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Dyslipidemia: the hidden sector of hypertension

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Abstract: Hypertension is one of the commonest leading causes to death with no one protected from developing it. It has many developing causes from idiopathic to stress and hyperlipidemia. 60.7% - 64.3% of hypertensive individuals were found to be hypercholesterolemic. From simply a faulty life style to a genetic cause of lipoprotein lipase mutation, dislipidemia develops and unfortunately patients remain unaware of their condition as it's asymptomatic so it's more likely to be discovered by chance.
Lipid absorption start with solubilisation by different lipase enzymes and detergent such as bile acids then transported through blood stream by lipoproteins to be stored as esters in liver. These circulating lipids may form plaques on the vessels' lining along with other components threatening the lumen to be closed and stiff walled thus decreasing blood flow.
Prevention and control of hyperlipidemia still remains to start with life style modifications. Like most disease, in recent years the consuming life style adapted affected our health aspect. With proper diet and physical exercise, patients improve their outcome with the medications aiding them in their long journey. But beware; controlling the lipid profile will not be complete without the control of the associated HTN due to their synergistic effect on cardio-vascular risk.

Key words: *Hypertension, dyslipidemia*

I. INTRODUCTIONS

Hypertension is one of the commonest leading causes to death[1]. It's a persistent lifelong elevation of blood pressure which may lead to serious effects as coronary artery disease, stroke, chronic renal failure and finally death from its complication. These days it's known that no one is protected from developing hypertension opposed to the past when it was considered a disease for old age. It affects all ages even youth[2]. Hypertension has many causes for developing such as idiopathic cause -most commonly-, smoking, lack of physical activity, excessive salt in diet, stress and hyperlipidemia[3].

Hyperlipidemia stands for abnormal elevation of lipid and/or lipoprotein in blood thus leading to atherosclerosis of arteries especially the aorta, coronaries, carotids and cerebral arteries [4]. Dyslipedemia is on the top of the concomitant condition associated with hypertension as 60.7% - 64.3% of hypertensive individuals found to be hypercholesterolemic[5]. Hypercholesterolemia also exacerbates the effect of hypertension on cardiovascular risk[6]. That's to say controlling hypertension alone would decrease that risk, but only through controlling other highly concomitant factors headed by dyslipidemia would this risk even slam further down[5, 7] .
But before we jump to the excessive lipids effect on the body let's go back to the very beginning of the process.
Lipid absorption start with solubilisation by different lipase enzymes and detergent such as bile acids then transported through blood stream by carriers called lipoproteins to be stored as esters in liver.

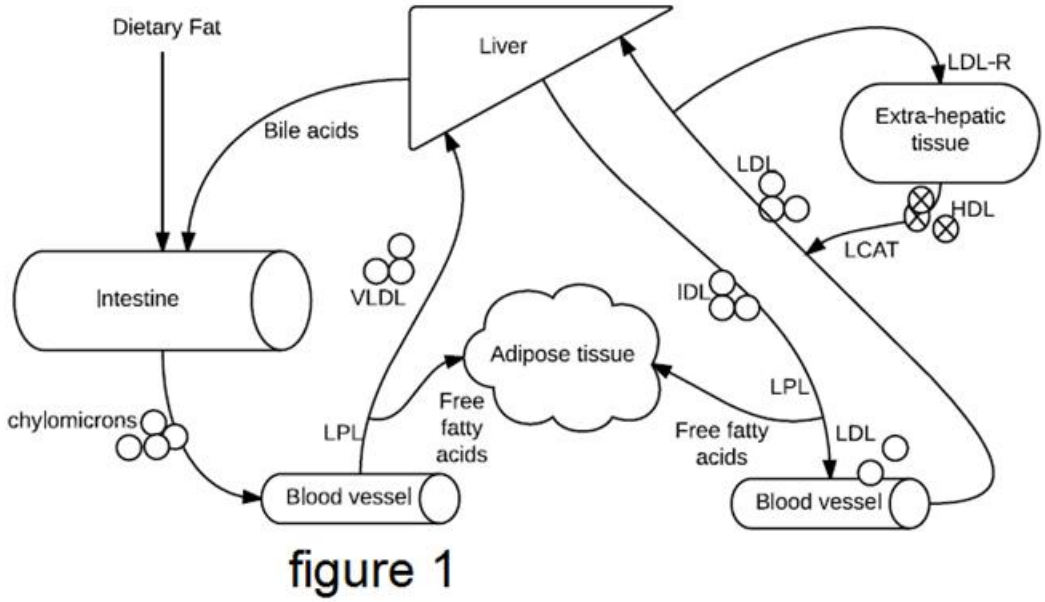
II. LIPOPROTEINS

The fat submarines that are responsible for transporting lipids through blood stream. They are formed of "lipo" meaning lipid and proteins. Since lipids are hydrophobic but proteins are hydrophilic, we know that lipoproteins are basically lipid inside a shell of proteins. There are different types of lipoproteins and each one carries lipid around the body by a different way as shown in table (1). Epienephrine, cortisol and insulin control the hormone-sensitive lipase responsible for releasing free fatty acids from the lipid storage sites.

