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"Pulse Pressure of Blood Flowing in Lumen of an Artery is Directly Proportional to Tunica Intimal Density of Lipid as well as Carbohydrate of that Artery" - The Theory of Atherosclerosis Created

Medical Science

KEYWORDS : Ascending aorta, Pulmonary trunk, Pulse pressure ,Lipid, Carbohydrate, Atherosclerosis.

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ABSTRACT

In order to observe proportionality, if any, between pulse pressure and tunica intimal density of lipid as well as carbohydrate, tissue of ascending aorta and pulmonary trunk was obtained during autopsy 1 cm distal to their commencement from 50 human adults to be preserved in 10% formalin (for carbohydrate) and in Baker's Calcium Cadmium Formal Solution-1944 (for lipid). Wall thickness and lumen circumference were measured in each arterial segment to calculate their pulse pressure in accordance with laws of arterial pulsation (Keshaw Kumar 1993).1

After processing paraffin sections of 10 micron thickness were cut with the help of rotary microtome to be stained with Sudan Black –B (for lipid) and PAS (for carbohydrate). It was observed that a ratio of 3:1 was existing between tunica intimal densities of lipid as well as carbohydrate in ascending aorta and pulmonary trunk resembling with the ratio of pulse pressures between these arteries i.e. (3:1). It was concluded that pulse pressure of blood flowing in the lumen of an artery is directly proportional to tunica intimal density of lipid as well as carbohydrate of that artery- the theory of atherosclerosis created by Dr. Keshaw Kumar.

INTRODUCTION

In the past studies of lipid in tunica intima of arteries have been done by Gross et.al. (1934)[2] , Harvey (1963)[3], Spiro and Wiener (1963)[4]. Clarification of relationship of systemic blood pressure with atherosclerosis has also been tried by Anitschkow (1913)[5], Bronte and Heptinstall (1954)[6], Davis and Klainer (1940)[7], Heptinstall et.al. (1958)[8], Morgan (1956)[9], Paterson et. al. (1960)[10], Sacks (1960)[11], Turnbull (1915)[12] and Wilkins et. al. (1959)[13]. Mucopolysaccharides of human arterial tissue were reported by Dyrbye and Kirk (1957)[14], Dyrbye, Kirk and Wang (1958)[15], Kirk and Dyrbye (1957)[16], Kirk, Wang and Dyrbye (1958)[17]. Bunting and Bunting (1953)[18] noticed acid mucopolysaccharides of aorta. Keshaw Kumar (1994, 1996, 2003, 2009, 2011)[19,20,21,22,23] described Anatomy of arterial lipid accumulation in coronary arteries and great arterial trunks. Somar and Schwartz (1971)[24] observed focal-H-cholesterol in pig aorta.

But as yet carbohydrate and lipid are not compared in ascending aorta and pulmonary trunk interrelating with their pulse pressure of blood by any author, therefore, present study was conducted to compare density of metabolic storage products (lipid and carbohydrate) in different layers of human ascending aorta and pulmonary trunk interrelating with their pulse pressures of blood.

MATERIAL AND METHODS

Hearts of 50 human adults were procured immediately after death due to accidents after knowing the history from their relatives that they were not suffering from any cardiovascular disease. Tissue of ascending aorta and pulmonary trunk was obtained I cm distal to their commencements. Wall thickness and lumen circumference were measured cutting the wall of arterial segments longitudinally to obtain mean of wall thickness and lumen circumference separately for ascending aorta and pulmonary trunk. Pulse pressure of ascending aorta and pulmonary trunk was calculated in accordance with following laws of arterial pulsation created by Dr. Keshaw Kumar (1993)[1].

1. Pulsatory power of an artery is equal to pulse pressure multiplied by volume of blood entering the lumen of that artery during each heart beat.
2. Pulsatory power of an artery is directly proportional to wall (tunica media) thickness of that artery having 1mm wall thickness is reported as 2000 Joule per heart beat.
3. Arterial lumen circumference in millimeters equals with volume of blood in milliliters entering the arterial lumen during each heart beat.

