Mastering cholesterol to optimise CVD prevention webinar series

Taking a holistic approach to lipid disorders (27 July 2023)

Q&A with Professor Jo Blair (JB), Dr Gavin Galasko (GG) and Dr. Sue Kemsley (SK)

Question 1

When should statins/lipid therapy be stopped? Is it purely at a certain age or more related to co-morbidities?

GG: Sue has talked about stopping therapy towards end of life. I think it's important to look at primary prevention and secondary prevention. There's very good evidence of benefits of secondary prevention, with people who have had cardiac events – heart attacks, strokes – with data well beyond the age of 75 and older. So, we know that it reduces events, improves outcomes and in otherwise healthy people with no significant issues of frailty and end of life care, secondary prevention should be continued. We treat lots of elderly people who present with heart attacks with high dose statins and there's good data to support that. I think primary prevention, there's less evidence of benefit as you hit high 80s and if we are looking at reducing medications, then certainly for primary prevention, that is quite reasonable. If there are frailty issues, tablet issues, comorbidities, cancer, end of life, then again, it's reasonable. It's a prevention therapy; there's less prevention 'bang for your buck', in primary prevention. So, I don't have a cut off; I think treat everyone individually. Secondary prevention; certainly there's evidence supporting it in more elderly populations. Primary prevention there's probably slightly less evidence and I'd be quicker to consider that if we are looking at a de-escalation plan at that stage.

Question 2

Can injectable lipid therapies be used in children?

SK: Easy answer; no. Not yet. I think there is some research ongoing in that regard, but no, not at present.

GG: There's some data, so I think you're right. I think Alirocumab is licensed for only over 18s. I think Evolocumab has got data for 10 [years] and above. I think America certainly can use that; there's a slight difference. We didn't mention PCSK9 inhibitors as much today, but that's another injectable therapy that has benefits in secondary prevention and in FH and that does require secondary care involvement. That's another indication for referral to secondary care if we are looking at using those agents.

SK: We've been working on this regionally, and at present we've not written it into our guideline that we will use PCSK9 in that age group. But it is in the pipeline, but I think at the moment, certainly in our region we are not looking to use them.

Question 3

How would you manage a child with an abnormal lipid profile who doesn't test positive for FH on genetic testing?

GG: Professor Blair covered this really well. Her tool was fantastic [see webinar slide deck for details]. First thing is to rule out secondary causes. So why have they got high cholesterol? Is this an underlying condition? Is this diabetes, nephrotic syndrome, hypothyroidism; those sorts of things. Definitely don't just jump to a conclusion. Make sure that we are not dealing with an underlying condition. Look at lifestyle, look at diet, look at exercise, look at weight; are there other things here that can be contributing? If it's still very high and I think the cut-off that we will take is an LDL-C of 5mmol/L, I think it's still a clinical diagnosis of FH and that's fine. If it's an LCL-C between 4mmom/L and 5mmol/L, then if there's a strong family history, again, you can use a clinical diagnosis and offer treatment.

We don't know everything yet about genetics. One exciting development in Blackpool is that we're part of the Manchester Biomedical Research Centre. This is basic science; it's a really exciting opportunity of translational research and one of the parts of that for all biomedical research centre sites is the NIHR BioResource data set. The BioResource dataset is looking at these conditions and finding underlying causes, other genomics, other genetics and there's going to be a lot of polygenetics in FH; it will be familial and yet we've not found a single gene defect and there's a lot of ongoing work. But we hope that the lipids cohort from Blackpool Teaching Hospitals will be part of the UK BioResource and then we can start looking at these other polygenic factors to try and find other reasons. So, they are basically acting as FH, but you don't find a single gene defect because it's multiple genes that are contributing. It's a quite exciting development in Familial Hypercholesterolemia. It's the commonest genetic abnormality in the country – about 1 in 250 people might have it – which is more than any other condition, more than Cystic Fibrosis, but there is also polygenic FH and that might be equally as prevalent and we are only beginning to scratch the surface. There is a long way to go with diagnosing FH I would say.

Question 4

My nurses are already pressed for time doing childhood immunisations. How long does it take to perform a point of care test to screen a baby for FH?

