Dr. Tevfik Ismail (00:17):

Welcome to the AHA Pericardial Disease Podcast, entitled Treatment of Acute Pericarditis. This is the third of a series of eight podcasts on acute pericarditis and recurrent pericarditis. My name is Dr. Tevfik Ismail. I'm a consultant cardiologist and clinical lead for inflammatory myocardial and pericardial diseases at Guy's and St Thomas' Hospital, London, United Kingdom.

Dr. Tevfik Ismail (00:40):

Today, I'm joined by two leading experts in the treatment of acute pericarditis. The first is Professor Antonio Brucato, who is director of internal medicine at the Fatebenefratelli Hospital, Milan, Italy, and also professor of internal medicine at the University of Milan. He's one of the authors of the European Society of Cardiology Clinical Practice Guidelines for the Diagnosis and Management of Pericardial Diseases. He has also led or been involved with some of the key clinical trials that provided the evidence base for these guidelines, such as the ICAP study for colchicine, which is published in the New England Journal of Medicine.

Dr. Tevfik Ismail (01:14):

I'm also joined by Dr. Robert Barcelona, who is a specialist cardiovascular clinical pharmacist and director of the year 1 post-graduate pharmacy residency program at the University Hospitals Cleveland Medical Center, Cleveland, Ohio.

Dr. Tevfik Ismail (01:27):

In the first of this series of podcasts, we focused on the diagnosis and initial assessment of acute pericarditis. In the second podcast, we reviewed the potential complications of acute pericarditis, their clinical features, and their management. Today, we are going to focus on the treatment of acute pericarditis, and in particular, review the relevant clinical pharmacology of the agents used. During the course of this discussion, we will discuss the use of drugs that are off-label for acute pericarditis in the United States and other jurisdictions. We hope we can provide some practical tips and tricks and pointers towards pitfalls to avoid while managing this condition.

Dr. Tevfik Ismail (02:05):

So to start off, Professor Brucato, can you start our discussion by taking us through your initial approach, the treatment of a first presentation of acute pericarditis?

Prof. Antonio Brucato (02:14):

Thank you. I am so happy to be here with all of you. The first approach to the treatment of acute pericarditis, in my opinion, is of paramount importance because I am convinced that the main cause of failure and of recurrences is simply the factor that the first episode of pericarditis has been treated improperly. And the mainstay of a therapy of a first attack, in my opinion, remains non-steroidal anti-inflammatory drugs and/or aspirin. And this is usually stated, but has some practical implication. Aspirin and non-steroidals must be used at full dose if tolerated, of course, and until complete symptoms' resolution.

Prof. Antonio Brucato (03:06):

What does it mean, full dose? Full dose are the dosages that you can find in the textbook, in the medical literature, and not the dose most of us are used to commonly use. For instance, aspirin. High dose of

aspirin is at least 3 grams daily. Ibuprofen. Ibuprofen, there is a problem because doctor are convinced that the dose is a simply 600 milligrams three times daily, but this is not full dose. Full dose of ibuprofen is easily 800 milligrams three times daily. Indomethacin is a very nice, useful drug. You can use it by mouth and intravenously. By mouth, well you have tablets, at least in Italy, 25 and 50 milligram, and you can reach till 150 milligrams daily.

Prof. Antonio Brucato (04:02):

But any non-steroidal is useful. The point is that whatever non-steroidal you will use, you have to use a dose that is appropriate to treat the inflammatory process that you want to treat. And if inflammatory process is explosive, you need for sure high dosages. And that if you use these drugs by mouth, please remember it is quite important to give them at least well-distributed every eight hours, because the majority of these drugs has a length of action that is seven, eight hours. And if you give just two dose, one in the morning and one in the evening, you will not reach the full control of disease. And this does not mean that the drug is not effective. It does mean simply that the action of the drug has ended.

Prof. Antonio Brucato (05:00):

An important point that I underline is also by mouth or intravenously. As far as I know, for instance, probably in US, probably also in UK, you don't have non-steroidal that you may use intravenously. This is a problem because if you have a patient who have a severe disease, who is hospitalized, high fever, severe heart pain, nausea, vomiting, I think it will be very difficult to reach a good control of that condition simply giving one pill of ibuprofen, 600 milligrams, at 7:00 PM. And this will not be able to control the disease.