Table 1: lipoproteins types

	HDL "good cholesterol"	LDL	VLDL	chylomicron
Made by	Liver and small intestine	Losing a lot of TGs form VLDL	By liver	Small intestine
Secreted	Blood stream	Blood stream	Into blood stream	Into lymph vessels then to blood stream
Rich in	cholesterol	cholesterol	TGs	TGs
function	Reverse cholesterol transport back to the liver "reverse heart diseases	Deliver cholesterol to all body	Deliver TGs to body cells	Deliver TGs to body cells
Contain Apo proteins	A,C,E&D	B100	B100,C&E	A,B48,C&E
Density	1.063-1.210	1.019-1063	<.95-1.006	<.95

Figure 1: action and sequence.



Causes of Dyslipidemia : shows a wide variation from simply a faulty life style to a genetic cause of lipoprotein lipase mutation. There's also diabetis mellitus type II, pregnancy, hypothyrodisim and medications such as Thiazde diuretics, cortisol, BB and estrogen, that may cause Dyslipidemia. And so forth with others.

III. SYMPTOMS

Though it's a highly prevalent disease[5], unfortunately patients remain unaware of their condition as it's asymptomatic so it's more likely to be discovered on screening investigations for atherosclerosis, other cardiovascular disease or a severe complications, for instance MI, stroke, premature coronary artery disease or pancreatitis.

IV. ATHEROGENIC EFFECT OF HYPERLIPIDEMIA

Circulating lipid may form plaques on the vessels' lining along with other components threatening the lumen to be closed and stiff walled thus decreasing blood flow through the following stages:

First the intimal lesion :- The subendothelial part of the intima shows lipids called Fatty streaks. The dissolved cholesterol crystals appear in paraffin sections in the form of needle shape clear clefts. There are also foam cells "macrophage engulfing lipid". The lesion could go further to be atheromatous plaque 'atheroma' with vascularization from the vasa vasorum, proliferated CT and smooth muscle cells and dystrophic calcification

appearing as dark blue granule in addition to the lipids and foam cells. Necrosis of the overlying endothelium would result in atheromatous ulcer.
Secondly the media: Opposite the intimal lesion, the internal elastic lamina atrophy and fragmentation emerges.

Discussion:-

In the last decade, the dream started, many studies had been made in preventing the hyperlipidemia in young age and so, decreasing the incidence of one of most commen causing factor for hypertension. With coexistence described by many studies of 15 to 31%.[8]

Prevention and control of hyperlipdemia still remains to start with life style modifications. Like most disease, in recent years the consuming life style adapted affected our health aspect.

DIET: it's proven to be the first line of combating hyperlipidemia and to be highly effective. Tackling one's diet is done through Decreasing saturated and Trans fat consumption[6], through decreasing fast food intake, Increasing fibers and plant stanol bring about parietal block of cholesterol absorption[9], Profetol diet which is a therapeutic vegetarian diet that showed marked reduction of LDL-c level[10] and finally Fish oil that would decrease TG[11] along with omega 3 PUFA augmenting the benefit of antihypertensive drugs[12, 13].

Regular physical activity: is also indicated. Weight reduction is shown to improve lipid profile picture. A clinical trial found that with aerobic exercise and a diet of high saturated fat, the lipid profile remain unchanged compared to that of only high saturated fat diet[14]. Another study found cardio-respiratory fitness in parental history of HTN would decrease the risk of developing HTN to 16% compared to those fit without family history. Parental history combined with low fitness individuals would have a 70% risk of developing HTN[15]. Another trial found in combined high intensity intermittent exercise, patients with altered baseline would have a decrease in total cholesterol and TG[16]. In contrast high intensity exercise also improved lipid profile only in hyperlipidemic women[17]. Exercise along with life style modifications would increase HDL level providing further protection from CVD[18].