Tissue from 25 human adults was preserved in 10% formalin (for carbohydrate) and tissue from remaining 25 human adults was preserved in Baker's Calcium Cadmium Formal Solution-1944 (for lipid). After processing paraffin sections of 10 micron thickness were cut with the help of rotary microtome to be stained with Periodic Acid Schiffs (for carbohydrate) and Sudan Black-B (for lipid). Density of reaction product of lipid and carbohydrate per magnified field was observed in tunica intima, tunica media and tunica adventitia of ascending aorta and pulmonary trunk.

Each layer of ascending aorta and pulmonary trunk was graded as +, ++, +++ and ++++ with + representing minimum density and ++++ representing maximum density of reaction product of carbohydrate as well as lipid. Results were obtained as visual assessment by single observer only.

OBSERVATIONS

Lipid : (Table-I, Fig-1 and 2)

Density of reaction product of lipid was observed ++++ in tunica adventitia ++ in tunica media and +++ in tunica intima of ascending aorta while pulmonary trunk showed density of reaction product of lipid ++++ in tunica adventitia + in tunica media and + in tunica intima.

TABLE-I

Density of reaction product of lipid in human great arterial trunks.

Arteries	Tunica intima	Tunica media	Tunica adventitia
Ascending aorta	+ + +	+ +	+ + + +
Pulmonary trunk	+	+	+ + + +

Carbohydrate – (Table-II, Fig 3 and 4)

Density of reaction product of carbohydrate was observed ++++ in tunica adventitia ++ in tunica media and +++ in tunica intima of ascending aorta while pulmonary trunk showed density of reaction product of carbohydrate ++++ in tunica adventitia + in tunica media and + in tunica intima.

TABLE – II

Density of reaction product of carbohydrate in human great arterial trunks.

Arteries	Tunica intima	Tunica media	Tunica adventitia
Ascending aorta	+ + +	+ +	+ + + +

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Pulmonary Trunk	+	+	+ + + +

TABLE- III
Ratio between tunica intimal lipid/carbohydrate densities of ascending aorta and pulmonary trunk.

Metabolic Storage products	Tunica intima of ascending aorta	Tunica intima of pulmonary trunk	Ratio
Lipid	+ + +	+	3:1
Carbohydrate	+ + +	+	3:1

(Fig. 1)

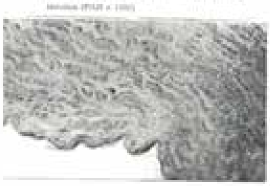
Transverse section of human ascending aorta showing +++ density of reaction product of lipid in its tunica intima (Sudan Black B x 100)

(Fig. 2)

Transverse section of human pulmonary trunk showing + density of reaction product of lipid in its tunica intima (Sudan Black B x 100)

(Fig. 3)

Transverse section of human ascending aorta showing +++ density of reaction product of Carbohydrate in its tunica intima (PAS x 100)



(Fig. 4)

Transverse section of human pulmonary trunk showing + density of reaction product of Carbohydrate in its tunica intima (PAS x 100)

A ratio of 3:1 was observed between tunica intimal density of lipid as well as carbohydrate of ascending aorta and pulmonary trunk. (Table-III)

Mean of wall (Tunica media) thickness was 1.5 mm in ascending aorta and 0.5 mm in pulmonary trunk while mean lumen circumference was 60mm in ascending aorta as well as in pulmonary trunk. (Table-IV)

TABLE – IV
Wall (Tunica media) thickness and lumen circumference of great arterial trunks.

Arteries	Wall (Tunica media) thickness	Lumen circumference
Ascending aorta	1.5 mm	60 mm
Pulmonary trunk	0.5 mm	60 mm

Pulsatory power of ascending aorta was calculated (1.5mm x 2000) = 3000 Joule per heart beat.

Pulsatory power of pulmonary trunk was calculated (0.5mm x 2000) = 1000 Joule per heart beat. It was calculated that 60ml. volume of blood (60mm=60ml) was entering the lumen of ascending aorta as well as pulmonary trunk during each heart beat.

On calculation pulse pressure of ascending aorta was obtained (3000» 60 = 50mm Hg.) and pulse pressure of pulmonary trunk was obtained (1000 »60=17mm Hg.) (Table –V).

TABLE-V
Pulsatory power, volume of blood entering the lumen during each heart beat and pulse pressure in human great arterial trunks.

Arteries	Pulsatory power	Volume of blood entering the lumen	Pulse pressure
Ascending aorta	3000 Joule per heart beat	60ml	50mm Hg.
Pulmonary trunk	1000 Joule per heart beat	60ml	17 mm Hg.