SK: We've been doing child parent screening in my own practice for about 12 months now, and my nurse does the immunisation and the heel prick test in 20 minutes. I have sat in with her actually and watched her do it. She's absolutely amazing. So, the heel prick test is really brief to do. The immunisation takes much longer. The point of care test takes seven minutes, during which time immunisation happens and so it's very swift and surprisingly easy to do.

Question 5

Am I right in thinking that heel prick testing in all children goes against the current advice against screening in children?

SK: So, what Professor Blair was talking about [see webinar slide deck for details] was the government guidance on whether screening should occur in children, which was the 2020 guideline. NHS England have commissioned the child-parent screening programme as a pilot to roll out across the UK, because there is good evidence to suggest that screening in children does improve outcomes. But because FH is under diagnosed, there's much still to be learnt about it, so we are still on a huge learning curve. So, the answer is child-parent screening is in pilot phase; it's NHS commissioned. The position statement from 2020, probably will be updated in light of the evidence of child-parent screening, which is due to report next year.

Question 6

What would you advise if patients are on Simvastatin 80mg, appear intolerant to other statins and are stable on this dose (given that MHRA warn to avoid this dose)?

GG: It's quite rare that they are on that, having tried lots of other statins, and they are up to 80mg. Most of the people on 80mg have been on it for a long time and were put on it from the original NICE guidelines, where Simvastatin was really the only cheap statin and NICE, because of cost reasons, said to start on Simvastatin 40mg and go up to 80mg. So some people are on it from then, for historic reasons and they may not have tried the other statins. I do move people who truly have only tried one statin and it's Simvastatin, I would probably move them to Atorvastatin, [Atorvastatin] 40mg is the equivalent dose because there are side effect profiles [with Simvastatin 80mg]; there is a higher risk of Rhabdomyolysis, a higher risk of muscle aches. If they have not tried the other statins, I probably would change them…I may or may not. If they have tried all the others though and that's the one for them, and they are on that, then that's fine. If they are well on that, I probably wouldn't do anything about it. We might drop it. We need to look very carefully at drug interaction. So, the problem is probably Simvastatin on its own in most people will possibly be ok. But once you take any drug that increases levels in the blood or gets rid of excretion of Simvastatin or affects metabolism, then you have side effects. So, you might even think about dropping it and adding an alternative such as Ezetimibe or things like that. So, it's case by case; have they actually tried other statins – they may not have done – do we want to continue them on this knowing that calcium antagonists might increase the effect, or other drugs may increase the effect? I'd try and get them off the 80mg and think about how we could do that.

SK: I absolutely agree. I don't think there are many patients left on Simvastatin 80mg, or there shouldn't be. But I guess the odd one could be knocking around or end up on it. I think if you try to prescribe on primary care systems now, you know that all the bells ring telling you not to because we shouldn't be using 80mg because of the risk profile. I probably would be looking to use Simvastatin 40mg and Ezetimibe instead, if we were left with just using Simvastatin. I guess if somebody absolutely wanted to stay on it and they were well, and didn't want to do anything else, then of course it's risk management for the long term in terms of using other medications alongside that.

Question 7

If the CVD risk is under 10% but the patient wants to have lipid therapies, should I prescribe, and if not, when should their lipid profile be repeated, and risk recalculated; is it still five years?

SK: So, if CVD risk is less than 10%, NICE currently say, if it's hovering just below 10% – and actually a CVD risk calculator may underestimate risk for some people, particularly young people who have other risk factors – then we can still start lipid therapies. It is entirely appropriate for some people to do that. You can look at QRISK®-lifetime, which will give you a trajectory of when they will cross that 10% risk. I think that's really useful to do because repeated lipid profiles are likely to be the same, give or take. Unless their risk factors develop otherwise; so they develop hypertension or diabetes or something else that will significantly push up their risk, or start smoking, which I guess is unusual, then using QRISK®-lifetime will tell you when they are going to cross that threshold without saying we'll do your lipid profile again next year on an ad hoc basis. So, I would use that as a way to predict risk.

