East Surrey CCG, Guildford & Waverley CCG, North West Surrey CCG, Surrey Downs CCG, Surrey Heath CCG,

Guidance on Metformin Titration to reduce gastrointestinal (GI) side effects

The evidence:

NICE guidance (5) and local guidelines (4) state that metformin should be considered as the drug of first choice in overweight or obese individuals with type 2 diabetes. (Metformin can also be effective in non-overweight individuals so it should be considered in this group too).

Evidence from the UKPDS showed that metformin reduces macrovascular complications and death. It is therefore the hypoglycaemic agent of preferred choice for all patients, particularly those who are overweight (6).While blood glucose control is important in type 2 diabetes, UKPDS showed that tight control of blood pressure was more effective in preventing diabetes-related endpoints and deaths. MeReC states that "Cardiovascular disease is the leading cause of morbidity and mortality in patients with type 2 diabetes, and managing cardiovascular risk factors is at least as important as managing blood glucose." (6)

For Surrey CCGs (excluding NWSCCG) the cost of metformin MR for the financial year 2014/15 was over £455,000 compared to £406,000 for 2013/14. The % of metformin MR of all metformin products for 2014/15 was 42%. (This varies across the CCGs from 39% to 45%). Approximately £180,000 could have been saved across the four CCGs if 75% of the metformin MR had been prescribed as Metformin.

Side Effects

Problems with side effects limits the use of metformin in some patients. The incidence of GI side effects is highest just after initiation and diminishes over time (2). Diarrhoea may be caused due to altered absorption of bile salts. Disturbances tend to be transient and will resolve quickly when the dose is lowered. Gastrointestinal (GI) side effects are experienced in up to 25% of patients **but less than 5% of patients cannot tolerate metformin (3)**.

Dose Titration

Educate patients – ensure patients are aware of the side effects of metformin and understand that often the side effects diminish over time. Effective care involves a partnership between patients and professionals, and all decision making should be shared (5).

- Careful dose titration is recommended to try to limit the problems with side effects.
- The dose should be titrated slowly upwards by 500mg every 2 weeks on the basis of blood glucose (fasting) levels to a maximum usual dose of 1g twice daily (however the maximum dose is 3000mg (3g) daily. (1)
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A typical dosing regimen would be;

500mg (One tablet) once daily for weeks 1 & 2

500mg twice daily for weeks 3 & 4

1g in the morning and 500mg in the evening for weeks 5 & 6

1g twice daily for weeks 7 & 8

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- Titration should be completed over a 2 to 3 month period and then the HbA1c (glycosylated haemoglobin) should be checked. A slow increase of dose may improve gastrointestinal tolerability.

- If metformin is increased and not tolerated, the dose should be reduced back to the previously tolerated dose and a slower titration attempted.

- At the tolerated dose if HbA1c is not reduced add in another oral hypoglycaemic drug as stated in NICE guidance. (5)

- Consider a trial of metformin MR if GI side effects are severe to prevent the person discontinuing metformin. Document and/or read code intolerance to immediate release metformin. If no benefit in GI side effects is seen, metformin MR should be stopped and an alternative oral hypoglycaemic agent commenced.

Also remember……

- Monitor renal function regularly (6 monthly) and more often in those with reduced function.

- Prescribe metformin with caution for those at risk of a sudden deterioration in renal function and those at risk of eGFR falling below 45 ml/minute/1.73-m2

- Reduce the dose of metformin if the serum creatinine exceeds 130 micromol/litre or the estimated glomerular filtration rate (eGFR) is below 45 ml/minute/1.73-m2.

- Stop the metformin if the serum creatinine exceeds 150 micromol/litre or the eGFR is below 30 ml/minute/1.73-m2.

- To clearly document metformin intolerance in the patient's records.

References

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