Depression and Blood Pressure Control: All Antidepressants Are not the Same

To the Editor:

In their cross-sectional study involving >2900 subjects, Licht et al demonstrated that depression was associated with reduced blood pressure, whereas the use of certain antidepressants, namely, tricyclic antidepressants (TCAs) and serotonin-norepinephrine reuptake inhibitors, were associated with higher blood pressure and greater incidence of hypertension. The authors proposed that the link between hypertension and the use of these antidepressants may involve an effect of these agents on vagal tone. Whether antidepressant-induced alteration in vagal function underpins the increase in blood pressure observed by Licht et al is problematic. We have previously documented a reduction in vagal activity, as indicated by a diminution in heart rate variability and baroreflex sensitivity, in patients with depression after serotonin-specific reuptake inhibitor therapy. Moreover, Licht et al, in an earlier analysis of data from the Netherlands Study of Depression and Anxiety, documented a reduction in heart rate variability in patients with depression. The association between diminished heart rate variability and depression was driven largely by the use and dose of antidepressants. Importantly, in the context of interpreting data from their present report, they found that the reduction in heart rate variability was not confined to TCAs and serotonin-norepinephrine reuptake inhibitors but was related to dose across all antidepressant classes, including serotonin-specific reuptake inhibitors. In the present report, serotonin-specific reuptake inhibitors were without an effect on blood pressure.

Activation of the sympathetic nervous system is one of the hallmarks of hypertension. We have demonstrated that sympathetic nervous activity in unmedicated patients with depression follows a bimodal distribution, with values in some patients being extraordinarily high. Serotonin-specific reuptake inhibitor treatment normalized sympathetic activity in those patients in whom sympathetic activity was elevated. Patients with depression and those with hypertension share a common phenotype in that they both exhibit signs of a defect in function of the norepinephrine transporter in the heart. In the heart, the majority of released norepinephrine is recaptured into sympathetic nerves, so it is more sensitive than all other organs to impairments in transmitter reuptake. Blockade of norepinephrine transporter by TCAs or serotonin-norepinephrine reuptake inhibitors may further exacerbate this and could sensitize the heart to sympathetic activation, increasing cardiac output and leading to an elevation in blood pressure. Indeed, whereas TCAs have a propensity to act centrally to inhibit sympathetic outflow, in the periphery, they block the norepinephrine transporter. In healthy subjects, desipramine increases cardiac norepinephrine spillover. Whether the same occurs in patients with depression is unknown but merits further attention.

Despite improved awareness, diagnosis, and the refining of treatment, depression remains a significant public health challenge. There is a reasonably sound theoretical basis indicating that certain antidepressants should be avoided in specific patients; TCAs are contraindicated in patients after a myocardial infarction, and serotonin-norepinephrine reuptake inhibitors may be unsuitable for those with existing hypertension or vascular disease because of their propensity to raise blood pressure. It is important to appreciate that not all antidepressants are the same. In this regard, the title of the article by Licht et al, suggesting that all antidepressants increase the risk of hypertension, while provocative, is perhaps misleading.

Sources of Funding

We are supported through grants from the National Health and Medical Research Council of Australia and the National Heart Foundation of Australia.

Disclosures

None.

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_Hypertension_. 2009;54:e1; originally published online May 18, 2009;
doi: 10.1161/HYPERTENSIONAHA.109.133272
_Hypertension_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://hyper.ahajournals.org/content/54/1/e1

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