

## Bile Acid Sequestrants

The next group of Gastrointestinally Active Lipid Lowering Drugs I will talk about are the Bile Acid Sequestrants. Like Zetia, this class of drugs works in the intestines. They have been used since the 1960s. Since they are not absorbed into the body they are inherently safe and also safe during pregnancy. They are a good class of drugs for young adults contemplating a potential lifetime of exposure to a medication and are the only class of drugs recommended by NCEP for use in children. The three most common adverse events that have been reported are constipation, rarely leading to obstruction, increase in plasma triglyceride levels, and decrease absorption of some medicines and certain vitamins. The newest agent, Colesevelam (Welchol)-available as a tablet, has greater affinity for bile acids compared with the older medicines such as Cholestyramine(Questran)-available as a powder, so it has fewer drug interactions and is less likely to cause constipation.

The main problem with this class of drugs for patients with hypercholesterolemia can be the taste, the amount that needs to be taken, and the bloating and constipation. I tell my patients to take a stool softener while on this class of drugs or to drink prune juice. Since the development of Welchol and the improved GI tolerance, more patients are willing to take BASs. In an analysis of 3 randomized, placebo-controlled trials of Welchol added to statin therapy, constipation was only reported in <10% of patients and <5% withdrew secondary to side effects.

These classes of drugs are anion-exchangers and cause increased clearance of LDL-C from the blood. As I said previously, they work in the intestines by binding bile acids, and thus, interrupt the circulation of bile acids back to the liver. Since there is less bile acid available, cholesterol is converted to bile acid and the concentration of cholesterol within the liver falls. As this happens, LDL receptor activity of the liver cell increases which then increases LDL clearance from the blood.

The largest set of data on BASs comes from the Lipid Research Clinics Coronary Primary Prevention Trial (LRC-CPPT). Reduction in coronary risk corresponded to LDL-C reduction. When the maximum dose of 24 grams/day of Cholestyramine was used, there was 28% reduction in LDL-C and a 39% reduction in CHD risk. The BASs have been used alone or in combination with other lipid lowering medications in one major trial with a clinical endpoint and in five with angiographic endpoints.

BASs should be avoided in patients with TGs >400mg/dl because they tend to raise TG levels. If it is be used in combination with medicines to lower TGs, this is not a major concern but if used alone should only be used if one's TG level is < 200mg/dl.

Finally, due to potential drug interactions, coumadin, thiazide diuretics, propranolol, tetracycline, penicillin G, phenobarbital, thyroid preparations, estrogens, progestins, and digoxin should be administered one hour before or four hours after taking the older BAS

agents. The current evidence has shown that Welchol can be taken concurrently with these medicines.