Evening Medical Update: Insights in Endocrinology and Diabetes
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Diabetes – updates in drugs and pumps – Dr Balakumar Muthukrishnan

What is your view dosage of empagli – is 10mg or 20mg a day the best dose?
The difference in glycaemic control between empagliflozin 10 mg and 25 mg is small but significant. The EMPE-REG outcome trial showed that the difference in HbA1c 12 weeks after starting 10 mg and 25 mg dose was -0.54 % and -0.60% respectively. This small difference persisted in week 94 (-0.42 and 0.47%) and on week 206 (-0.24 and 0.36%). So consider increasing the dose to 25 mg daily after 3 months if renal functions remain stable and eGFR >60. Stay on 10 mg if eGFR drops less than 30.

Thank you for clarifying the most appropriate use of antidiabetic drugs. Following lifestyle and metformin, in very obese patients, would you consider GPL-1 over a Gliflozin?
Weight loss is common with GLP-1 RA. Weight loss between 5-10 kg is possible depending upon the agent used. Semaglutide is more effective in causing weight loss than others in this group. SGLT2 inhibitors can also lead to sustainable mild reduction in weight up to 3 kg. I would consider GLP-1 RA, preferably semaglutide first. But consider other factors such as oral route vs injections, need for education for s.c. injections and potential side effects when deciding which one to start first. Both GLP-1 RA and SGLT2 inhibitors can also be used together.

How can we approach DKA in someone with a pump? Is it a matter of stopping the pump and how do we restart it?
Remove the pump if the patient is unwell and follow DKA protocol. Once the patient is well enough to self-manage with pump, pump therapy can be restarted. Consider overlapping the pump (start basal rate) and i.v. insulin therapy for a period of time before stopping i.v. insulin and let the patient start the boluses.

Hyponatraemia – what to check, when and why? – Dr Owain Leng

What is your approach to anti-depressant induced hyponatraemia in an acute medical admission?
This is a good question and a common problem. It depends on a variety of factors, including the degree of biochemical hyponatraemia and whether there are any other likely drivers of SIADH. The severity and timeline of the mental health issues will also have a bearing. If there is a complex psychiatric history or recent cause for concern regarding mental health, I would have a low threshold for involving the psychiatry team in decisions regarding whether antidepressants can be safely discontinued or whether a switch to an alternative agent is warranted.

In general, unless there is a very strong indication to stay on the antidepressant in question, I would favour stopping the antidepressant and monitoring the sodium concentration. If the [Na] is <125, I would favour stopping the antidepressant immediately and fluid restricting. If the patient has developed SIADH on an SSRI or venlafaxine, it might be worth their considering changing to a tricyclic antidepressant, a MAOI or mirtazapine as these agents are less prone to cause SIADH, but whoever is looking after their mental health will need to weigh the potential increased risk of adverse effects or overdose (particularly with the TCAs).

How long after stopping diuretics would you recommend re-checking the urinary sodium and osmolality?
The urine sodium can still provide some useful information when on diuretics. If the urine sodium concentration ≤30 mmol/l suggests low effective arterial blood volume, even in a patient on diuretics. In terms of when to re-check the urine sodium and osmolality, that would depend on the clinical picture. If the serum sodium is gradually normalising after discontinuation of the culprit diuretic (most often a thiazide diuretic), there is probably no need to repeat urine studies. Traditional teaching has generally been that diuretics can still be having residual effects for up

to two weeks, but this effect dissipates with time. Practically speaking, if the sodium is not correcting as expected with stopping the culprit agents, I tend to re-check the urine studies every 2-3 days.

Can we measure ADH directly for SIADH diagnosis?
In short, we do not measure ADH/vasopressin for this purpose. ADH levels are very variable depending on a multitude of factors, and has a very short half-life (~20 minutes), and so it makes it tricky to measure. When we want to measure ADH, we tend to measure co-peptin which is a by-product of ADH production. However, it is not the "absolute" amount of ADH produced that is relevant here, it is the level of production relative to the serum osmolarity/tonicity. This is more elegantly (and conveniently) demonstrated by evidencing inappropriately concentrated urine in the context of dilute serum - from which we can infer that whatever the absolute level of ADH production is, it is inappropriately high for that situation.

Would you agree (particularly medication induced) SIADH is under-recognised? Should we be more aware of SIADH when prescribing from these common drug groups (such as antidepressants, anticonvulsants, antipsychotics, antinflammatories)?
This is again a great question.

Depending on how you look at it, I believe SIADH is both under- and over- recognised.

I am sure you are right that perhaps there is a lack of consideration of the possibility of SIADH when prescribing medication. This is particularly true of those at greater risk - particularly the elderly and those on multiple drugs which can perturb sodium balance. I think particularly in these cases, a re-check of U&Es a couple of weeks after starting a new medication could be very helpful.

But also, I think there is sometimes a rush to prematurely label hyponatraemia as SIADH, at least in the inpatient population. I quite frequently see people who have been treated as SIADH without having had important conditions excluded (e.g. adrenal insufficiency) or without having had the prerequisite biochemistry tested.

Antenatal metabolic disease – Professor Rebecca Reynolds

Is maternal Metformin during pregnancy an additional independent risk factor for child obesity?
This is a very interesting question. Available evidence from systematic reviews would suggest 'yes' - see Tarry-Adkins et al., 2019 PMID: 31386659 - but more follow-up is clearly needed

Are the metabolic effects of combine hormonal contraception, and their reversibility to normal metabolism after stopping, completely understood? Should we measure/guarantee more good micronutrient levels (e.g. zinc magnesium), before trying placenta crossing medication?
At the moment we don't recommend measuring any micronutrients prior to conception (as measurements need to be carefully timed to be interpretable) but we would recommend a healthy lifestyle when planning pregnancy

Is there any evidence for the effectiveness in interventions to address obesity in women who are attending pre-conception in infertility clinics, where the obesity may have already been identified?
This is a very interesting question and pertinent as women who are attending pre-conception infertility clinics may be more motivated to make changes. My colleagues in Amsterdam are conducting some studies in this space and we look forward to their findings.