EDITORIAL

Should sertraline be used in CKD patients with depression?

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SERTRALINE IS INEFFECTIVE IN PATIENTS WITH CHRONIC KIDNEY DISEASE (CKD) AND DEPRESSION, a randomised controlled trial, from the USA, has found.[1]

Patients with stage 3, 4 or 5 non-dialysis-dependent CKD were screened for depression in primary and secondary care settings. Those with major depressive disorder, diagnosed by structured diagnostic interview, were invited to participate in the trial.

A total of 201 participants, mean age 58.2 years, 27% female, successfully completed a one-week placebo run-in period and were randomised to receive either sertraline, at an initial dose of 50 mg daily, or placebo. Eight patients left the trial before the first follow-up assessment and were excluded from the primary analysis. The sertraline dose was increased at two weekly intervals according to tolerability and response, up to a maximum dose of 200 mg daily. Depressive symptom severity was measured at baseline, during and at the end of the 12-week intervention using the 16-item Quick Inventory of Depression Symptomatology in the clinician rated format (QIDS-C16). This tool has been validated for depression screening and shown to be independently associated with outcomes in patients with CKD.

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The QIDS-C16 assesses the severity of the nine DSM-IV diagnostic criteria. Each item is rated from 0 to 3 giving a total score ranging from 0 to 27.[2] At baseline the mean QIDS-C16 score was 14.0 in the sertraline group (n = 97) and 14.1 in the placebo group (n = 96). These scores suggest moderate depression (QIDS-C16 score range 11-15). However, when compared with the gold standard depression severity measurement, the 17-item Hamilton depression rating scale, the QIDS tends to overrate the severity of depression.[2] The median achieved sertraline dose was 150 mg daily.

At study exit, the mean change in the QIDS-C16 score was -4.1 in the sertraline group and -4.2 in the placebo group; between-group difference 0.1 (95% CI: -1.1 to 1.3). Both nausea/vomiting and diarrhoea occurred more frequently in the sertraline than in the placebo group; between group differences 12.3% (95% CI: 1.9-22.6%) and 10.3% (95% CI: 2.7-17.9%) respectively.

The inclusion criteria were changed early in the study to exclude patients with CKD 3a (eGFR 45-59). Consequently only 11% of the participants had CKD 3a and the negative findings of the study may only be applicable to those with CKD 3b-5 (eGFR $\leq$ 44).

Current guidelines recommend SSRIs as the antidepressants of choice in CKD.[4,5] However, patients with moderate to advanced CKD have generally been excluded from previous antidepressant trials and this is the first large randomised placebo controlled trial to investigate the safety and efficacy of SSRIs in CKD patients. SSRIs undergo hepatic oxidative metabolism but their potentially toxic metabolites are excreted mainly by the kidneys. Therefore, CKD patients may be at increased risk of side effects such as arrhythmias, bleeding and gastrointestinal side effects.[4]

Sertraline was chosen for this trial as its active metabolite, N-desmethylsertraline, is further metabolised to an inactive form before renal excretion. It is therefore considered to be relatively safe and no dose adjustment is recommended. Particular care should be taken with citalopram as its active metabolite may cause QTc prolongation and torsades de pointes; the starting dose should be 10 mg daily and it should not be used if the eGFR is less than 20 ml/min.[4]

This study suggests that the prescription of sertraline, and indeed any SSRI, to stage 3b-5 CKD patients with depression can no longer be justified. CBT is probably the best option and there is some evidence of its efficacy in end-stage CKD patients.[4]

The study authors conclude: 'Future studies need to explore whether non-SSRI medications or nonpharmacological therapies can result in improvement in depressive symptoms among patients with non-dialysis-dependent CKD, who are at a disproportionately higher risk for depression and its complications than the general population.'

REFERENCES
1 Hedayati SS, Gregg LP, Carmody T et al. Effect of sertraline on depressive symptoms in patients with chronic kidney disease without dialysis dependence. The CAST randomised clinical trial. *JAMA* 2017;318:1876-90
2 www.ids-qids.org
3 NHS Quality Improvement Scotland. Assessing the validity of the PHQ-9, HADS, BDI-II and QIDS-SR16 in measuring severity of depression in a UK sample of primary care patients with a diagnosis of depression. Aberdeen. 2011
4 Hedayati SS, Yalamanchili V, Finkelstein FO. A practical approach to the treatment of depression in patients with chronic kidney disease and end-stage renal disease. *Kidney Int* 2012;81:247-55
5 National Institute for Health and Clinical Excellence. CG91. Depression in adults with a chronic physical health problem: treatment and management. NICE. London. 2009