Prevention of Alzheimer Disease in People with Down Syndrome

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We have been asked questions regarding preventing Alzheimer disease (AD). One question is about the use of statin medications to prevent Alzheimer disease in people with Down syndrome. Statins include such medications as Lipitor (atorvastatin), Mevacor (lovastatin), Pravachol (pravastatin), etc. Statins are commonly prescribed to reduce cholesterol and prevent heart attacks (myocardial infarctions). We are hesitant to use statins in people with Down syndrome to prevent heart attacks because the incidence of heart attacks is already so low in people with Down syndrome. Out of over 5000 patients, we have one well-documented heart attack in our practice. It has been hypothesized that there is something on the 21st chromosome that is protective against atherosclerotic disease (hardening of the arteries, narrowing of the arteries). What may protect against atherosclerotic disease is not known.

Even though the incidence of atherosclerotic disease is so low that the benefits of statins to prevent the disease is so limited, might there be a different reason for taking statins for people with DS?

Mangialasche and others (2012) studied Alzheimer disease in people without Down syndrome and wrote, “Multidisciplinary research involving epidemiology, neuropathology, and neuroimaging has provided sufficient evidence that vascular risk factors significantly contribute to the expression and progression of cognitive decline (including dementia).” Therefore, since vascular risk factors such as elevated cholesterol contribute to dementia (such as Alzheimer disease), it has been speculated that using statins might reduce Alzheimer disease.

Initial observational studies were encouraging in people without Down syndrome. Observational studies do not involve intervention by an investigator. The investigator “simply ‘observes’ and assesses the strength of the relationship between an exposure and disease variable” (Song & Chung 2011). There is not a control group in the same way as in a randomized controlled trial (RCT) in which participants in the study are randomly assigned to take the medication or a placebo. RCT studies are often done in the “double blind” fashion such that the subject and the experimenter do not know who is taking the medication and who is taking the placebo. This helps prevent bias and study inaccuracy. Data from controlled studies such as RCT are generally considered stronger than data from observational studies.

After the observational study data was available, randomized controlled trials were performed. McGuiness et al (2009) concluded, “There is good evidence from randomized controlled trials (RCTs) that statins given in late life to individuals at risk of vascular disease have no effect in preventing AD or dementia. Biologically it seems feasible that statins could prevent dementia due to their role in cholesterol reduction and initial evidence from observational studies was very promising. Indication bias may have been a factor in these studies however and the evidence from subsequent RCTs has been negative.”

No medication has been shown to prevent Alzheimer disease. The reviews of studies lead to the conclusion that “active engagement in social, physical, and mentally stimulating activities may delay the
onset of dementia” in people without Down syndrome (Mangialasche 2012). Therefore, active engagement in activities, physical exercise, and social and mentally stimulating activities seem to be the only known ways at this time to prevent AD in people without Down syndrome.

How about in people with Down syndrome?

In an observational study of 123 adults with Down syndrome, Zigman and others (2007) found that statins might be beneficial for people with DS. They found that “controlling for covariates, participants with total cholesterol (TC) >or=200mg/dL were more than two times as likely to develop AD as subjects with lower TC. In contrast, participants with higher TC levels who used statins during the study, had less than half the risk of developing AD than participants with higher TC levels who did not use statins.”

What do we know?

- The incidence of Alzheimer disease in people with Down syndrome is higher than people without DS.
- People with DS tend to develop Alzheimer disease about 20 years earlier than people without DS.
- There are data in people without DS that show being active in social, physical, and cognitive activities may help prevent Alzheimer disease.
- Observational studies in people without DS suggest that statins might prevent AD in people without DS. However, randomized controlled studies were then performed and showed that taking statins does not prevent AD in people without DS.
- The incidence of atherosclerotic disease seems to be quite reduced in people with DS and, therefore, the benefit of taking statins to prevent atherosclerotic disease (heart attacks) would seem to be much reduced (although randomized controlled studies have not been done).
- Observational data has demonstrated benefit of taking statins in people with DS as far as preventing AD. Randomized controlled studies have not been done.
- We have observed memory impairment as a side effect of statins in people with DS.

What do we recommend for our patients with DS?

Given that,

- (a) Only observational data for people with DS (in the study of 123 people) is available as far as preventing AD with statins,
- (b) in people without DS, randomized controlled studies disproved the earlier encouraging findings of observational studies on the use of statins to prevent AD,
- (c) the benefit of statins in people with DS for preventing heart disease seems limited since atherosclerotic disease seems to be so low anyway, and
- (d) we have observed memory impairment as a side effect of statins,

We are cautious about recommending statins for people with DS. We need further study (i.e. randomized controlled studies or other strong data) that demonstrates that statins reduce Alzheimer disease.
disease in people with DS. Therefore, we don’t recommend statins for this purpose at this time. Active involvement in social, physical, and cognitive activities is a good idea for so many reasons in people with and without DS so that, even though data are not available as to their benefit in preventing AD in people with DS, we still recommend these activities for our patients.

References


