Lipid-Lowering Therapy for the Primary Prevention of Cardiovascular Disease in the Elderly

Background:

Cardiovascular disease—such as heart attacks and strokes—causes about 4 out of 10 deaths in people 75-84 years old, and almost half of deaths in those age 85 years and older. It is the leading cause of death in elderly. Additionally, 74 out of 100 men aged 85-94 who haven't had a stroke or heart attack will have one during these years. This is in contrast to about 3 out of 100 men aged 35-44 years who will have a stroke or heart attack.

Since 7 out of 10 strokes and 6 out of 10 heart attacks are first cardiovascular events, it is important to find ways to prevent a person's first cardiovascular event. Drugs that lower lipids, i.e. cholesterol, can help prevent heart attacks, strokes, or other cardiovascular events in people who have had them. This is called secondary prevention. Since they provide this benefit, it's reasonable to think they might also prevent these events in people who haven't had them before. Prevention of first strokes, heart attacks, or other cardiovascular events is also called primary prevention. Drugs that lower cholesterol are thought to reduce cardiovascular events by preventing cholesterol from clogging blood vessels. It's important to find out if this theory holds true by seeing if there are actually fewer heart attacks and strokes in people that take the drugs.

Goals of the study:

To evaluate the potential for medium and high dose statin therapy to safely reduce first cardiovascular events and associated deaths in people over 65 years old.

Who was included in this study?

This study was an analysis of 14 studies that looked at the effectiveness of statins in people with diabetes or cardiovascular disease. It also reviewed 7 studies of statins in those without pre-existing cardiovascular disease. The studies included men and women with an average age range of 55-75 years. Also, this Fact Sheet was updated with the results of some studies that were finished after the analysis of 14 studies was written, including one with participants as old as 97 years.

What was the study design and intervention?

The studies included in the analysis assigned patients to either the control group or a statin group. The control groups varied between placebo or a different statin—depending on the study. Placebos are pills without any actual drug in them. People were randomly selected to different treatments. This means something like a coin flip was used to decide which drug they received, or whether they received a placebo. The statins studied were: atorvastatin, extended-release fluvastatin, lovastatin, pravastatin, rosuvastatin, simvastatin and a simvastatin/ezetimibe combination. The patients' baseline LDL (low-density lipoprotein—the "bad" cholesterol) cholesterol was measured and cognitive level assessed at the start of the trial. At the end of the follow up period, the LDL cholesterol was measured. Changes to cognitive level, rate of stroke, mortality (death), nonfatal heart attacks and coronary heart disease were also determined. Rates of drug side effects were reported.

What did the study find?

Primary Prevention—i.e. prevention of first heart attacks and strokes

- Less information was available on the effectiveness of statins in older persons. People in the studies often died for reasons other than cardiovascular disease.
- In another study of males aged 70-79 with high blood pressure and 3 other cardiovascular risk factors, but no past serious cardiovascular events, atorvastatin 10mg reduced LDL cholesterol by 35% and reduced the risk of stroke.
- The most common type of stroke, ischemic stroke (where the brain doesn't get enough blood), was less common in people taking statins. For every 5 people that had an ischemic stroke in the placebo groups, only 4 people taking statins had an ischemic stroke. That means statins prevented about 1 out of 5 ischemic strokes that would have happened without the statins.
- The protective effects of moderate dose statins were mainly found in males. A higher dose statin, rosuvastatin 20mg, was effective in both women and men.
- The JUPITER study was published after this study. It included the largest number of persons >70 years, including about half women. It found a benefit for both coronary heart disease and stroke reduction in people with risk factors, even if their LDL cholesterol was in the normal range. About 1 in 5 serious cardiovascular events was prevented. This study used rosuvastatin 20 mg and had a greater reduction in LDL (or bad) cholesterol than did previous studies, about 50%.

Secondary Prevention—i.e. prevention in people who have had heart attacks or strokes before

- The reduction in the actual number of heart attacks and strokes with statins compared to placebo was greater in people who had already had a heart attack or stroke, compared to their effect in people who had never had a heart attack or stroke. The overall risk in this group is higher. This makes the overall impact of statins greater even though the fraction of events prevented was similar.
- Statins reduced the number of major cardiovascular events, e.g. heart attacks and strokes, in patients 65-80 that had either diabetes or cardiovascular disease by 19%—compared to placebo. That means about 1 in 5 cardiovascular events was prevented by statin use.
- The decline in risk is similar across the age range with patients 70-74 and 75-80 years old. About 1 in 5 events was prevented in both age groups.
- Statins also reduce the overall risk of death in older secondary prevention patients.

Safety in Elderly Patients

When prescribing in an elderly population, the safety of statins is important to consider. Medium doses of statins don't seem to cause many side effects. The highest doses, such as atorvastatin 80 mg, simvastatin 80 mg, or rosuvastatin 40 mg, are of greater concern. The risk of muscle problems due to statins is slightly greater in elderly people, and these are more common at higher doses. Uncommonly, older patients may experience liver function test elevations with higher statin doses. Despite some concern raised in the past, statins do not appear to increase the risk of cancer.

Special Considerations for Elderly Patients

- The safety and effectiveness of cholesterol-lowering drugs other than statins is unknown and their use should be avoided. There is more research on statins.
- If statins are used, it's still important to address other risk factors for heart attacks and strokes such as smoking, high blood pressure, diet, and physical activity.
- Elderly people may develop health problems that may make cholesterol lowering a low priority. These other health problems may lead to death before the statin produces any benefits. For example, statins did not benefit people with serious heart or kidney failure.
- The elderly have a greater risk of drug side effects.

Conclusions:

- Statins may help prevent first heart attacks or strokes in older adults. At least a 50% reduction in LDL (bad) cholesterol may be needed to see benefits for both heart attacks and strokes in both men and women. The JUPITER study suggested that men > 50 years old or women > 60 years old with at least one risk factor for cardiovascular disease could have reductions in serious cardiovascular events with rosuvastatin, even if they have normal LDL cholesterol levels. Examples of risk factors include smoking, high blood pressure, low HDL cholesterol (good cholesterol), and diabetes.
- Statins are useful in secondary prevention, reducing the number of major cardiovascular events by 19% in those 65-80 years old. That means they prevent about 1 in 5 major cardiovascular events in people who have already had these events.
- While medium dose statins are well tolerated in the elderly, it is important to realize:
    - Side effects in muscles and the liver may be more common in the elderly
    - If someone has a serious disease like end-stage heart or kidney failure that gives them a short life expectancy, statins may not benefit them.

This summary is based on a review by Jennifer Robinson, MD, MPH, of the University of Iowa. The full article appears in Drugs Aging 2009;26(11):917-31. This work was partially supported by an Agency for Healthcare Research and Quality (AHRQ) Centers for Education and Research on Therapeutics cooperative agreement #5 U18 HSO16094. The summary was updated with information from recent clinical trials and meta-anlayses. These references are listed below.

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