

The authors acknowledge that the results may have been caused by channelling bias e.g. venlafaxine may have been more likely to be prescribed to patients at increased risk of suicide (as it is recommended as a third-line treatment for resistant depression) whereas tricyclics may have been less likely to be prescribed (because of their toxicity in overdose). They tried to reduce this bias by adjusting for attempted suicide at baseline, but were unable to adjust fully for depression severity.

NICE recommends generic SSRIs as first-line treatment for depression. For those who do not respond adequately, NICE recommends switching to either a different SSRI or a 'better tolerated newer-generation antidepressant' i.e. mirtazapine.

If patients still do not respond, third-line treatment with venlafaxine, a tricyclic or an MAOI can be considered.³

It is unclear how the results of this study should be interpreted. However, as the risk of suicidal behaviour associated with antidepressant use appears to be strongly age dependent, I would suggest that we avoid prescribing mirtazapine and venlafaxine to young adults (under 25 years).⁴ Lofepramine is thought to have a very low toxicity, comparable with that of the SSRIs,⁵ and may be preferred to mirtazapine as a second-line treatment.

Suicide rates were highest in the first 28 days after starting treatment: if we do prescribe mirtazapine or venlafaxine, we should monitor patients closely during this initial period.

DR PHILLIP BLAND

● **Coupland C, Hill T, Morriss R et al. Antidepressant use and risk of suicide and attempted suicide or self harm in people aged 20 to 64: cohort study using a primary care database. *BMJ* 2015;350:h517 doi:10.1136/bmj.h517**

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Cardiovascular disease

Does renal denervation improve BP control in resistant hypertension?

Renal denervation plus a standardised stepped care antihypertensive treatment (SSAHT) regimen reduced ambulatory blood pressure more than the drug regimen alone in the DENERHTN trial, published in the *Lancet*.

The study was a prospective, open-label randomised controlled trial with blinded endpoint evaluation in patients, aged 18-75 years, with resistant hypertension. It was carried out in 15 French tertiary care centres specialising in the management of hypertension.

Patients received indapamide 1.5 mg, ramipril 10 mg (or irbesartan 300 mg), and amlodipine 10 mg daily for four weeks to confirm treatment resistance by ambulatory blood pressure monitoring before randomisation.

Patients were then randomly assigned to receive renal denervation plus SSAHT or SSAHT alone as a control group. The stepped medication regimen involved sequentially adding spironolactone 25 mg per day, bisoprolol 10 mg per day, prazosin 5 mg per day, and rilmenidine 1 mg per day from months two to five if home blood pressure was more than or equal to 135/85 mm Hg.

The primary endpoint was the mean change in daytime systolic blood pressure from baseline to six months measured by ambulatory blood pressure monitoring. The authors also

analysed safety outcomes such as the incidence of acute adverse events following the renal denervation procedure and the change in renal function, by eGFR, from baseline to six months.

There were 101 patients with completed endpoints (48 in the renal denervation group, 53 in the control group).

The mean change in daytime ambulatory systolic blood pressure at six months was:

- -15.8 mm Hg (95% CI: -19.7 to -11.9) in the renal denervation group
- -9.9 mm Hg (95% CI: -13.6 to -6.2) in the group receiving SSAHT alone
- This represented a difference of -5.9 mm Hg (95% CI: -11.3 to -0.5; $P = 0.0329$)

The number of antihypertensive drugs used was similar between the two groups as was drug adherence at six months.

There were three minor renal denervation-related adverse events and a mild and similar drop in eGFR in both groups.

Renal denervation has rather fallen from grace as a strategy for the management of resistant hypertension. This is largely due to the disappointing results from the SYMPLICITY HTN-3 randomised trial which failed to show a reduction in systolic blood pressure with renal denervation when compared with medical therapy alone.

The DENERHTN trial provides further hope for supporters of this interventional therapeutic option in the battle against resistant hypertension.

The authors conclude that renal denervation plus a stepped care antihypertensive treatment regimen reduces ambulatory blood pressure more than the same drug regimen alone at six months. They postulate that this may contribute to a reduction in cardiovascular morbidity if maintained in the long term after renal denervation.

Whether or not commissioners and clinicians will be enthused by this new data remains to be seen.

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● **Azizi M, Sapoval M, Gosse P et al. Optimum and stepped care standardised antihypertensive treatment with or without renal denervation for resistant hypertension (DENERHTN): a multicentre, open-label, randomised controlled trial. *Lancet* 2015. pii: S0140-6736(14)61942-5**