handed to him. So when I reminded him and I read the detail of the letter my colleague sent me he said, 'Yes you're right, I was so much better off.' I did say to him, 'I do understand why you went back on them, maybe you are stressed.' But I said to him, 'If you cannot manage without the opioids, I would suggest we do start the neuromodulators.' In the past, he managed to cut down the opioids, to stop the opioids, [and] he didn't even go back to the neuromodulators. But I suppose, because of the current situation, the worries that he had, in particular, he agreed to go on the neuromodulators, and [he agreed] to a regime to try and cut back [the opioids]. And the habits of a few patients like that, that did say, 'I stopped it, because I decided I didn't want to be on this anymore.' And suddenly their symptoms improve. Whether they need to be supported with some form of treatment, either regulating their bowel habits better, or giving them a form of neuromodulator to avoid any of the symptoms coming back. And reinforcing this sort of dependence, if you like, is important as well.

Evans: You mentioned giving out leaflets – education is absolutely crucial.

Eugenicos: I have got special interest in that. We have developed, with medical students, educational leaflets to give to the patient. We did a trial where we have designed the symptoms, lifestyle measures, medications to take, which are safer for long term, which are perhaps less often prescribed long term etc. And when we gave the patient the questionnaire, what we wanted to know more about, was the pathophysiology behind their symptoms. So what they enjoyed coming and listening about when they were coming to the clinic, is myself, showing them a picture of the [CT scan] and explaining [to] them the journey of the food through their stomach, through their small bowel [and] the large bowel, the function of each one of these organs, the function of the rest of the endocrine, if you like, the enzymes that we produce, how our bowel reacts to that [and] why we develop the symptoms we develop.

They were really fascinated, and I think if we allow the patient to be well educated, to know why they get the symptoms they get, what makes their symptoms appear certain times [in the] month, if you like, hormonal changes maybe, stress situations, and they know to address those and prevent their symptoms happening. And if they are in control, this perhaps is the key to successful treatment in general. We manage to know more about how a patient can control their symptoms better through the biofeedback when we were giving the patient the treatment modalities to take home and do it on their own. And because they had to educate themselves, how to work a biofeedback machine: 'What does it do? What does relaxation mean?' They were much better [at] controlling their symptoms and much more successful. So I do [routinely] give them leaflets, but nowadays I give them leaflets relating to their own symptoms. What my task in the future [is], is to make a booklet which would contain all the information [they need], so they don't need to depend either [on] the GPs they're visiting and [being told] this and that, or [depend on] following any healthcare professional. They need to have ownership of their symptoms, of their treatment [and] know what to do in the future.

Evans: Dr Maria Eugenicos, clinical gastroenterologist at Edinburgh's Western General Hospital. Now, as always, I remind you that we, in Pain Concern, believe the information and opinions on ***Airing Pain*** are accurate and sound, based on the best judgments available. You should always consult your health professional on any matter relating to your health and well-being. He or she is the only person who knows you and your circumstances and, therefore, the appropriate action to take on your behalf. You can find all the resources to support the management of chronic pain, including details of our videos, leaflets, all editions of ***Airing Pain***, of course, and ***Pain Matters*** magazine at painconcern.org.uk. And Pain Concern is currently preparing an information leaflet and an article for ***Pain Matters*** magazine on how to manage opioid induced constipation. So please look out for that in the future. Dr Maria Eugenicos also recommends the IBS network websites as an excellent online resource for the management and understanding of IBS and other related conditions. The address is theibsnetwork.org. There are no gaps.

Eugenicos: In that website, they would be able to ask any questions. These bodies are linked to specialists and if anybody asked questions, they usually would address them to us, and we would answer back. So it's a big cohort of patients who usually try to collaborate. It's

more about IBS, but all of these conditions are addressed under this umbrella, it doesn't have to be only IBS. So people, for example, who may have bile acid diarrhoea [and] may ask questions – nobody would tell them, 'By the way, this is not IBS', or if somebody says. 'I have been commenced on the hydrocodone that develop these symptoms, what can I do? Can we address all of these symptoms?'

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More information:

- ***Airing Pain*** 123: Opioids and Chronic Pain
- The IBS network – theibsnetwork.org
- British Pain Society – britishpainsociety.org
- IASP Global Year for the Prevention of Pain 2020 – iasp-pain.org/GlobalYear.

With thanks to:

- Maggie's Centre, a resource network designed to help cancer patients and their families – maggies.org.