Prof. Antonio Brucato (05:44):

In this patient with this severe phenotype who is hospitalized, high fever, you will give all the drug intravenously, the antibiotics proton pump inhibitors, everything. And you should use also non-steroidal anti-inflammatory drugs intravenously if you really wanted to control the disease, because if you have only option to give these drugs by mouth, and for instance, the patient is severely ill, nausea, vomiting, you will not be able to control the disease. And this is a typical condition in which the doctor will be forced to use corticosteroids that the doctor will give intravenously, usually.

Prof. Antonio Brucato (06:25):

Non-steroidal are really important. They are the mainstay of treatment, and they should be given at high dosages, of course, if tolerated. If not tolerated, you will move to another non-steroidal, and you will easily find a drug that will be well-tolerated by the patient.

Prof. Antonio Brucato (06:44):

So when you start, the therapy must be strong and active. And then how long? Of course, as long as it will be necessary. What does it mean in practice? In most cases, I think that you should give these drugs, for instance, one month, in most cases. I think that one or two week is not enough in most cases. Maybe I am biased because I saw a lot of complicated patient, but one or two weeks is not enough. At least one month.

Prof. Antonio Brucato (07:15):

And after that, tapering non-steroidal, as tapering of any drug, is not automatic. But tapering must be guided by symptoms and by the value of CRP, that in most cases would be elevated at the beginning. So

in practice, after one month, if symptoms are almost completely absent and if CRP is completely normalized, I personally, in my practice, at that point begin to taper the drug, and tapering will last two, three, four weeks according to the clinical condition.

Prof. Antonio Brucato (07:56):

Of course, from the beginning, I propose to the patient also to add colchicine. Colchicine, we may discuss later on at some point on mechanism of action, but colchicine is useful also in the first attack of pericarditis, and low dose. Non-steroidal must be used at high, but colchicine, the opposite, low dose and no loading dose at all.

Prof. Antonio Brucato (08:24):

And which is the dose? In Europe, we have tablets of 0.5 or 1 milligram. In US, you have tablets of 0.6 milligrams. Personally, I start with the low dose, the minimum dose. It is 0.5 milligram. In US, I will say 0.6 milligram. And I see which is a good tolerance, well-tolerated immediately for the patient. If a patient do not develop diarrhea or other gastrointestinal symptoms, but mainly diarrhea, after three, four, five days, I will increase the dosage. In Europe, 1 milligram. In US, 0.6 milligrams twice a day.

Prof. Antonio Brucato (09:11):

In the trial we published, we proposed that the of colchicine will depend on the weight of patient. This is of course acceptable and is true in any case. In the trial, we had to propose dosages. But you have patient of any weight that will tolerate well 1 milligram of colchicine, then on the other side, you have patient of any weight who will tolerate just 0.5 milligram. So my personal approach is to start with 0.5 or 0.6 milligram, and after a few days, if well-tolerated, I try to increase to a full dose. It is 1 milligram in Europe, or 0.6 milligram twice daily in US. This is, in my opinion, the best approach to initial treatment of acute pericarditis with CRP elevation, fever, and inflammatory symptoms that are important.

Prof. Antonio Brucato (10:13):

There is also a problem of pain. If pain remains not well-controlled, I advise you not to start corticosteroid just because pain is not well-controlled. I advise you in the case to try analgesics, for instance, codeine or tramadol or something like that, and not on demand, but at fixed intervals. For instance, every day, every night, a low dose of tramadol, of codeine. That will be quite important to avoid pain during the night, because this is a classical mistake. If you give the last dose of a nonsteroidal, for instance at 8:00 PM, after eight hours, the effect will be disappeared. And so, the patient will awake early in the morning with pain. To avoid this, I advise to give to a patient, for instance at 10:00 PM, 11:00 PM, the dose of codeine or tramadol. That will help him to sleep well without pain and without calling for a doctor on charge.

Prof. Antonio Brucato (11:27):

Basically, this is my approach, non-steroidal anti-inflammatory drugs or aspirin of high dosages, and colchicine at low dose, plus eventually, analgesic. Eventually we might discuss later conditions such as patient with ischemic heart disease or a contraindication to high dose of this, of non-steroidal.

Dr. Tevfik Ismail (11:45):

Thank you very much, Professor Brucato. That's a fantastic overview of initial approach. Dr. Barcelona, for aspirin and other non-steroidals and colchicine, what are the key cautions and contraindications that prescribers should be aware of?

