Amiloride, fluoxetine or riluzole to reduce brain volume loss in secondary progressive multiple sclerosis: the MS-SMART four-arm RCT

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Plain English summary

The MS-SMART four-arm RCT

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Plain English summary

Multiple sclerosis is a disabling and progressive neurological disease that affects approximately 120,000 people in the UK. Many people with multiple sclerosis experience two phases of disease called relapsing–remitting multiple sclerosis and secondary progressive multiple sclerosis. Relapsing–remitting multiple sclerosis is often characterised by periods of 'attacks' (relapses) interspersed with periods of 'remission' with no or few disease symptoms. The attacks are due to inflammation of the nerves and the insulation (called myelin) that surrounds the nerves. Secondary progressive multiple sclerosis, which ultimately affects most people with multiple sclerosis after 10–15 years from disease onset, results from nerve death (called neurodegeneration) and relentless disability. Unlike relapsing–remitting multiple sclerosis, there are few treatments with limited effects that can slow down the disability accrual in secondary progressive multiple sclerosis. MS-SMART (Multiple Sclerosis-Secondary Progressive Multi-Arm Randomisation Trial) was a randomised and blinded trial that investigated three drugs (i.e. amiloride, fluoxetine and riluzole) that showed potential to prevent nerve death in multiple sclerosis. Randomisation means that participants can get any one of the three active drugs or the inactive placebo/dummy; blinded means that neither the participants nor the investigators will know which drug (or placebo) the participants are receiving. All participants in MS-SMART were planned to have brain magnetic resonance imaging scans before starting the trial and after 96 weeks, which were used to measure brain shrinkage – a normal process of ageing that occurs faster in people with multiple sclerosis and is thought to reflect nerve death (neurodegeneration). Across 13 UK clinical neuroscience centres, 445 people with secondary progressive multiple sclerosis were enrolled and each person was followed up for 96 weeks between December 2014 and July 2018. When we completed our analyses, we found no difference in the brain shrinkage rates between participants receiving amiloride, fluoxetine or riluzole and the dummy, suggesting that these drugs do not prevent nerve death (neurodegeneration). The results also suggest that testing three drugs simultaneously in one trial (rather than one by one) is feasible in secondary progressive multiple sclerosis.

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