Potassium-sparing diuretics might reduce risk of Alzheimer's disease

It has been suggested that high blood pressure might increase the risk of developing Alzheimer's disease (AD). Some studies have indicated that antihypertensive drugs might reduce this risk. Researchers in the US investigated the relationship between antihypertensive drugs and the incidence of AD among 3,217 residents of Cache County, UT, aged 65 years or older, 1,456 of whom were taking antihypertensive treatments.

Use of β -blockers and dihydropyridine calcium-channel blockers was associated with reduced incidence of AD in this study; non-dihydropyridine agents had no effect on AD risk. By far the greatest effect, however, was observed with the use of potassium-sparing diuretics, which was associated with a 70% reduction in the risk of AD. No association was found between other diuretic medications and AD risk.

The protective effect of potassium-sparing diuretics might be related to their effect on potassium levels. Potassium-sparing diuretics cause an increase in plasma potassium levels, whereas other diuretics reduce plasma potassium concentration. Increased plasma potassium level has been associated with a reduced risk of dementia; low potassium levels are associated with oxidative stress, inflammation, platelet aggregation and vasoconstriction, all of which have been linked to the pathogenesis of AD. As the specific association between potassium-sparing diuretics and reduced incidence of AD is a new finding, further investigation is required to confirm the anti-AD effect of these drugs.

Jim Casey

Original article Khachaturian AS *et al.* (2006) Antihypertensive medication use and incident Alzheimer disease: the Cache County Study. *Arch Neurol* [doi: 10.1001/archneur.63.5.noc60013]

Celecoxib has beneficial effects in the treatment of major depression

Major depression is associated with a deficiency in serotonergic and noradrenergic neurotransmission. Although the cause of this deficiency is unclear, it is thought that an inflammatory process might be involved. Use of

the inflammatory mediators interferon or interleukin-2 to treat cancer or multiple sclerosis has been associated with an increased incidence of depression, and high levels of prostaglandin E_2 have been reported in the serum of depressed patients. Cyclo-oxygenase 2 (COX2) inhibitors inhibit the production of prostaglandin E_2 and of proinflammatory cytokines, and have been reported to have antidepressive effects.

Researchers in Germany evaluated the antidepressive effect of the COX2 inhibitor celecoxib in combination with the noradrenergic antidepressant reboxetine in 20 patients with depression. The control group contained 20 matched patients who received reboxetine alone.

Both groups of patients improved over 6 weeks of therapy, but the improvement was much more pronounced in the celecoxib group. Nine patients achieved remission in the celecoxib group, while four patients achieved remission in the control group. Nine patients in the control group dropped out because of lack of efficacy, compared with five in the celecoxib group. In total, 7 of 40 patients dropped out because of adverse effects.

The authors state that the results implicate the inflammatory process in the pathogenesis of depression, although they point out that COX2 inhibitors have also been shown to influence neurotransmitter release. Although the mechanism of action remains to be elucidated, celecoxib and other COX2 inhibitors are potentially powerful therapies for depression.

Jim Casey

Original article Müller N *et al.* (2006) The cyclooxygenase-2 inhibitor celecoxib has therapeutic effects in major depression: results of a double-blind, randomized, placebo controlled, add-on pilot study to reboxetine. *Mol Psychiatry* [doi: 10.1038/sj.mp.4001805]

A single siRNA injection combats flavivirus-induced encephalitis

The neurotropic flaviviruses Japanese encephalitis virus (JEV) and West Nile virus (WNV) are emerging pathogens of considerable importance, with the ability to cause acute encephalitis and death. Currently, there are no effective drug treatments for infection with either of these viruses. A recent study in mice, however, has produced promising data indicating that administration of a single synthetic short interfering ribonucleic acid (siRNA) can suppress both JEV and WNV.