

STATINS – ITS ROLE IN CLINICAL USE

WHAT ARE STATINS

The 3-hydroxy-3-methylglutaryl-coenzyme (HMG-CoA) reductase inhibitors, also known as statins, are the most effective class of drugs for lowering serum low-density lipoprotein cholesterol concentrations.

They are first-line agents for patients who require drug therapy to reduce serum low-density lipoprotein cholesterol concentrations. The purpose of this review is to compare the benefits and harms of different statins in adults and children with hypercholesterolemia.

TYPES

According to their solubility, statins can be categorised as hydrophilic and lipophilic.

The predominantly lipophilic statins (simvastatin, fluvastatin, lovastatin, pitavastatin, and atorvastatin) can easily pass more deeply into the membranes where they interact with the surrounding acyl chains.

Based on such data, rosuvastatin and pravastatin are commonly clinically referred to as hydrophilic statins, while cerivastatin, simvastatin, fluvastatin, and atorvastatin are called hydrophobic statins.

DIFFERENCE BETWEEN A HYDROPHILIC AND LIPOPHILIC STATIN

Lipophilic statins are widely distributed in different tissues, whereas hydrophilic statins are liver specific.

Hydrophilic statins employ carrier-mediated mechanisms for uptake, which could reduce their ability to exert non-lipid effects on extrahepatic tissues and they are suggested to be less pleiotropic.

MECHANISM OF ACTION

Statins work by competitively blocking the active site of the first and key rate-limiting enzyme in the mevalonate pathway, HMG-CoA reductase.

Inhibition of this site prevents substrate access, thereby blocking the conversion of HMG-CoA to mevalonic acid.

LIPOPHILIC STATINS

Lovastatin and simvastatin

In terms of lipophilic nature, lovastatin and simvastatin are the most lipophilic, followed by atorvastatin, fluvastatin, and pravastatin.

Rosuvastatin is a relatively new statin, having a polar methane sulphonamide group, and it can be placed between fluvastatin and pravastatin.

ADVANTAGES OF STATINS.

Statins are worth it for people who already have cardiovascular disease. Statins are also worth it for people who are at high risk for getting cardiovascular disease in the future. Statins are not worth it for people at low risk of cardiovascular disease.

Sex and gender disparities play a role in determining the efficacy and safety of the most commonly used medications suggesting the need for a sex-tailored approach in prescription.

Statins are a cost-effective strategy for cardiovascular disease (CVD) prevention. While

statins are similarly effective in secondary CVD prevention, some concerns raised by conflicting data reported in primary CVD prevention clinical trials.

The small representation of women in clinical trials and the fewer rates of events due to the lower female baseline CVD risk may have conditioned contradictory meta-analysis findings.

Statins help lower low-density lipoprotein (LDL) cholesterol, also known as “bad” cholesterol, in the blood. They draw cholesterol out of plaque and stabilize plaque. This issue needs a little clarification.

With rosuvastatin the added advantages are it raises the HDL(good cholesterol)a well as lowers triglycerides (high triglycerides, above 1000 are a potential risk for pancreatitis), unlike other statins.

The plaques which form in the major arteries of heart or brain start as cholesterol deposits in the intima of arteries. This calls for macrophages which give rise to an inflammatory process and gives permanent plaques. While some of these plaques are hard (stable –having less chance of dislodgement), some are soft plaques and have the chance of dislodgement and causing heart or brain attacks. So it is to be remembered that even in people with normal cholesterol, statins are helpful as they convert soft to hard, non dislodgable plaques.

Hence it is mandatory to take statins in secondary prevention and high risk patients (with co-morbidities like diabetes) even if the lipid profile is normal.

FOODS THAT SHOULD BE AVOIDED WHEN TAKING STATINS

While taking atorvastatin (most commonly used) as well as other statins, high-fat and high-cholesterol foods should be avoided as part of the overall treatment.

