

Fibrates vs Niacin

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Therapeutic Decisions: Fibrates versus niacin.

There are no head to head trials to answer the question of drug superiority. We know with statins and resins that outcome reduction is related to lowering apoB and what is not definitively proven is whether raising HDL-C is related to outcomes (NCEP 2004 addendum).

There are numerous outcome trials using various fibrates: The WHO trial, the Coronary drug project, The Stockholm Ischemic trial, The Helsinki Trial, The Bezafibrate Intervention Prevention (BIP) trial, the VA-HIT study and the FIELD trial. There are also several angiographic trials. In VA HIT part of the benefit was related to the 6% rise in HDL-C (~1.89 mg/dL) and 50% of the benefit was nonlipid related (pleiotropic effects). Fenofibrate has a very successful angiographic data in a study enrolling only diabetics (DAIS).

Niacin has one seriously empowered clinical outcome trial: the Coronary Drug Project where high dose immediate release niacin was used as well as several angiographic trials including HATS (statin plus slow release niacin) and FAT (niacin and bile acid sequestrants). Does niacin's angiographic and outcome benefit in HATS have anything to do with raising HDL-C? Many would suggest it does and post hoc analysis confirms it. However, the combination drug (niacin and statin) effect on apoB data from HATS is also impressive. Niaspan (extended release) has no outcome data and one carotid intimal thickening trial (with a statin) which failed to show statistically significant improvement at one year was successful in longer term follow up.

We can all agree that fibrates and niacin have multiple lipoprotein benefits including increasing HDL-C and reducing apoB. However, may I quote the recent NCEP addendum and the authors of NCEP certainly know the data of HATS and every other trial:

"Although the potential benefit of HDL-raising therapy has evoked considerable interest, current documentation of risk reduction through controlled clinical trials is not sufficient to warrant setting a specific goal value for raising HDL-C. Recent lipid-lowering drug trials provide no new evidence in this regard."

NCEP: "Another drug that raises HDL-C is nicotinic acid. Clinical trials support the efficacy of nicotinic acid for reduction of CHD risk, both when used alone and in combination with statins. The combination of a statin with nicotinic acid produces a marked reduction of LDL-C and a striking rise in HDL-C. Although the majority of patients can tolerate nicotinic acid therapy, **a sizable minority are intolerant because of a variety of side effects.**"

And of course the potential glucose issue is niacin's biggest metabolic drawback. Until there are long term empowered studies proving the niacin induced glucose elevation has nothing to do with anything, especially microvascular disease, it remains an issue especially in younger lower risk patients. In conclusion, **NO ONE DISPUTES NIACIN REDUCES ATHEROTHROMBOTIC EVENTS.** Many dispute its tolerability and the glucose/insulin resistance issue.

- 1) Fibrates and niacin have outcome data that is unimpeachable (fibrates have significantly more). Both have positive angiographic trials.
- 2) There is no specific NCEP goal of raising HDL-C but there are goals for LDL-C, apoB and non HDL-C (apoB surrogate). Both niacin and fibrates help statins lower apoB and non HDL-C.
- 3) There are more tolerability problems with niacin than any other lipid drug.
- 4) Niacin causes metabolic perturbations: especially glucose, uric acid, homocysteine issues
- 5) Fenofibrate can raise homocysteine and occasionally creatinine, but lowers uric acid
- 6) Fibrates may have more pleiotropic effects than niacin and one (bezafibrate) has been shown to delay the onset of diabetes. Fenofibrate is associated with microvascular benefit.
- 7) Fibrates seem to have their best efficacy in insulin resistant patients (especially T2DM) who have high TG and low HDL-C.
- 8) Niacin raises HDL-C more than fibrates, but in monotherapy outcome trials the benefit of fibrates and niacin is very similar.

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9) Both niacin and fibrates improve macrophage reverse cholesterol transport.

So when deciding on what to add to a statin in people with atherogenic dyslipidemia (most of whom are insulin resistant with impaired glucose metabolism), the choice of lipid therapy comes down to issues # 3 and 4 and 5 and 6 and 7.