GG: There's some draft guidelines for 2023 and I don't think they are out yet, but those are quite interesting and pertain to this question. What they've said is that, yes, above 10% it's recommended and we should follow the pathways. But if there are people who are keen to take statins and their risk is below 10%, and after informed discussion of benefits and risks, then NICE approves it and it's cost effective and they've calculated that with a 5% risk, if you treat a thousand people with statins you will protect against 20 events over 10 years. At 10% it's about 40; it's about double. So, for minimal cost, NICE are going to change their guidelines and say, yes, above 10%; everyone. But below 10%, there may be other factors that haven't been taken into account that you could take into account. Some people say, measure LPA to see if that's high, as another factor. But it will be up to people.

But that's going to, maybe, lead to social economic uptake and it's probably the worried well who will ask to go on it younger. We do need to see what the guidelines are like when they come out. But they are probably going to go back and back and back. I think the QRISK®-lifetime life score is very helpful because you can say, yes, you don't quite hit it now but you're going to hit it in three years' time. And also you say it's 10% now but look, it's going to be 15% in five years' time; please start a statin. It's quite useful to show patients, to realize that starting now is a good idea; like saving for a pension. Starting now for lipids is a good idea. We saw it for young people and FH and if you treat people from the age of 10 for FH, although we didn't see a lot of data, there's good data now that life expectancies are normal and cardiac events are markedly reduced, 75%+ reduced. It's a tremendous treatment and the earlier you start the more the cumulative benefits. So, I think the guidelines will change.

Question 8

How many different statins would you advise to try before one would consider it to be statin intolerance?

GG: All of them. It's a good question. It's really up to patients as well and some people, after one they are just going to refuse to take statins and some people will try the [other] statins. We try in the clinic to talk them through the side effects; they shouldn't be asking 'what are they?' Statins are the

best drugs. They've got the best data, they're taken by the most number of people, there's tons of outcome data, they lower your cholesterol very well. They have other effects; they stabilize plaque, they don't just lower cholesterol. They seem to work above and beyond cholesterol lowering. So, they are amazing therapies. Yes there can be people with side effects; yes there can be people with side effects on all of them. We certainly will try Simvastatin, Atorvastatin, Rosuvastatin, we may not try Pravastatin as it's quite a weak statin and we probably don't try Fluvastatin. I would say those three are the three that we would probably want to try them on. Anaphylactic reactions are very rare and there might be issues of class effect. But we would generally try them on those three before thinking about saying that they are truly intolerant.

Question 9

[In relation to Professor Blair's description of the patients visiting her clinic.] It's interesting to hear that FH affects children in the least deprived deciles. Do either of you have any idea as to the possible reasons for this?

SK: I don't think FH affects children in the least deprived areas the most. I think we are picking it up in those areas the most because the parents are able to articulate that to us. Whereas perhaps people in areas of deprivation don't. I think that Gavin can probably talk more about the fact that genetics don't gravitate to deprivation. It's just that patients will not come and flag it to us.

GG: I think it's more about who attends screening; who has bloods taken, who wants to know 'I've got this high cholesterol, could it be in my family?' It's access to healthcare and access to testing. It's more a measure of access than a measure of prevalence. There is evidence around the world; there are different frequencies in different populations, that is true, there are genetic differences. Unfortunately, part of the argument is we probably we don't know the prevalence in some communities as well as we know the prevalence in other communities. So certainly, white Caucasian, we know the prevalence, but maybe we don't actually know the prevalence that well in other communities. So we do need to get these big databases and big bio resources and get ethnic minorities represented there, to find out what the needs and the differences are. They may have different genetic abnormalities as well. So, it's a good question. Maybe there are some subtle differences in prevalence, but I think the point was that its more about access to healthcare than underlying prevalence of disease.

IA addendum (question not addressed during webinar due to lack of time):

Question 10

Can Bempedoic acid be used as a monotherapy?

NHS Cheshire formulary:
https://www.cheshireformulary.nhs.uk/chaptersSubDetails.asp?FormularySectionID=2&SubSectionRef=02.12&SubSectionID=A100&drugmatch=6901#6901

NHS Pan Mersey Area Prescribing Committee:
https://www.panmerseyapc.nhs.uk/recommendations/ and
https://www.panmerseyapc.nhs.uk/media/2465/bempedoicacid_hypercholesterolaemia.pdf

Lancashire and South Cumbria Medicines Management Group:
https://www.lancsmmg.nhs.uk/medicines-library/bempedoic-acid-without-ezetimibe/