

Lipidaholics: Greetings from the most politically corrupt and embarrassing part of the Union, the Garden State. If we practiced medicine like **Jersey** Democrats practice politics, we would all be behind bars. Too bad there is no such thing as political malpractice and that no politicians ever get put behind those bars.

BREAKING LIPID NEWS: 1) Crestor has now been on the market for one year. No FDA warnings, no deaths! The safety record that we all desire and wanted to see is emerging rapidly. 2) Vytorin (Zetia plus Zocor at 10/10, 10/20, 10/40 and 10/80 mg tabs) are available. Next week we will get into a nice discussion of lipid absorption. Most of us have long forgotten or were never taught this physiology and pathophysiology. Like everything else, more complex than originally thought!. Please know Zetia (ezetimibe) hinders sterol, not fat absorption.

Although the dog days of August are here, Lipiding must go on. I received the following from a gynecologist down South; "I have a 57 year old black woman with the following"

Her current BMI is 42 (ht 5'2", wt 202); She is on a "blood pressure medicine" but her blood pressure at this visit was 150/90; Her family history is riddled with heart disease-sister with 2 MI's, brother with MI, mother and father with CVA, MI's; She walks and doesn't smoke (thank god); She has a primary MD but also reports seeing a cardiologist; She reports a negative nuclear stress test (not sure when); I made her come in and talk about her HIGH risk for heart attack; Her labs are as followed:

TC = 252 Trig = 209 HDL-C = 42 VLDL-C = 42 LDL-C = 168
Non HDL-C = 252 - 42 = 210 TC/HDL-C = 6.0 TG/HDL-C ~ 5.0
Her glucose nonfasting was 145. Last year it was 126

"She is going to go see cardiologist; If nothing happens with him, where should I start and is nuclear stress test a good predictor of vessel disease; She obviously has metabolic syndrome and will likely need combo therapy but she makes me nervous because I think she is a heart attack waiting to happen; HELP!!"

DAYSRING ANALYSIS

I am so proud of the gynecologist's diagnostic acumen (unlike that of the primary care doc) as she indeed is a heart attack waiting to happen. The family history tells you that. The nuclear stress test only rules out significant obstructive coronary disease. It makes no major statement about her risk of MI or the presence or absence of atherosclerotic plaque. One can still have substantial intimal coronary atherosclerosis with negative stress testing. Those intimal plaques are potentially vulnerable to rupture and inducing thromboses and clinical events.

The patient is a diabetic (glu = 126) and that puts her in the highest risk classification there is: Coronary Heart Disease Equivalent. If the Cardiologist does nothing (and that is inconceivable) never ever refer to him/her again.

Since she is a CHD equivalent aggressive treatment is warranted. First step is to analyze the lipids: Her profile reveals elevated (high risk) TG, elevated VLDL-C (should be less than 30), reduced HDL-C (less than 50 in a woman) and seriously elevated LDL-C (>160 is in the high risk zone). Her Non HDL-C is extremely elevated at 212 (252 - 42). The TC/HDL-C ratio is 6.0. The TG/HDL-C is > 5 (indicative of small LDL particles if > 3.0). Every possible lipid is abnormal. She has very high levels of small LDL, VLDL remnants and significantly impaired reverse cholesterol transport.

She needs the following additional tests: TSH, Homocysteine, urine microalbumin and HgbA1c. Baseline LFT (she may well have fatty liver) and renal function are needed. One could order an hs-CRP, but it really would not add anything, since we already know this woman is high risk. We will treat her exactly the same no matter what her CRP is. A baseline CPK is warranted as it is virtually a certainty that we will be using combination lipid therapies.

The goals of therapy will include

Normalizing the HgbA1C (or to get it below 6)

Get the BP to less than 120/80: (Lotrel/Avalide works wonders: two combination therapies of 4 drugs, that will provide to the patient an ACEI, ARB, diuretic and calcium channel blocker). If her pulse tends to be fast, consider Tarka/Avalide. The CCB is verapamil which can slow HR. With these combos you get 4 drugs for two co-pays.

Get LDL-C to < 100 or at least a 30-40% reduction from baseline. Since we have no existing evidence that she has atherosclerosis, she would not qualify for the new Very High Risk category recently introduced by NCEP (National Cholesterol Education Program) which gives us an optional goal of LDL-C of less than 70.

Once the LDL-C goal is achieved if the TG are still abnormal, then a secondary goal is normalizing Non HDL-C to 130 (or the new optional 100 in the very high risk category). NCEP wants us to assume that by normalizing LDL-C and Non HDL-C we will have reduced her abnormal lipoproteins to normal. Of course those of you doing advanced lipoprotein testing that quantitates particles, know even non HDL-C lets us down in many cases.

Based on the above lipids, advanced students can guess what type of lipoproteins we are dealing with in the above patient. The elevated LDL-C and Non HDL-C tells us there are likely way too many VLDL, IDL and LDL particles (the carriers of atherogenic cholesterol): since all of these particles carry a single molecule of apolipoprotein B, the apoB level will be up. On NMR the LDL-P will be elevated. The abnormal TC/HDL-C and TG/HDL-C is highly suggestive of small highly atherogenic LDL particles. The high TG and low HDL-C suggest the lack of large HDL particles and a reduced apoA level. The patient will have impaired reverse cholesterol transport (RCT) and not enough HDL particles to perform their increasingly recognized antiatherogenic functions. Lastly, this woman almost certainly has postprandial hypertriglyceridemia diagnostic of remnant chylomicrons and VLDL (more atherogenic apoB particles).