Dr. Robert Barcelona (11:59):

Obviously, for those patients who had allergic reactions to these medications in the past where they've developed shortness of breath, chest tightness, wheezing, definitely should avoid these medications in those patients because we're using such high doses, as Dr. Brucato alluded to.

Dr. Robert Barcelona (12:16):

Bleeding is a problem that may be seen, particularly in the GI tract. But especially at the high doses used, you have to monitor for any kind of bleeding. Dr. Brucato also alluded to potentially using intravenous therapy. So ketorolac may be used, but as far as duration of therapy, that would have to be limited to five days, again, because of the risk of bleeding complications.

Dr. Robert Barcelona (12:38):

These medications, especially NSAIDs, can cause volume retention. So those patients who have severe heart failure or uncontrolled hypertension, you'd want to be very careful or avoid using them if the disease is severe enough. As far as colchicine, this medication is contraindicated in patients who have both renal and hepatic dysfunction because of how it's metabolized. The other aspect of both colchicine is that it's a cytochrome 3A4 substrate. Especially those patients with their strong CYP3A4 inhibitors should avoid this medication, especially if they have either renal or hepatic impairment.

Dr. Tevfik Ismail (13:16):

What about diarrhea, particularly with colchicine, any tips for that?

Dr. Robert Barcelona (13:22):

As far as diarrhea, this can be common, especially used at higher doses. Again, as Dr. Brucato alluded to, starting at a lower dose, getting the anti-inflammatory effect with colchicine at the low dose, and then seeing as patients tolerate it, increasing the dose as tolerated.

Dr. Robert Barcelona (13:37):

As far as non-steroidals and aspirin, main side effects include GI distress, abdominal pain, heartburn. Taking those with food or water may help minimize some of the side effects. In the clinical trials that use especially these high doses, a proton pump inhibitor was commonly used to mitigate some of these side effects.

Dr. Tevfik Ismail (13:57):

That's great. I think sometimes with patients who get diarrhea, there's a temptation to potentially stop the colchicine altogether. But I think a better approach if you do end up with side effects is to consider reducing the dose, typically by 50%. And something that we occasionally find helpful as well is considering putting the patient on a lactose-free diet. Particularly, if the patient's been on colchicine for a little while, it does seem to cause a degree of acquired lactose intolerance. It can sometimes contribute to diarrhea.

Dr. Tevfik Ismail (14:27):

Professor Brucato, we know from podcast two that recurrent pericarditis is one of the most common complications of acute pericarditis, particularly when the latter, as you've been mentioned earlier,

hasn't been correctly treated. You briefly touched this already, but how important is colchicine in preventing recurrence and how effective is it?

Prof. Antonio Brucato (14:44):

First, let me give a brief comment on diarrhea. Of course, colchicine may cause diarrhea. But in practice, I remember that diarrhea may be facilitated also by antibiotics that are quite commonly, unfortunately, improperly used in these patients. And also, proton pump inhibitors often used at high dose such as in this patient may cause diarrhea. When you have a patient who is taking colchicine, antibiotics, and proton pump inhibitors, diarrhea is common, and most doctors will taper or discontinue colchicine. But in many of these cases, some weeks later, you can restart colchicine at low dosages. And in most case, colchicine will be tolerated after that. So this is an important trick for the use of colchicine.

Prof. Antonio Brucato (15:46):

Regarding the efficacy, effect of colchicine in acute pericarditis, in this podcast, we are talking about the first attack of acute pericarditis. We have demonstrated with my friend Massimo Imazio that colchicine is useful both in the first attack and for recurrences. Here, we discuss the first attack.

Prof. Antonio Brucato (16:10):

And in this particular condition, we published the two paper, the COPE trial and the ICAP trial. The COPE trial was a open-label, randomized, the single-center trial. But the final findings came from the ICAP trial. That was a multicenter, randomized, double-blind control trials in which we randomized 230 patients, half to usual therapy, and the other half to usual therapy plus low-dose colchicine. And what we found? We found that recurrence occurred in approximately 30% of patient with usual therapy, and in approximately 15% of patient treated with colchicine.

