THE WIRE

ECONOMY

Big Pharma is Subtly But Surely Spinning Statins Out of Control

BY DEEPAK NATARAJAN ON 20/08/2015 • LEAVE A COMMENT

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Recently, the journal *JAMA Internal Medicine* published a massive retrospective study (http://archinte.jamanetwork.com/article.aspx?articleid=2301148) that included almost a million subjects. Almost half a million people taking statins were compared to an

equivalent population not popping in any. They also added more than 26,000 patients on non-statin lipid lowering drugs. The authors observed, in their own words, a strong association between first exposure to statins and acute memory loss diagnosed within 30 days immediately following exposure. The increase in memory loss was 4.40 times compared with non-statin users; in other words statins hiked up loss of memory by 440%.

The non-statin lipid lowering drugs also increased memory loss 3.6 times compared with people not on lipid lowering medicines. Both statin and non-statin drugs substantially dented acute memory to a similar degree. This was the evidence gathered in this study, which ensured that people with dementia, Alzheimer's, brain tumors, and brain infection were excluded. The odds ratios were adjusted bearing in mind confounders such as diabetes, hypertension, stroke, hypercholesterolemia, alcohol abuse and other such health indicators.

The conclusions however that were drawn were remarkable to say the least. "Both statin and non-statin lipid lowering drugs were strongly associated with acute memory loss compared to nonusers but not when compared with each other. Thus, either all lipid lowering drugs cause acute memory loss regardless of drug class or the association is the result of detection bias rather than a causal association."

What does *The New York Times* report? It astoundingly prints on 11th June 2015 a story based on the above study with the headline, "Statins May Not Affect Memory, Study Suggests (http://well.blogs.nytimes.com/2015/06/11/statins-may-not-affect-memory-study-suggests/)". The story ends with a quote from the lead author from the study as, "But the question of impairing memory is a nonissue." Such a twisted spin wasn't expected from the NYT, and

it's not clear if there's a need to do so.

But TIME magazine too has reported the same study (http://time.com/3912512/statins-memory/) with the remarkable title, "Memory Loss Not Caused By Cholesterol Drugs After All." The TIME story takes enormous pain to explain that albeit there is substantial memory compromise with statins, this may be because of detection bias that is people on statin drugs are more sensitive to memory changes and are willing to report them to their physicians.

Expenditure on marketing and administration

The Western media just refuses to divulge the truth that statins can roger your memory to a large extent. The headlines are brazenly misleading and conclusions drawn by the correspondents are clever untruths. An impression is being hammered down that statins are safer than a puff of pristine pure air, when actually nothing can be further from the truth. Statins most certainly can cause severe muscle aches, cataracts, impaired memory, dented cognition, and also diabetes, in spite of repeated shrill and strident denials by the industry (examples here (http://archopht.jamanetwork.com/article.aspx?articleid=1739520) and here (http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm293330.htm)) Atorvastatin (a statin) has been the largest selling pill for years; generating billions of dollars of revenue for its makers. Pfizer was making almost US $10 billion year after year on sales of Lipitor alone.

In the year 2002, the combined profits of the 10 drug companies listed in Fortune 500 was more than the combined profits of all the other 490 businesses put together ($35.9 billion vs. $33.7 billion). Moreover the biggest single item in the budget was 'marketing and administration.' The combined worldwide sales of

these 10 companies had been to the tune of $217 billion, of which 14% was spent on research and development ($31 billion approximately) and the profits were in the range of 17% ($36 billion approximately).

Remarkably, 31% ($67 billion) were spent on marketing and administration. This information is drawn from the industry's own annual reports to the Securities and Exchange Commission (SEC) and to the stockholders. The exact details of expenditure into 'marketing and administration', however, are not revealed, but it is estimated that more than $50 billion of this is used annually for 'marketing' alone (http://www.amazon.in/Truth-About-Drug-Companies-Deceive-ebook/dp/B000FC1V1A/ref=sr_1_1?ie=UTF8&qid=1440056616&sr=8-1&keywords=truth+about+drug+companies+marcia+angell).

The JUPITER trial (http://www.nejm.org/doi/full/10.1056/NEJMoa0807646) studied the role of the drug rosuvastin (a statin) in 18,000 healthy people who had raised high sensitivity C-reactive-protein of 2.0 mg % or higher, and low-density lipo-protein level less than 130 mg%. The trial was terminated after a mere 1.9 years when the data and safety monitoring board observed a significant reduction in the primary end point in the group assigned to rosuvastatin.

Myocardial infarction, stroke and cardiovascular death were reduced from 157 events in placebo group to 83 on rosuvastatin, a relative reduction of 47%. The company publicised the results with great pomp and ceremony. *The New York Times* reported the study as 'Cholesterol-Fighting Drugs Show Wider Benefit (http://www.nytimes.com/2008/11/10/health/10heart.html?pagewanted=all&_r=0)', writing 'those people were almost 50% less likely to suffer stroke or need angioplasty or bypass surgery, and they were 20% less likely to die during the study.'

