New drugs

Terlipressin

Approved indication: hepatorenal syndrome type 1
Lucassin (Ikaria)
vials containing 0.85 mg powder for reconstitution
Australian Medicines Handbook section 10.6.3

Hepatorenal syndrome occurs when hepatic failure is complicated by renal failure. It often develops in patients with decompensated cirrhosis and severe ascites. Type 1 hepatorenal syndrome develops over a couple of weeks and the mean survival time is also about two weeks.

The kidneys are thought to fail because of the changes in vascular resistance induced by liver failure. There is severe vasoconstriction of the renal arteries. The best treatment is liver transplant, but there is a need to manage the hepatorenal syndrome while a transplant is being considered.

One strategy for improving renal blood flow is to reduce blood flow in the splanchnic circulation. This effect can be achieved with vasopressin (antidiuretic hormone), but this risks mesenteric ischaemia.

Terlipressin is a long-acting analogue of vasopressin, given by slow intravenous injection. Its vasoconstrictor effect comes on more slowly and it has a pharmacological half-life of about six hours. As the vasoconstrictor effect is mainly in the splanchnic circulation, terlipressin has been used in the treatment of variceal bleeding.

A systematic review included three randomised trials of terlipressin in patients with hepatorenal syndrome. Terlipressin increased creatinine clearance and urine output. Only five of the 25 patients given terlipressin died compared with 15 of the 23 patients in the control group.1

A later pooled analysis aimed to find out if increases in blood pressure improved renal function. The 21 trials of vasoconstrictors for hepatorenal syndrome included 15 studies of terlipressin. An increase in mean arterial pressure was associated with a decrease in serum creatinine, but had no significant effect on urine output.2

A decrease in serum creatinine was used to assess the reversal of hepatorenal syndrome in some of the eight randomised controlled trials included in another systematic review. Terlipressin was significantly more efficacious than placebo. The syndrome was reversed in 55 of 117 patients given terlipressin and 14 of 117 patients given placebo. Blood pressure increased and urine output was significantly higher.3

Giving an intravenous vasoconstrictor can cause hypertension, and arrhythmias may occur. Terlipressin should not be used in patients with unstable angina. Other adverse effects include myocardial ischaemia, necrosis at the injection site, vomiting, diarrhoea and abdominal pain.

The effectiveness of terlipressin is not completely clear. Many patients will not respond. Although terlipressin may improve survival, the larger systematic review did not have enough data for a meta-analysis of survival.3 Assessment of the trials is further complicated by the use of different doses of terlipressin and the role of other treatments such as albumin. Two small studies found no difference between terlipressin and noradrenaline.3 Few patients survive without a liver transplant.

REFERENCES


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The T-score (T) is explained in ‘New drugs: T-score for transparency’, Aust Prescr 2011;34:26–7.