Prof. Antonio Brucato (16:56):

What does it mean in practice? In practice, first of all, number needed to treat is four. It is you have to treat four patient to avoid one recurrence. And the second point is that colchicine is effective, but of course it's not a magic bullet that will eliminate any recurrence. So after starting colchicine, you will continue to see some patient who might experience some recurrences. That is, colchicine is useful, but it is not a magic bullet that will eliminate any recurrence. In particular, the use of colchicine, I say, that it mandatory in the recurrent cases. In the first attack, I discuss with the patient the opportunity to use it, to start it, because for sure we'll have the risk of recurrences.

Prof. Antonio Brucato (17:48):

They have also demonstrated and published that starting colchicine will accelerate disappearing of symptoms and will reduce the rate of hospitalization. So it is best used also in the first attack if well-tolerated.

Dr. Tevfik Ismail (18:06):

It's clear that colchicine plays a key role in preventing recurrences, speeding up recovery. Are there any particular types of pericarditis where you wouldn't recommend using colchicine, or any circumstances you wouldn't use it?

Prof. Antonio Brucato (18:19):

Honestly, not a lot. For sure, if a patient has not tolerate well colchicine, I will avoid for sure. Other condition in which I will be cautious for sure are advanced renal failure, elderly people, patients who are taking a lot of drugs, particularly for instance, cyclosporine or clarithromycin. In Italy, there is some reluctance to use colchicine during pregnancy, but actually we know now that colchicine may be used also in pregnancy. It's a useful drug. So I do not see many conditions in which colchicine is not indicated apart from the cases in which the patient clearly do not tolerate well it. Cautions, for sure, in patient with a renal failure, elderly, taking a lot of drugs, a lot of comorbidities.

Dr. Tevfik Ismail (19:17):

That's great. On that subject, Dr. Barcelona, are you able to walk us through the pharmacokinetics of colchicine?

Dr. Robert Barcelona (19:25):

After you take colchicine, about half the medication is absorbed one to two hours after ingestion, so some of the effects may start at that period of time. It gets into lots of different cells, especially white cells, as far as decreasing some of the inflammatory components that they may release. Such that the concentrations in leukocytes are very high. Again, it's why the anti-inflammatory properties of colchicine are so pronounced.

Dr. Robert Barcelona (19:50):

As far as some of the metabolism, it is again, metabolized as a substrate through the cytochrome 3A4 system, and then is excreted in the urine mostly as unchanged drug. The half-life is about 24 hours in those patients with normal renal as well as hepatic function.

Dr. Robert Barcelona (20:08):

As far as other metabolism of colchicine, it is a substrate of P-glycoprotein. Metabolic pathways are found in variety of areas, including the liver, the kidney, as well as the GI tract.

Dr. Tevfik Ismail (20:19):

So you mentioned that the cytochrome P450 3A4 system and also P-glycoprotein are really important in terms of the metabolism clearance of colchicine. These are systems that are commonly involved in multiple other drug processing. Are there any clinically relevant drug interactions prescribers should very commonly be aware of? Because if you look at the typical pharma computer, everything interacts with everything else. And sometimes, it's difficult to work out what interactions are really, truly significant, which others are cautionary tales to be aware of but not necessarily in practice a major problem most of the time. Are there any situations where you would be particularly cautious combining one agent with another? With the instance, your colchicine.

Dr. Robert Barcelona (21:00):

For these agents, it's really the strong inhibitors of that enzyme system, items or medications like clarithromycin, some azole antifungals that are used, especially itraconazole, ketoconazole. The antidepressant nefazodone is a strong inhibitor of the system, as well as some of the antiretrovirals. Some of these are not used as commonly, things like indinavir, nelfinavir, saquinavir. However, ritonavir, which is a component of some medications, as well. Also, sometimes in my center, we may use this as a booster for those patients on immunosuppressants, so that's something just to be cautious of.

Dr. Robert Barcelona (21:37):

As far as P-glycoprotein, my center is also a transplant center. Cyclosporine is a inhibitor of this pathway. Using colchicine in combination with cyclosporine really should be used, if at all, cautiously. For example, cyclosporine and colchicine, I would do maybe the 0.5 or 0.6 every 72 hours, maybe sometimes once a week, really to make sure that the concentrations don't get too high as far as causing any of the adverse effects we talked about earlier.

