Metformin in patients with moderate renal impairment: reduce the dose

The European Medicines Agency recommends reducing the dose of *metformin* for diabetic patients with moderate renal impairment. To reduce the risk of lactic acidosis, it is important to monitor the renal function of patients taking *metformin* and to pay attention to interactions.

Metformin, a biguanide, is the first-choice oral glucose-lowering drug in type 2 diabetes. In this situation, it appears to reduce mortality and prevent some of the complications of diabetes, while the adverse effects it provokes are usually acceptable. The adverse effects of *metformin* mainly consist of gastrointestinal disorders, which are frequent, and macrocytic anaemia. It can also provoke lactic acidosis, a rare but sometimes fatal adverse effect (1,2).

Lactic acidosis with metformin: various risk factors. *Metformin* is excreted unchanged in urine. Lactic acidosis is an adverse effect linked to *metformin* accumulation. It can occur in patients with renal failure and in situations that contribute to the development of renal failure, such as: dehydration; acute disease; and the use of drugs that are nephrotoxic or can provoke prerenal failure, such as nonsteroidal anti-inflammatory drugs, diuretics, angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARBs) or *aliskiren*. Other situations sometimes cause lactic acidosis in *metformin* users, in particular: acute alcohol intoxication, heart failure, respiratory failure, recent myocardial infarction or hepatic failure (1-4).

Metformin in patients with moderate renal impairment: no consensus. In patients with moderate renal impairment (i.e. whose glomerular filtration rate estimated by creatinine clearance is between 30 ml/min and 60 ml/min), there is no consensus over whether it is best to discontinue *metformin* or to continue *metformin* therapy at a lower dose (4). As of early 2017, in France, both of these options are suggested in the summaries of product characteristics (SPCs) for various *metformin*-containing drugs (5).

According to the EMA doses for patients with moderate renal impairment should be reduced. In late 2016, given the disparities between SPCs within the European Union, the European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) conducted a review of clinical guidelines and data from the literature. It concluded that *metformin* has a positive harm-benefit balance in patients with moderate renal impairment, provided it is used at a lower dose: a maximum of 2000 mg per day when the glomerular filtration rate is between 45 ml/min and 59 ml/min, and a maximum of 1000 mg per day when it is between 30 ml/min and 44 ml/min. The CHMP recommended that *metformin* should remain contraindicated in patients with a glomerular filtration rate less than 30 ml/min (3,6).

In practice To minimise the risk of *metformin* overdose, attention should be paid to drug interactions, with regular monitoring of the patient's kidney function, and more frequent monitoring in high-risk situations. For patients with moderate renal impairment, if the choice is to continue *metformin* therapy, it makes sense to reduce the dose.

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