V. MEDICATIONS

They include anti-hyper lipedimic drugs that either a) decrease lipid absorption or b) remove excess cholesterol from blood "statins". Detailed classification in table 2.

Table2: anti-hyperlipidemic drugs

	Statins	Niacin	Fibrates	Bile acid-binding resins	Inhibitors of intestinal sterol absorption	CEPT inhibitors
Mechanism of action	• Competitive inhibition of HMG-CoA reductase increasing LDL liver uptake • Pleiotrophic effects	• Adipose tissue: decrease fatty acids mobilization thus decrease TG and VLDL • Liver: decrease VLDL production • Plasma: increase lipoprotein lipase activity	As Niacin + • Increase HDL level	• Decrease LDL level By binding bile acids in the intestine preventing their reabsorbtion forcing liver up-regulating LDL receptors.	Decrease dietary and biliary cholesterol absorption	produced large increases in plasma HDL-C of around 140% with no observable adverse effect on CVS parameters [19,20]
Use	All types of hyperlipidemias	Mixed hyperlipidemia	Hypertriglyceridemia, Mixed hyperlipidemia	Primary hypercholesterolemia		Under trials

In familial hypercholesterolemia, the goal is reducing LDL-c at least 50% or less than 100mg/dl. Statins and proper life style are the treatment of choice[21]. Through this decrease of LDL-c level, the cardio vascular risk decrease by decreasing the atherosclerosis. It was found that 10% decrease of LDL will lead to 20% decrease of coronary heart disease. Statins alone was found to decrease the CVD by 30%[22]. Through the removal of major risk factors of CVD, life expectancy will increase almost 7 years[22]. So it's important to start control early.

From here comes the importance of genetic screening for gene mutations in families with positive history. If unavailable, highly elevated levels of LDL-C alongside cutaneous or tendon xanthomas before 10 years are suggestive of Homozygous Familial Hypercholesterolemia[23, 21].

Statins is the most described drugs in guidelines. The indications of different types depend on the severity of the LDL-C level. Rovastatin in HTN patients showed LDL-C decrease and marked improvement of coronary flow reserve[24]. Studies found atrovastatin to have effects on both lipid and blood pressure. It decrease lipids, improves endothelial function and decrease vascular tone. Thus improve the BP control of the prescribed antihypertensive drug[25, 26]. Combination of amlidipine and atrovastatin was found to markedly decrease BP and reverse left ventricular hypertrophy compared to amlidipine monotherapy[27]. In a 2010 review they found more patient achieve control of BP and LDL-C on combination. Also there was no modification of either drug action on the other[28].

Statins also showed an improve in BP control not shown in any other lipid lowering drug[7]. Though statin could cause myalgia, it's not combined with decrease strength or performance[29].

In an experiment on Hypertensive-induced rats (not hyperlipidemic) , amlodipine was found to further provide vasculature benefit with atrovastatin[30]. Another experiment on hyperlipidemic rats to assess the combination of atrovastatin and colchicine showed a synergistic effect in improving the endothelial function thus providing further protection from atherosclerosis and subsequently CVD[31]. The flushing effect of niacin has limited its use despite reports on improved CVR[32]. Though the current aim of treatment is to lower LDL-C, increasing HDL level seems just as important or even more so as 55% of patients admitted for CVD had low HDL-C levels at the time.[18]

Controlling the lipid profile will not be complete without the control of the associated HTN. Though Simultaneous control was less likely as severity of the underlying conditions increased, and more likely as medication adherence increased[33], Studies found that controlling HTN alone would decrease the risk approximately 25% while with combined cholesterol control the risk would decrease more than 35%[5]. Thus, achieving this control would give a highly beneficial outcome. BB and diuretics were also found to affect plasma lipids while CCB, ACEI and alpha agonist show no such effects. A dose dependant increase of cholesterol level was found with diuretics and the increase was worse in black. BB increased TG however, when cardio-selective with intrinsic sympathomimetic activity it reduce total cholesterol and LDL-C[34].

VI. CONCLUSION

The synergistic effect of Dyslipidemia and hypertension on the CVR left us to deduce hypertension control alone would not be enough to improve the patient outcome.

The aim should be to have controlled:-

1. Diet: through decreasing content of fat or its absorption
2. Drugs that help elevate HDL level and decrease LDL and VLDL
3. Proper combination of anti-hypertensive and anti-hyperlipidemic drugs
4. We hypotheses that decreasing liver intake of VLDL would limit the body content of saturated fatty acids.

Conflict of interest:

The authors declare no conflict of interest.

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