Two very interesting articles were just published (references listed below). In the first Alan Sniderman ("Dr ApoB") states: It is important to appreciate the basis for this advantage for apoB: apoB is superior to LDL C when small-LDLs are present because the cholesterol indices will, by definition, underestimate LDL particle number in this circumstance. Statin therapy does produce similar proportionate reductions in the levels of LDL C, non-HDL C and apoB. But if small-LDLs predominate, the plasma level of apoB, relative to the distribution of apoB levels in the general population, will be higher than the levels of the cholesterol indices are to their distribution in the general population. This critical therapeutic point is illustrated by the results from the ACCESS study. In a group of patients treated with atorvastatin, both LDL C and non-HDL C reached their target levels – approximately the 25th percentile of the population, whereas plasma levels of apoB were just above the 50th percentile of the population. Given the evidence that clinical benefit is directly related to the extent of apoB reduction, this represents a major therapeutic gap.

In the second article, a great review of fasting TG, HDL-C and relationship to postprandial remnants: Conclusions: we found that a slower clearance of TG-rich lipoproteins from circulation postprandially results in low fasting levels of HDL cholesterol. Additionally, fasting plasma TG concentration is the primary determinant of the magnitude of postprandial lipemia. The delayed TG clearance postprandially seems to result in low HDL cholesterol even in subjects with low fasting TG. **The fasting TG > 121 mg/dl are predictable for abnormal response to fatty meal. Just think how many of your patients have fasting TG > 121. TGs lower HDL-C because cholesteryl ester transfer protein (CETP) swaps cholesterol from HDL for TG of VLDL and LDL, thereby depleting the HDL of cholesterol and lowering HDL-C levels. PLEASE STOP IGNORING POSTPRANDIAL TG LEVELS AND DO NOT BRING THE PATIENTS BACK FASTING AND ASSURE THE PATIENT IF TG LOWER WITH FASTING.**

THERAPY for the above patient

In addition to aggressive therapeutic lifestyle changes (needs low carb diet) using proper portion control) and exercise:

1) Initial lipid therapy Statin:

OPTIONS: Start Pravachol40/Zetia 10 mg or Vytorin 20 or Crestor 10 mg

2) ASA 81 mg daily

3) Metformin titrated slowly over 4-6 weeks to 2000 mg (make sure renal function OK)

4) 8 week follow up lipids and LFTs:

If LDL-C is not less than 100 and Non HDL-C not < 100-130 or LDL-P not < 1100

add TriCor 160 mg to the statin or statin/Zetia (TriCor and Zetia are off package label but a recent study revealed fantastic synergy).

5) If metformin does not get her HgbA1C to goal, add a TZD like Avandia or Actos. Might consider Avandamet (metformin and Avandia in the same pill). Downside is the weight gain that will occur with the TZD.

I close with the conclusions from just published data from the GENOA study here in the US: Conclusions: Dyslipidemia is highly prevalent in hypertensive adults. **Fewer than one third of these adults are drug-treated**, and **fewer than half of those treated achieve recommended goals**. Our findings suggest that an alarming 9 of 10 dyslipidemic hypertensive adults have untreated or undertreated dyslipidemia. WE ALL HAVE TO CHANGE THESE DISMAL STATS. SPREAD THE WORD TO ALL OF YOUR COLLEAGUES AND STUDENTS.

REFERENCES OF THE WEEK: (articles discussed above)

1) Ethnic and Sex Differences in the Prevalence, Treatment, and Control of Dyslipidemia Among Hypertensive Adults in the GENOA Study Arch Intern Med. 2004;164:1313-1318

2) Low fasting low high-density lipoprotein and postprandial lipemia. Genovefa D Kolovou*1, Katherine K Anagnostopoulou, Nektarios Pilatis, Nikolaos Kafaltis, Konstandina Sorodila, Eleftherios Psarros and Dennis V Cokkinos. Lipids in Health and Disease 2004, 3:18 This article is available free from: <http://www.lipidworld.com/content/3/1/18>

3) Applying apoB to the diagnosis and therapy of the atherogenic dyslipoproteinemias: a clinical diagnostic algorithm Allan D. Sniderman Current Opinion in Lipidology 2004, 15:433-438. Must reading for those of you who believe you can impact on CVD by relying on LDL-C calculations.

DAYSPRING UPCOMING TRAVELS

Austin, TX

Denver, CO

Bridgewater, Cherry Hill, NJ

Chicago, Rosemont, IL

Greenville, NC

Brooklyn, Newburgh, NY

Atlanta, GA

New Orleans, LA

West Palm Beach, Indian Shores (Tampa area) FL

If you ave not joined the National Lipid Association, what are you waiting for????

<http://www.lipid.org/>

As always I salute our men and women at arms here and abroad and to first responders here in the US. They should have our thoughts, prayers and support.

Good luck and happy lipiding,

Tom

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