Dr. Tevfik Ismail (22:06):

That's right. So far, our discussion's focused on a case of uncomplicated acute pericarditis. But what about patients with significant comorbidities, particularly we've already mentioned earlier as well, renal dysfunction. Any particular precautions you're taking with someone with renal failure?

Dr. Robert Barcelona (22:24):

Colchicine can accumulate in renal dysfunction, adverse effects including diarrhea. The rare adverse side effect is bone marrow suppression, which we hardly see. But for those patients where the metabolism will be really significantly decreased, such as real dysfunction, something to keep out an eye for in this population. I find this somewhat challenging because referral center for our main health system, we get lots of transfers, very complicated patients with renal failure getting referred for transplant.

Dr. Robert Barcelona (22:52):

As far as using colchicine in this population, again, is very problematic. Again, at most, in this population, I would recommend half a tablet. So in our country, 0.3 milligrams. In Europe, 0.25. Again, very infrequently, at most twice a week, maybe once a week, but really for a short period of time as possible such as three months.

Dr. Robert Barcelona (23:17):

In this population again, because of the risk of complications besides diarrhea, like bone marrow suppression, you'd want to periodically get a CBC, look for any abnormalities and decrease in cell counts. For those patients again, as we alluded to, if they have both renal failure as well as if they're on any potent inhibitors of 3A4, definitely would not use colchicine and use alternative agents, NSAIDs if you can, corticosteroids. And then we talked about pain management as well to control the disease.

Dr. Tevfik Ismail (23:50):

What about dialysis? Is that any use in terms of clearing the drug. How effective is dialysis?

Dr. Robert Barcelona (23:56):

Dialysis does not clear the medication. So definitely, that's very a tricky population as far as using the medication in. And as I said before, using it at most twice a week, and again, as a short duration of time with the lowest dose possible to control symptoms.

Dr. Tevfik Ismail (24:13):

Professor Brucato, we've talked about aspirin, non-steroidals, and colchicine as cornerstone for the management of acute pericarditis. What's the role for corticosteroids in this condition?

Prof. Antonio Brucato (24:23):

Corticosteroids in pericarditis are similar to the devil, because when you start corticosteroid, you will sell your soul to the devil. They are very effective, but then you will anticipate lot of problems in tapering and finally, discontinuing corticosteroids. I personally use corticosteroid as a third drug, typical patient without any particular contraindications. That is young patient with very active inflammatory clinical film pictures. Young patients are no risk of renal failure, no comorbidities. So these young patient usually tolerate well high dosage non-steroidals and colchicine. But for instance, elderly patients, patient with a lot of comorbidity, maybe problem of renal failure, you cannot use this high dose of a non-steroidal.

Prof. Antonio Brucato (25:26):

So I will consider a corticosteroid drugs in two condition. First, the minority of patient with classical acute pericarditis who do not respond to intravenous non-steroidal inflammatory drugs but colchicine, who really not respond, and patients with comorbidities or renal failure, advance age, the anti-coagulated or something like that, in which I think it is not safe to push too much use of non-steroidal or aspirin.

Prof. Antonio Brucato (26:02):

But when I start corticosteroids, you had to consider some important point. That also in pregnancy, for instance, corticosteroid may be used. Of course, low-dose corticosteroid may be used. And in this time low-dose corticosteroid may be used in patient who had pericarditis after COVID disease and also after COVID vaccine, for instance. Most of these patient complain of asthenia, myalgia, and low-dose corticosteroid may be useful in this patient.

Prof. Antonio Brucato (26:40):

When I use a corticosteroid, absolutely I recommend to use minimal effective dose. And when I start, personally I start, for instance, prednisone 5 milligrams twice daily, low-dose prednisone. These dose are low, but believe me, when you add them to non-steroidals and colchicine, they are often able to obtain final control of the disease. Exceptionally, I use higher dose, but no more than 25 milligram of prednisone or 20 milligram of methylprednisolone intravenously, because the vast majority of pericarditis will respond to these low medium-dose of corticosteroids. And if they do not respond, the diagnosis is doubtful.

Prof. Antonio Brucato (27:38):

When you start corticosteroids, please, particularly if you are a cardiologist, remember that for sure, this will be a chronic therapy. It is impossible to start a corticosteroid in pericarditis and give them just for two weeks. I've never seen this. When you start, you went for two, three, four, five months, and you have to apply or what is recommended for chronic corticosteroid therapy. Basically, first of all, the use of vitamin D and for instance, in many patient, the use of a bisphosphonate to reduce the risk of osteoporosis. That is a really risk when you start the corticosteroids, for instance, in a middle-aged woman, and you will give corticosteroid for two, three years to this lady.