Large quantities of grapefruit or grapefruit juice, which can increase the risk of serious side effects. Also, avoid excess alcohol use, as this may cause serious liver problems.

OTHER FOODS TO BE AVOIDED ARE:

- Bacon, sausage and other processed meats.
- Potato chips and other processed, packaged snacks. .
- Dessert..
- Too much protein. .
- Fast food.
- Energy drinks.
- Added salt.
- Coconut oil.

STATINS - SIDE EFFECTS

COMMON

- Muscle pain and damage. One of the most common complaints of people taking statins is muscle pain.
- Liver damage. Occasionally (rarely) statin use could cause an increase in the level of enzymes that signal liver inflammation.

Increased blood sugar or type 2 diabetes. Here there is an issue.

This is observed in a handful of patients in certain research, but the statin rosuvastatin has its advantage over other statins in this regard (discussed before). With rosuvastatin CoQ10/LDL-C levels at 6 months were increased in the (+23.5%, $p < 0.01$) and percent changes in

CoQ10/LDL-C were correlated with the myocardial salvage. It has this added advantage which can cause no harm as far as glycaemic status is concerned too.

Others:

- Diarrhoea
- Constipation
- Nausea
- Rash or flushed skin
- Stomach cramps

NEUROLOGICAL SIDE EFFECTS.

Common side effects of cholesterol drugs include:

- Muscle soreness, pain, or weakness

The lipophilic nature of medical compounds and the lowering of the cholesterol level in the blood, however, seem to play an important role in the occurrence of this side effect.

As stated above, it has been determined that HMG-CoA inhibitors block the production of mevalonate, which leads to deficient production of coenzyme Q10, isopentenyl, and dolichols.

Deficiency of these 3 chemical compounds can lead to the muscle cell injury and toxicity. Predominantly lipophilic statins penetrate muscle cell at a higher degree than predominantly hydrophilic statins.

- Taking CoQ10 supplements to get relief.

- Another option, L-carnitine, might help, too.
- Fatigue
- Problems sleeping
- Memory loss or confusion
- Often patients on statins complain of insomnia and cognitive changes.

These particular 2 side effects are especially important for the elderly population. Once elderly patients are put on a statin, they take it for a long period of time, and, in addition, they may tend to have sleep disturbances and cognitive problems. (these are still questionable)

DIABETES & STATINS

Hydroxyl methyl glutaryl coenzyme A reductase (HMGCoAR) is the target of statin therapy and the activity of this key enzyme in cholesterol synthesis is reduced by statins in a partial and reversible way.

Mendelian randomization studies suggest that the effect of statins on glucose homeostasis reflect reduced activity of HMGCoAR. In vitro and in vivo data indicate that statins reduce synthesis of mevalonate pathway products and increase cholesterol loading, leading to impaired β -cell function and decreased insulin sensitivity and insulin release.

While this effect has been thought to be a drug class effect, recent insights suggest that pravastatin and pitavastatin could exhibit neutral effects on glycaemic parameters in patients with and without diabetes mellitus.

The inhibition of HMGCoAR activity by statins appears to be a key mechanism. It is difficult to offer a comprehensive view regarding the diabetogenic effect of statins because our

understanding of the most widely recognized potential mechanisms, i.e. underlying statin-induced reduction of insulin sensitivity and/or insulin secretion, is still far from complete.

Of all agents available, rosuvastatin produces the greatest reduction in LDL-C, LDL-P, and improvement in apoA-I/apoB, together with a favorable safety profile due its action on increasing enzyme Co-Q. Several recent proposals and methods to lower cardiovascular risk are reviewed.

SUMMARY

In conclusion it can be said that lifestyle modifications(weight reduction, dietary changes, exercises) still remain the hallmark for primary prevention for patients at risk of cardiovascular and carotid disease.

But in certain patients ,at high risk like (Patients with metabolic syndromes, strong family history post or peri-menopausal females etc) statins can be a part of primary prevention as well.