TABLE-VI
Ratio between pulse pressures and tunica intimal lipid/carbohydrate densities of great arterial trunks.

Pulse Pressure and Metabolic storage products	Ascending aorta	Pulmonary trunk	Ratio
Pulse pressure	50mm Hg.	17mm Hg.	3:1
Tunica intimal densities of lipid/carbohydrate	+++	+	3:1

It was observed that a ratio of 3:1 was existing between pulse pressures as well as between tunica intimal lipid/carbohydrate densities of ascending aorta and pulmonary trunk (Table –VI)

Therefore it was proved that pulse pressure of blood flowing in lumen of an artery was directly proportional to tunica intimal density of lipid as well as carbohydrate of that artery- The theory of atherosclerosis created by Dr. Keshaw Kumar.

DISCUSSION
As yet exact cause of arterial atherosclerosis has remained uncertain to smoking, alcoholism, anxiety and hypertension but the theory of atherosclerosis created by Dr. Keshaw Kumar declares the increasing pulse pressure as exact cause of atherosclerosis in arteries because atherosclerosis begins with increasing tunica intimal lipid density and it is the arterial pulse pressure

which is directly proportional to lunica intimal lipid density. Because increase or decrease in pulse pressure causes increase or decrease in tunica intimal lipid density in the same ratio, therefore, it is the increasing pulse pressure and nothing else which can be the exact cause of arterial atherosclerosis.

On the basis of theory of atherosclerosis created by Dr. Keshaw Kumar the mechanism of arterial atherosclerosis is established as follows:-

(1) Pulse pressure of blood is directly proportional to pinocytotic activity of endothelial cells of tunica intima.
(2) Pinocytotic activity of endothelial cells of tunica intima is directly proportional to amount of lipoproteins entering the tunica intima.
(3) Amount of lipoproteins entering the tunica intima is directly proportional to density of tunica intimal lipid as well as carbohydrate.
(4) Density of tunica intimal lipid as well as carbohydrate is directly proportional to relative inadequacy of metabolic removal of metabolic storage products (lipid and carbohydrate) in tunica intima.
(5) Relative inadequacy of metabolic removal of metabolic storage products (lipid and carbohydrate) in tunica intima is directly proportional to atherogenesis.

Due to increase in pulse pressure of blood pinocytotic activity of endothelial cells of tunica intima is also increased which results into increased density of tunica intimal lipid as well as carbohydrate causing increased amount of lipoproteins entering the tunica intima due to which relative inadequacy of metabolic removal of constituent lipid as well as carbohydrate is produced because inner 1/3 of tunica media and entire tunica intima is devoid of blood vessels and in this way atherogenesis occurs.

The mechanism of atherosclerosis laid down by Dr. Keshaw Kumar on the basis of theory of atherosclerosis created by him is supported by findings of following workers.

1. Harvey (1963)[3] presented some observations on the mechanism of arterial lipid accumulation in human coronary artery atherosclerosis. These observations supported the concept of plasma proteins entering the arterial wall from the lumen and because of localised relative inadequacy of metabolic removal of the constituent lipids accumulated in selective areas of the arterial intima the lesions of atherosclerosis are produced.
2. Gross et. al. (1934)[2] reported earlier appearance and more marked deposits of lipid crystals in the intima of anterior interventricular branch of left coronary artery in human beings.
3. Spiro and Wiener (1963)[4] have also observed membrane enclosed droplets and large vacuoles within the endothelial cells of rat coronary artery probably presenting transport phenomenon within the cells. According to them pinocytotic activity might be of importance in certain pathological phenomena particularly the accumulation of lipid in atherosclerosis.

Because the density of subintimal lipid which is directly proportional to pulse pressure of blood can not increase without increase in the pinocytotic activity of endothelial cells due to which amount of lipoproteins entering the tunica intima is increased which is responsible for producing relative inadequacy of metabolic removal of constituent lipids therefore, mechanism of atherosclerosis established by Dr. Keshaw Kumar is supported by the findings of above authors.

The opinion of Dr. Keshaw Kumar that increasing pulse pressure of blood is the exact cause of arterial atherosclerosis is supported by the findings of following workers.