Prof. Antonio Brucato (28:38):

In practice, I start the corticosteroid low medium dose, for instance, prednisone 5 to 25 milligram daily. And I take this dosage again for how long? Till complete resolution of symptoms and complete normalization of CRP. That takes approximately for 20, 30 days, one month. After one month, not automatically I will taper. But when symptoms have completely disappeared and CRP is normalized, I'll taper very gradually. For instance, means 5 milligram of prednisone if a patient was taking 25.

Prof. Antonio Brucato (29:26):

Tapering of corticosteroids is similar to an airplane who is landing, must be quite slow and quite cautious, particularly when you reach very low dosages such as 5 milligram. It is a mistake to taper from 5 milligram to 0, because 5 milligram seems a small dosage, but if you reduce from 5 milligram to 0 is 100% reduction, and it is very at risk of recurrence. So with tapering, for instance, 25 milligram, then 20, then 15, then 12.5, then 10, then 7.5, then 5, 5 alternate to 2.5, 2.5, 2.5 alternate to 0. Extremely slow tapering, particularly when you reach the very low dose, because acute pericarditis is extremely sensitive to reduction of corticosteroids. Extremely sensitive.

Prof. Antonio Brucato (30:41):

And this is very reason for which the corticosteroid are the devil. In any case, it may be very useful if we use it properly, low dose, very gradual tapering. And during the tapering, we have to anticipate the risk of recurrence. It is possible. It's best that you anticipate the patient. "Do not worry if when we will reach 2.5 milligram of a prednisone, you will experience a recurrence. This is possible. Don't worry. Don't panic." The important point is at that point, not to increase again the dose of corticosteroids. You will do any effort not to increase again the dose of corticosteroids, will stay on that dosage. You will push the dose of non-steroidal anti-inflammatory drugs, eventually adding analgesics. Tranquilize the patient. "Don't panic. This is anticipated. This is not a tragedy. This may happen, and we will manage it together. The recurrence, eventually, you will experience during tapering of corticosteroids." This is my way to use corticosteroids.

Dr. Tevfik Ismail (31:55):

That's fantastic. So, Dr. Barcelona, we've talked about aspirin, non-steroidal anti-inflammatory drugs, colchicine, and steroids in a patient who is otherwise well. We've also talked about patients with comorbidities. What's your advice on the use of these drugs in pregnancy and breastfeeding? We've already mentioned, I think colchicine traditionally has been thought to be something we can't use in pregnancy, but actually the data doesn't entirely support that. Well, what is your view?

Dr. Robert Barcelona (32:25):

As far as colchicine, maybe start with that first. There is data, some data in familial Mediterranean fever that it can be used in pregnancy. The data, as far as adverse effects, are mainly in animal studies, so that this may be used if there's no other therapies. Also, colchicine does get in breast milk, but most of the references you will find will commonly say that is compatible with breast milk.

Dr. Robert Barcelona (32:50):

As far as aspirin, NSAIDs, these may be used really until the second trimester of pregnancy, especially at the high doses, you can use them. However, after that, they really should be avoided. As far as breastfeeding with these agents, you can use NSAIDs. However, with high dose of aspirin, probably should not use that in anything more than 100 milligrams. And then one way to potentially mitigate some of the complications in those patients who are breastfeeding is to breastfeed and then take the medication following, so then the concentrations are much lower after breastfeeding is finished.

Dr. Tevfik Ismail (33:23):

Dr. Barcelona, one of the commonly encountered situations, a patient who needs to take dual antiplatelet therapy or even formal anticoagulation. What's your advice in these circumstances?

Dr. Robert Barcelona (33:35):

As far as those patients on dual anti-platelet therapy, I think it's really important to know what the indication is, and if it's for a coronary stent, when the stent was placed, where was placed, was it in the setting of electively in stable ischemic heart disease, or is it in the setting of acute coronary syndrome?

