Contraindications to metformin

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Metformin hydrochloride is the first line oral hypoglycaemic agent in Australia for the treatment of type 2 diabetes mellitus. It is the medication with the best evidence base for preventing macrovascular complications (1).

However, it is not without problems. Lactic acidosis is a life threatening complication. Luckily, it is fairly rare with an estimated number of cases of 0.03 per 1000 patient years (or 1 case per annum in 30,000 patients on metformin) (2) (3). The mortality of lactic acidosis is close to 50%.

I find the follow guide useful (adapted from the somewhat alarmist editorial in the Medical Journal of Australia by Nisbet, Sturtevant and Prins) (4):

Renal dysfunction

- *Absolute cut-off*:
  - serum creatinine > 150 nmol/L *or*
  - creatinine clearance < 30 mL/min
- Use metformin with extreme caution:
  - creatinine clearance: 30-50 mL/min

Acute illness that alter renal function

- *For example*: dehydration, shock and septicaemia.
- Cease metformin completely until resolution of illness and renal function has been shown to be normal.

Acute illness that tissue hypoxia and acidosis

- *For example*: acute myocardial infarction, pulmonary embolism, acute cardiac failure.
- Significantly reduce the dose of metformin or cease altogether.

Iodinated contrast agents

- Withhold metformin 48 hours prior to procedure.
- Recommence 48 hours after the procedure after renal function has been shown to be normal.

Be aware there is controversy

It should be recognised that there is some controversy surrounding some of these guidelines. Although it is true that lactic acidosis is probably more common that actually recognised and diagnosed (4), it also means that it is less lethal.

As recognised by Nisbet et al., a large proportion of patients on metformin have contraindications to the medication. This fact was discussed in an opposing point of view in a commentary in the Canadian Medical Association Journal by McCormack, Johns and Tildes, who pointed out that despite this, lactic acidosis (fatal or otherwise) is extremely rare (5). The benefits in macrovascular endpoints in using metformin must be weighed against the very small risk and McCormack, et al., conclude that "the evidence at present suggests that the use of metformin in patients who are over the age of 80 years, have congestive heart failure or have renal insufficiency leads to a benefit that far outweighs the potential harm".

Reference articles

(1) Twigg, S. Individualising initial therapy for hyperglycaemia in type 2 diabetes. *Medicine Today (Update on diabetes). September 2005*.

(2) Tam, M. How to start oral hypoglycaemic therapy [electronic article]. *The Medicine Box.* Last updated 19 August 2006. [Link]

(3) Diaformin (metformin hydrochloride). *MIMS Online*. Last updated: 20 January 2006.

(4) Nisbet J., Sturtevant J., Prins J. Metformin and serious adverse effects [editorial]. *MJA 2004; 180 (2): 53-54* [download PDF :: 53 Kb]

(5) McCormack J., Johns K., Tildes, H. Metformin's contraindications should be contraindicated. *CMAJ. August 30, 2005; 173 (5)*. [download PDF :: 132 Kb]

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