Automated Citrate Delivery: Does it Work?
Matthieu LeGrand, MD

Speaker 1:	00:00	And now it's a pleasure to introduce Dr Legrand, we all heard from this morning and he's going to discuss, Automated Citrate Delivery: does it work? I hope so.
Speaker 2:	00:14	Thank you very much, it is a pleasure to be here and after this great talk to discuss the automated citrate delivery, how many of you actually here use a machine ready for automated citrate delivery?, So my conflict of interest
Speaker 2:	00:42	As introduction will be short because you heard about that, we know that citrate works very well to, increase the duration of sation to reduce the risk of citrate loss and for those of you, who already use citrate and you know, that once you have tried citrate it is very complicated to go back to another, and I've heard of the story about, the calcium shortage and I can understand that heparin will be very complicated, especially for the nurses who are used to replace only once every two three days the future.
Speaker 2:	01:26	So the citrate works very well and it works very well, because, it decreases, the ionized calcium, in the citrate. But, is that in line of, with my talk, there is a very short therapeutic interval for the calcium, and the calcium leveled in it as the coagulation in the future and you'll see that you have to have very low level of humite calcium clearly have the coagulation in here, when you look at the coagulation, you'll see the symmetry you'll see that coagulation is inhibited about below open 4 open 35. And then, completely averaged below this target you don't need to be here. And the right target would be enough to average coagulation but not too low. to avoid a citrate overload and citrate high doses nephration, will won't be needed for your, citrate.
Speaker 2:	02:38	So in most protocols, the ionized calcium target sits around open 25 and open 4 especially your targets is a risk of benefits, balance of inhibition of the, ionized Calcium in the citrate, and to reach this target of ionized calcium in the citrate how much citrate you need of course, there is some viability, but most of the time it's around 3 to 4 per liter of blood entering the citrate . And with this target of citrate administration and concentration, you will most of the time, reach target of calcium concentration, in the citrate between open 4 and open at 25. It

means that this is like a short therapeutic interval for calcium. rather short therapeutic interval for citrate.

Speaker 2: 03:39

Below. You want to have a low calcium level enough to inhibit the coagulation and above you will, face some, metabolic consequences and possible accumulation of citrate If you load your patient with a high doses of citrate, which will be a bit more difficult to clear. And here as final introduction for the talk .of course, what we have in mind using citrate are the metabolic consequences of citrate and, citrate goes together with, sodium, especially a high concentration and we talk about 4% citrate and, but it comes along with sodium. In a high load of sodium. And to be short, actually when the citrate is associated with the sodium, we have potential metabolic consequences due to sodium and the metabolic, alcaloses but also with the citrate.

Speaker 2: 04:50

And if the citrate is not well metabolized but it shall cause consequences with metabolic acidosis in these patients.Shortly, you're probably familiar with the Stewart model, Stewart model means that you have equal, amount of anions and cations, in your plasma. And as soon that, an imbalance of strong cations and anions, you will have changes in the strontium difference and inducing, metabolic consequences. the metabolic alcalosis comes from the good metabolizer of citrate, it means that citrate goes to the patient. So secretion is well metabolized mainly by the liver. but then in the consequences of the metabolites of the citrate, have, an acute load of sodium, which goes along with the citrate. And as this, by increasing, the sodium concentration without including the chloride of the patient increase the strontium difference and induce, metabolic alcolosis

Speaker 2: 06:04

So that's the future of good metabolizers of calcium citrate. The metabolic acidosis are rather the consequences of poor citrate metabolizer. And that's the other way around. you don't have a combination of sodium, but you have accumulation, of course, you have a lot of sodium, like before, but you have mostly accumulation of citrate and this increase of ions will decrease a strontium difference induce metabolic acidosis, with, increase of anion gap and decrees of strontium difference. So now, if you want to, avoid the metabolic consequences of citrate you have to know exactly actually which modality since this, paper before very well done review, on the citrate and, how citrate is used for regional anticoagulation.

Speaker 2: 07:10

But to avoid this complications, the metabolic consequences, especially the metabolic alkalosis due to citrate, you need to use

balanced combination of citrate and CRRT solution. What does it mean that, you have to match your,citrate solution to CRRT solution to balance, especially the sodium concentration or if you use a citric acid concentration in the CRRT solution to balance this administration. So there are many already available, commercially available solution, too much as the CRRT solutions to the citrate, the citrate solution you use, in your protocols. And, I won't go through all, but, I'll show you, in my unit actually. I have two units and, we use two different available commercial solution and a machine ready for citrate administration concurrent, industry and, here is one of the protocol ready for the machine and which is using continuous hemodialysis and 4% citrate.

New Speaker: 08:40 it was a ----------for example, we use, once again for the Baxter and the Prisma Flakes., and what I meant is, as mentioned before, and administrating 4% citrate it is 136 mmol liter of citrate loading, which goes along with forward for citrate concentration of sodium in the solution. And if you want to avoid this acute load of sodium, the concentration of sodium have to be balanced, with chloride If you want to avoid the metabolic alcalosis and to avoid this imbalance between load of sodium and chloride concentration of sodium and chloride.

