Drug Monitor

Doubling Up on New Hypertension

Treating new hypertension with more than 1 drug is becoming more common. For one, clinical trials have shown that most patients can't get to their blood pressure (BP) goal on 1 drug alone. Moreover, combining drugs allows for lower doses of both. But how does combination therapy measure up in the real world of clinical practice? Pretty well, say researchers from the University of Colorado in Aurora, Kaiser Permanente in both Denver, Colorado, and Oakland, California, and the Denver VA Medical Center in Colorado. At 12 months, combination treatment is associated with better long-term BP control.

The researchers evaluated data from the Cardiovascular Research Network Hypertension Registry on 161,585 patients with newly diagnosed hypertension and had started treatment between 2002 and 2007.

Patients were divided into 2 groups: stage 1 and stage 2 (initial systolic BP ≥ 160 mm Hg or diastolic BP ≥ 100 mm Hg). In both groups, the proportion initially treated with 2 drugs rose from 2002 to 2007, but more so in the stage 2 group (from 21.6% to 44.5%). Between 2002 and 2007, fewer patients were treated initially for stage 2 hypertension, which the researchers say may be related to earlier recognition of hypertension. Nearly 90% of initial combination therapy was accounted for by 2 combinations of classes: thiazide plus a potassium-sparing diuretic and thiazide plus an angiotensin-converting enzyme inhibitor.

At 1 year, 78,095 (62.5%) of the 124,984 patients available for analysis had controlled BP. Initial treatment with 2 antihypertensive drugs was associated with higher odds of control.

The researchers also looked at adherence, comparing patients on single-drug and combination-drug therapies. The difference between the 2 groups was statistically but not clinically significant; however, the association between combination therapy and improved BP control remained consistent after the researchers adjusted for adherence to antihypertensive medications. Patients started on combination therapy were less likely to have an increase in the number of classes of antihypertensive medications during the year of follow-up compared with patients on single-agent therapy (32% vs 37%). Dosing increases were similar (24.6% vs 24.9%).

The researchers say their findings highlight not only the increasing role of combination antihypertensive agents in routine practice (in line with the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure guidelines), but also the potential long-term benefits for patients.

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Investigating Antidepressants' Effects in the Elderly

Many older people are treated with antidepressants, although there are still gaps in knowledge about adverse events, especially in cases of comorbidity, age-related physiological changes, and polypharmacy. As research and experience revealed serious drawbacks with tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs) became more popular. But even SSRIs may have unforeseen effects in the older adult, according to researchers from the University of Nottingham and the University of East Anglia, both in the United Kingdom. To help fill the knowledge gap, they conducted a cohort study of 60,746 patients with new episodes of depression between the ages of 65 and 100 years. The researchers believe their report is the first published systematic assessment of the safety of commonly used antidepressants in older patients across a range of serious adverse outcomes.

Of the patients in the study, 54,038 (89%) received at least 1 prescription for an antidepressant during follow-up. Of 1,398,359 prescriptions, 54.7% were for SSRIs, 31.6% were for TCAs, and 0.2% were for monoamine oxidase inhibitors; the remaining prescriptions were for other antidepressants. The analysis excluded the least-prescribed drugs.

The researchers followed the cohort for up to 12 years. While 10.7% of patients received only 1 prescription for an antidepressant, 10.9% received 60 or more during follow-up. The median duration of treatment was 364 days.

The researchers looked at 7 outcomes: all-cause mortality, attempted suicide or self-harm, stroke/transient ischemic attack (TIA), falls, fractures, epilepsy or seizures, and hyponatremia. All classes of antidepressants were associated with significantly increased risks of all-cause mortality, attempted suicide or self-harm, falls, fractures, and upper gastrointestinal (GI) bleeding, compared with when the drugs were not used. SSRIs and the group of "other antidepressant drugs" were associated with higher risks of stroke/TIA and epilepsy or seizures. SSRIs were also associated with increased risks of myocardial in-

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farction (MI) and hyponatremia. In fact, the researchers say, older patients are disproportionately affected by hyponatremia associated with antidepressant use, and hyponatremia is associated most strongly with SSRIs.

When the risks were broken down by class, the researchers found significant differences for all 7 outcomes. When compared directly with TCAs, SSRIs had significantly higher rates of all-cause mortality, stroke/TIA, epilepsy/seizures, hyponatremia, falls, and fracture. The researchers cite other studies that have found that older patients taking SSRIs have as much as double the risk of falls. Their finding of a "more marked and prolonged increase in risk" of fractures with SSRIs may be due to a greater risk of falls, but the researchers also cite some evidence that SSRIs reduce bone mineral density.

The group of other antidepressants had significantly higher rates compared with TCAs for all-cause mortality, attempted suicide/self-harm, stroke/TIA, fracture, and epilepsy/seizures. The researchers found no significant difference for falls or hyponatremia.

TCAs were not associated with significantly higher rates of any of the outcomes when compared with SSRIs or the other antidepressants.

Looking at the drugs individually, the researchers found that trazodone, mirtazapine, and venlafaxine had the highest rates for some outcomes. Venlafaxine, for instance, has been linked to a particularly high risk of GI bleeding.

Adverse events tended to be most common in the first 28 days after starting an antidepressant and in the first 28 days after stopping. For all-cause mortality, MI, stroke/TIA, adverse drug reactions, and hyponatremia, the researchers found some evidence that rates were reduced after 85 days of use.

Unexpectedly, TCAs seemed to be the safest class of antidepressants for older people. The differences may be explained in part by the fact that TCAs were prescribed in lower doses, the researchers say. Low-dose TCAs were as effective as higher doses, but whether they're as effective as SSRIs is not established. Moreover, TCAs have been associated with higher rates of discontinuation due to adverse effects such as sedation and dry mouth.

Clearly, more randomized trials are needed to confirm the findings, with long-term follow-ups to help assess risks and benefits, the researchers say. In the meantime, they advise careful consideration of not only class, but also individual drug risks and benefits when prescribing antidepressants for older patients.

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