Absolute v. relative reduction of events

The *New England Journal of Medicine* published a sobering editorial (http://www.natap.org/2008/HIV/111808_09.htm) in 2008 that emphasised that hard cardiac events were reduced from 1.8% in the placebo group to 0.9% in the rosuvastatin group; "thus, 120 people were treated for almost two years to prevent one event", while significantly increasing diabetes from 2.4% to 3% with the statin. The public was told of reduction of more than 50% in heart attacks while actually the absolute reduction was less than 1%. Put another way the chances of avoiding a heart attack were more than 98% without treatment, but 99% if you took a tablet of rosuvastatin every day for two years.

The ASCOT-LLA trial (http://www.thelancet.com/journals/lancet/article/PIIS0140673603129480/abstract) studied more than 10,000 patients of hypertension who also had three of the following risk factors: diabetes, peripheral arterial disease, stroke, left ventricular hypertrophy or smoking. Half received 10 mg atorvastatin, the other half placebo and the primary endpoint was fatal and non-fatal coronary heart disease. This study too was stopped after 3.3 years because as the company declared, "cholesterol lowering with atorvastatin conferred a 36% reduction in fatal coronary heart disease and non-fatal myocardial infarction compared with placebo".

The absolute reduction of events was however only 1.1%; atorvastatin reduced events from 3% in the placebo group to 1.9% in the treated cohort; this of course is 36% of 3. This again implies that even a person with hypertension accompanied by 3 more risk factors has a 97% chance of not having a heart attack despite not taking a statin in a follow up extending more than 3 years.

More than 20,000 subjects aged between 40-80 years and having cardiovascular diabetes and/or diabetes were included in the British Heart Protection Study (HPS) which compared efficacy of 40 mg simvastatin vs. placebo in a randomised manner. The results were trumpeted as 'stunning'; 'extreme 38% reduction in first nonfatal myocardial infarction'; 'a 27% reduction in the incidence rate of nonfatal myocardial infarction or coronary death.' The absolute reduction of events was only 1.5%; from 9.1% in the placebo group to 7.6% with simvastatin. More than 26% of patients had withdrawn from the trial in the run in period because of adverse effects (http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(02)09327-3/abstract).

All cause mortality was reduced from 14.7%% in the placebo group to 12.9% with simvastatin; absolute reduction of 1.8% only. Simvastatin was able to lower coronary deaths as compared to placebo by a mere 1.2% (5.7% vs.6.9%). These reduction of clinical events albeit statistically significant do not translate to meaningful clinical efficacy. Heart attacks or heart attack deaths were reduced from 11.7% to 8.7%; almost a quarter lowering of events relatively but in absolute terms only 3%.

A conditional risk-benefit ratio

Statins therefore may not be the best treatment for primary prevention because as we have observed clinical benefits are at best marginal and we should be wary of adverse effects that are always downplayed. *Diabetologia* published a study from Finland in March 2015 (http://www.ncbi.nlm.nih.gov/pubmed/25754552) that reported statins increased the risk of type 2 diabetes by 46% after adjusting for confounding factors. The risk of diabetes was dose dependent and the authors advised that low dose statin should be prescribed in people who are at higher risk such as the obese, or

having a family history of diabetes.

In this study diabetes was diagnosed by an oral glucose tolerance test and HbA1C >6.5%. The study included 8749 non-diabetic men aged 45-73 years in 6 years follow up. Subjects on statins had 24% decrease in insulin sensitivity and 12% reduction of insulin secretion. The statins largely involved were atorvastatin and simvastatin. The authors concluded that statins are not the best drugs for primary prevention and particularly not so in women. The risk benefit ratio may favour statin in patients who have already suffered a cardiac event.

Another study published in May 2015 (http://www.ncbi.nlm.nih.gov/pubmed/25917657) in the *Journal of General Internal Medicine* has also observed that 14% of almost 26,000 healthy adults developed diabetes following statin consumption. The researchers' propensity score matched 3351 statin users with 3350 nonusers. Statin users subsequent to adjustment for confounders had an 85% higher risk of new-onset diabetes and more than double the risk of diabetes with complications.

The FDA has added diabetes and memory loss to statin labels. Statins were the third largest selling drug in the US for 2010 with sales of $18.8 billion. So what should be the take home message on statins? Statins should be prescribed to patients who already have had a cardiovascular event but simple life style changes should be advised for primary prevention of heart disease in normal healthy middle-aged people. The life style change measures should include cessation of smoking, a sensible diet, getting optimal weight and a little exercise in the form of 10-15 minute jog or some yoga.

It may not be inappropriate to report this scorching quote provided by Peter Gotzsche in his book "Deadly Medicines and

Organized Crime: How big Pharma has corrupted healthcare (http://www.amazon.in/Deadly-Medicines-Organised-Crime-Healthcare/dp/1846198844)", of a former vice president of Pfizer:

> It is scary how many similarities there are between this industry and the mob. The mob makes obscene amounts of money, as does this industry. The side effects of organised crime are killings and deaths, and the side effects are the same in this industry. The mob bribes politicians and others, and so does the industry...

Deepak Natarajan is a cardiologist in New Delhi.

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