Speaker 2: 09:39 We use this commercially available dialysate solution with a low concentration of sodium to balance with accumulation and load of sodium from this citrate 4% concentration. So during that, actually we don't face many metabolic alkalosis. And if we, see most of the times, easy to to correct if we set correctly the machine, and point which was, addressed before, which is very important actually. if you want to avoid most of the metabolic consequences, you have to be careful of the citrate dose, and the sodium dose you give to your patient. And since the concentration here is completely related to the quality of anticoagulation of citrate of course, if we have to reach this concentration, the higher will be the blood flow in your machine the higher will be citrate delivered to the patients.

Speaker 2: 10:49 And of course, limiting the blood flow. we limit the administration of citrate to your patient. And of course the metabolic consequences, both, because of sodium, administration will be lower, but also on the other way around because the citrate accumulation will be less likely since you give less citrate to your patient and here are the determinant of a citrate load to the patient. And, as I said before, the blood flow is a major, it's a major contributor or the citrate, input to the patient. Of course, the citrate concentration of the solution and the blood citrate target, which should be, titrated based on

ionized calcium concentration in your citrate. And of course, citrate load to the patient would be also, dependent on the clearance from the machine because you give citrate to the patient with a machine, we'll get rid of some of the ciitrate and sodium before, as the citrate goes to the patient.

Speaker 2: 12:01

Here is a simulation, for example, which shows how, modifying every parameter from, your device can affect the citrate load but also the calcium losses, in your citrate. And for example, here, the blood flow, just like I mentioned, for example, so I target my citrate dose at 5 mmol per liter because I realized that was the right concentration to target my calcium concentration of open 30 For example, in my citrate. And,, this leads to a citrate load of 13.39 mmol per hour. If I decide for any reason, to increase my blood flow to 150 per minute you'll see, the citric load which more than double, to maintain this anticoagulation in my citrate

Speaker 2: 13:06

So changing the blood flow makes a big impact on the citrate load to my patient. And then once again, acting on every setting on of my citrate will impact also the clearance of the citrate, but also of course the calcium because the calcium will bind citrate and, citrate and calcium both are very high Cv coefficient and are very easily cleared by the machine either using convective or diffusive, techniques. But, here is an example of continuous hemodialysis and you'll see that about half of my citrate calcium, will be removed, administrated citrate will be removed by, the machine, which means that as soon as you modify your settings, especially the direct flow, the convective flow, if you choose a convective techniques and you impact also the predilution balance of your techniques and all together, that will impact the calcium loss in your citrate which also depends of course on citrate administration you'll see that, many factors impacts the calcium loss.

Speaker 2: 14:36

And so better potentially, the calcium concentration in the blood of your patients, in this setting. Once again for example, if I only change the food removal from your machine, you - increase it from 1 onward to 2 onward meter per hour. and what you see that, you will modify your calcium losses. So therefore you will need to increase your calcium compensation n your device. The other way round, I set my replacement phorate at 2 liter per hour with a citrate dose of 13. with af blood flow of 100. If I decide for any reason, to increase my replacement phorate what's will happen is that I will decrease the citrate load to the patient, but also increases the calcium loss to the citrate and therefore need to increase the calcium compensation, for maintaining the

Speaker 2:	16:08	blood calcium concentration of my patients, together you'll see that every, modification of the setting of your device will impact citrate adminstration the citrate laod to the patient and the calcium lost to the patient. And to be honest, it is complicated to manage all of this parameter together and to maintain, a safe procedure, to the patient why,? I know it's a bit different in US but in France now, in Europe, we, almost only use integrated infusion systems and RCA, dedicated software which, corrects all the citrate administration, the calcium compensation to the settings which have been, decided and based on simulation and estimation of the calcium losses and citrate losses into the effluent of the dialysate? Of the patients.
Speaker 2:	17:15	So it makes it much easier. it decreases the workload for the doctor, for the nurses. And, we have almost never, some side effects of the citrate. And if we do most of the time, a slight, metabolic consequences, which can be easily modified. What can do this automated system is to detect the citrate accumulation so we can anticipate the calcium loss. So we can anticipate what would be the citrate load to the patient, but we cannot, of course, detect using these techniques, as citrate metabolism, in the patient, especially in patient with multiple organ failure. And liver failure is why we still need to monitor patient calcium, level and especially calcium ionized level to detect, potential citrate accumulation and also to detect using a blood catharasis metabolic acidosis due citrate accumulation
Speaker 2:	18:28	So in the future we'll be complete automated system that could be a new future. There has been several papers on that. it was using intermittent dialysis and the calcium concentration was estimated using the ionic dialysance to maintain good anticoagulation together compensate the calcium losses based on the calcium dialysance but even more fancy will be the online monitoring of citrate concentration and calcium concentration. And then we could of course, imagine that a close loop of calcium administration, not only based on estimation of the losses but through observation of the calcium concentration in the machine, but also in the patient and, completely automized, citrates. So I would like to thank you for your attention and, I leave for some questions.
Speaker 2:	19:44	I think we could take a couple of questions and now we are going to have a panel at the end of all three speakers. Is there anyone with a burning question at this time?
Speaker 2:	19:57	Yeah, maybe I could just point out that, you know, you've got to have the citrate flowing all the time. I mean, this is obvious when you're there, but you don't need to keep the calcium

flowing all the time. Changes in ionized calcium take time to become a problem. But if you start the citrate flow while you're, changing bags or something else, then if you end up putting non citrated blood into the machine, you may regret it. So everyone worries about ionized calcium, but it takes some time, takes half an hour to get from satisfactory, done satisfactory, even in the worst of conditions when you're doing CRRT