Dr. Robert Barcelona (33:50):

I think as we've seen more data coming out that shorter durations maybe poor for some patients. Generally speaking, for patients with, for an example, a recent acute MI, a recent stent placed, I would generally avoid high doses of non-steroidals, high doses of aspirin, because they'll be on dual anti-platelet therapy during that initial period, and use colchicine, analgesics as needed. For those patients who the stent was more distant, maybe consider if it's appropriate to stop the thienopyridine, utilize the high dose of aspirin, NSAIDs, colchicine at that period of time.

Dr. Robert Barcelona (34:25):

As far as anticoagulation, again I think it's key to know what the indication for anticoagulation is. Is it someone who had a remote veno thromboembolic events, or is it for atrial fibrillation? Were they chronically on it? Again, because of the agents and the dose we're using of aspirin, NSAIDs can cause significant bleeding. We'll generally avoid those if you cannot come off anticoagulation, and utilize colchicine. And then analgesics on top of that, if needed, patients are experiencing significant pain.

Dr. Tevfik Ismail (34:56):

Professor Brucato, is there any role for therapies specifically directed at IL-1 or the IL-1 receptor in the management of acute pericarditis, as opposed to recurrent pericarditis where obviously they have a clear role? Are there any circumstances where you've had to result to using anakinra or rilonacept for a patient with a first presentation of acute pericarditis?

Prof. Antonio Brucato (35:17):

Of course, this is an uncommon situation in the context, in the setting of a first attack of acute pericarditis. Still, there is a possibility. I consider the use of anti-interleukin-1 agent directed against both interleukin-1 alpha and interleukin-1 beta with our anakinra and rilonacept in two settings, in two condition.

Prof. Antonio Brucato (35:50):

First of all, these agents are effective only in patient who are a clear inflammatory phenotype. That is, you must have a patient who typically has a fever, strikingly elevated values of C-reactive protein, quite commonly pleuropulmonary involvement that represents the inflammation that involves also the pleura and the surrounding, all in the context of pericardial pleura. First of all, selection of a patient is quite important. Patient with a clear inflammatory phenotype, fever, pleuropulmonary involvement, C-reactive protein elevation. This patient, I treat for sure with non-steroidal anti-inflammatory drugs intravenously, colchicine, and eventually load those corticosteroids. In the rare cases in which this is not able to control disease, I will consider anakinra.

Prof. Antonio Brucato (36:53):

Honestly, it is more common, a different condition. That is a patient had this typical phenotype, but was treated improperly. He was treated with the low dose anti-steroidal, high dose colchicine, very rapid

tapering of corticosteroids, and experiencing a series of hospital admissions, emergency room visits. And so the patient is exhausted. The patient is in a tunnel. Lot of hospital admission and so on, and he cannot accept enough attempt with classical therapy, even if classical therapy were used improperly before. And in this condition, of course, after three, four hospital admission due to therapies with low dose, high dose, in the condition, later it's the same attack. In this case, it is difficult to differentiate first attack, recurrence, incessant clinical course. You have a patient who was ill for two months. And at the end of these two months, he's exhausted, and I will try anakinra or rilonacept.

Prof. Antonio Brucato (38:15):

The other condition is another condition. For instance, if a patient has undergone cardiac surgery and he developed a renal failure, or the patient developed acute gastrointestinal bleeding during the first attack due probably related to non-steroidal corticosteroids, or the patient has undergone a general surgery in any case, or the patient has strongly anti-coagulated. This patient, if has a typical phenotype of inflammatory phenotype, may be treated for sure with an anakinra or rilonacept because these drugs are very effective, are not contraindicated in these conditions, but it can be used in renal failure or cardiac surgery, general surgery, renal failure, heart failure, and may even have a good cardiovascular safety profile. But they maybe used also in patient with ischemic heart disease and several comorbidities that are condition in which non-steroidal and corticosteroid, of course, may be dangerous.

Dr. Tevfik Ismail (39:29):

Well, thank you, Professor Brucato and Dr. Barcelona, on behalf of the American Heart Association for taking part in the podcast today. This is part of a series on recurrent pericarditis that's supported by an educational grant from Kiniksa Pharmaceuticals UK Limited. For more educational material on this topic, please visit the AHA website at learn.heart.org and look out for our series of webinars on this topic. Future podcast in this series will address the diagnosis, assessment, and treatment of recurrent and chronic pericarditis, and a number of other topics related to inflammatory pericardial disease. Thank you so much for your attention.