1. Turnbull (1915)[12] observed that atheromatous plaques were common in the pulmonary arteries of patients with mitral stenosis and he suggested that the high pulmonary pressure might be a factor in their production.
2. Davis and Klainer (1940)[7] demonstrated a relationship between coronary disease severity and arterial pressure.
3. Paterson et.al (1960)[10] established that the total extractable lipid in the coronary, cerebral and femoral arteries was related to blood pressure.
4. Wilkins et.al. (1959)[13] and Sacks (1960)[11] used heart weight as a guide to blood pressure and inadequacies of heart weight as an indicator of arterial pressure.
5. Anitschkow (1913)[5], Bronte-Stewart and Heptinstall (1954)[6], Heptinstall et. al (1958)[8] noticed that lesions found in cholesterol fed rabbits are not the same as those found in human arteries and the effects of experimental hypertension in these animals may not be relevant to human vascular disease.

Because pulse pressure of blood is always increased with an increase in blood pressure, therefore, the theory of atherosclerosis created by Dr. Keshaw Kumar is supported by the findings of above workers who have observed the relationship of atheromatous plaques with increasing blood pressure in past.

The theory of arterial atherosclerosis created by Dr. Keshaw Kumar is supported by following evidences also.

1. Normally atherosclerosis does not occur in pulmonary trunk and its branches unlike the ascending aorta and its branches unless there is pulmonary hypertension because pulse pressure of blood in pulmonary trunk is three times less than the pulse pressure of blood in ascending aorta (Keshaw Kumar 2003)[21].
2. In cases of myocardial infarction the anterior interventricular branch of left coronary artery is the most effected artery and posterior interventricular branch of right coronary artery is the least effected artery because tunica intimal density of lipid as well as pulse pressure of blood in anterior interventricular artery is three times more than the tunica intimal density of lipid as well as pulse pressure of blood in posterior interventricular artery (Keshaw Kumar 2003, 2009) [21, 22].
3. Lower prevalence of atheromatous plaques in the neck arteries and upper aorta as compared with the higher prevalence in the distal aorta and iliac arteries in view of the fact that femoral to carotid pulse pressure ratio is approximately 3:2 as quoted by Hurthle (1934, 1935 cited by Wehn 1957)[25].
4. In the veins pulse pressure of blood is zero therefore veins are never effected by atherosclerosis (Keshaw Kumar 2003) [21].

   Pulse pressure of blood in ascending aorta is thrice more than pulse pressure of blood in pulmonary trunk due to which tunica intimal density of reaction products of lipid as well as carbohydrate is thrice more in tunica intima of ascending aorta than the density of reaction products of lipid as well as carbohydrate in tunica intima of pulmonary trunk as has been reported in present study. Findings regarding reaction products of lipid in present study resemble with the findings regarding reaction product of lipid in ascending aorta and pulmonary trunk reported by Keshaw Kumar (1994, 1996) [19,20].

+ + + density of reaction product of lipid in tunica intima of ascending aorta and + density of reaction product of lipid in tunica intima of pulmonary trunk observed in present study confirms the theory of atherosclerosis i.e. "Tunica intimal density of lipid in an artery is directly proportional to pulse pressure of blood flowing in the lumen of that artery" created by Keshaw Kumar

(1994, 1996, 2003)[19,20,21].

Carbohydrate and lipid both are metabolic storage products, therefore, density of their reaction products resemble with each other in different layers of ascending aorta and pulmonary trunk depending upon the pulse pressure of blood there (Keshaw Kumar 2011)[23]. Tunica intimal accumulation of carbohydrate also takes place like the tunica intimal accumulation of lipid reported by Keshaw Kumar (1996, 2003)[20,21] supporting the mechanism of lipid accumulation described by Harvey (1963)[3] Spiro and Weiner (1963)[4] and findings regarding, metabolic storage products in present study resemble with the findings of metabolic storage products in great arterial trunks reported by Keshaw Kumar (2011)[23].

On the basis of 50mm Hg. pulse pressure of blood with +++ tunica intimal density of lipid as well as carbohydrate in ascending aorta and 17mm Hg. pulse pressure of blood with + tunica intimal density of lipid as well as carbohydrate in pulmonary trunk observed in present study it is concluded that pulse pressure of blood flowing in the lumen of an artery is directly proportional to tunica intimal density of metabolic storage products (lipid as well as carbohydrate) of that artery.

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