Effect of Smoking on Serum Amylase and Lipase Enzymes

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Abstract: Introduction: Cigarette smoking is a recognized risk factor for the induction of pancreatic diseases and is suspected to play a major role in the development of metabolic syndrome. It has been demonstrated that nicotine may also alter normal exocrine pancreatic function. However, these changes have not been fully elucidated. Aim of the work: To assess the effect of smoking on serum amylase and lipase as markers of exocrine pancreatic function. Methods: Fifty smokers and 20 age matched non smokers were compared as regards the level of serum amylase and lipase. There was18 mild, 11 moderate and 21 heavy smokers. Then, non smokers and mild smokers were compared to moderate and heavy smokers as regards the level of the same enzymes. Results: Both serum amylase and lipase were significantly decreased in smokers than non smokers (p=0.002 and 0.000, respectively). There was a significant difference between mild smokers and both moderate and heavy smokers as regards the same enzymes and a significant negative correlation between Pack. Year index and their levels. Conclusions: Low serum amylase levels may reflect impaired exocrine-endocrine relationship in the pancreas. Lipase level decreased (undiscriminating its different types), with a net result of dyslipidaemia.
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1. Introduction

Smoking, one of the avoidable causes of mortality, is considered a major risk factor for cardiovascular, pulmonary and metabolic diseases [(1)].Cigarette smoking leads to the uptake of many hazardous compounds and their metabolites extracted from burning tobacco lead to changes in the essential parameters in body homeostasis [(2).]

The pancreas is one of the first organs pathologically affected by the tobacco smoking. However, the mechanism of development of these changes is not eventually recognized [(3)].

Modern research relies on biomarkers, which are defined as any substance, structure, or process that can be measured in the body or its products, and which influence or predict the incidence of outcome or disease [(4)].

Serum amylase levels may reflect metabolic abnormalities and abnormal glucose metabolism, both of which are associated with impaired insulin action [(5)].

Lipase is the enzyme produced by the pancreas to metabolize fats. So, its deficiency can adversely affect the digestion of fats. There are several types of lipase enzymes, out of which pancreatic lipase is the most common lipase found in the human digestive system. Lipase is also produced by the stomach and the liver and they are known as gastric lipase and hepatic lipase respectively. Apart from pancreatic lipase, some related enzymes can be found in the human body such as, lipoprotein lipase and endothelial lipase. Deficiency of this enzyme can adversely affect the digestion of fats [(6)].

Some experimental studies have examined the direct effect of smoking on pancreatic dysfunction; however, any molecular mechanism for its impact remains highly speculative.

Aim of the work

This work aims at studying the effect of smoking on serum amylase and lipase levels as well as the impact of different smoking indices on these enzymes.

2. Subjects and Methods

The study was carried on 50 smokers and 20 age matched non smokers. Smoking history was elicited in detail and smoking pack year index was then calculated by using the formula:

{Number of cigarettes smoked per day × Number of years smoked) /20}

Both groups were compared as regards the level of serum amylase and lipase.

Smokers were classified into mild, moderate and heavy based on the number of pack. years as ≤ 10, 11 to 19 and ≥20, respectively. There was18 mild, 11 moderate and 21 heavy smokers.

Then, non smokers and mild smokers were compared to moderate and heavy smokers as regards the level of the same enzymes.

3.Results:

The study was carried on 50 non- alcoholic smokers and 20 age-matched non smokers.

Table I. Comparison of smokers and non-smokers as regards demographic data

		N	Minimum	Maximum	Mean	±SD	t	*P*
Age (years)	Smokers	50	32.00	58.00	43.78	±7.7	0.601	0.550
	Non-smokers	20	19.00	58.00	42.35	±11.7		

Both serum amylase and lipase were significantly decreased in smokers than non smokers ($p = 0.002$ and 0.000, respectively) (Table II).

Table II: Comparison of smokers and non-smokers as regards exocrine pancreatic enzymes

		N	Minimum	Maximum	Mean	±SD	t	*P*
S. Amylase (U/L)	Smokers	50	36.00	54.00	46.60	±6.8	3.197	0.002*
	Non-smokers	20	34.00	71.00	54.15	±12.9		
S. Lipase (U/L)	Smokers	50	24.00	48.00	29.46	±8.1	4.007	0.000*
	Non-smokers	20	22.00	62.00	38.85	±10.5		

*P** is significant if < 0.05.

Table III shows that there was a significant difference between mild smokers and both moderate and heavy smokers as regards the same enzymes (0.000 in both amylase and lipase).

Table III: Comparison of different smoking indices as regards exocrine pancreatic enzymes

	Smoking index	N	Mean	±SD	*P*	LSD
S. Amylase (U/L)	Mild	18	53.39	±0.6	0.000*	Mild vs moderate and heavy
	Moderate	11	44.91	±6.8		
	Heavy	21	41.67	±4.6		
S. Lipase (U/L)	Mild	18	36.56	±10.2	0.000*	Mild vs moderate and heavy
	Moderate	11	24.46	±0.5		
	Heavy	21	26.0	±1.7		

*P** is significant if < 0.05

Table IV describes the significant negative correlation between Pack.Year index and both serum amylase and lipase levels (0.000 and 0.001 respectively).

Table IV: Correlation between exocrine pancreatic enzymes and smoking index

		Smoking index	
S. AMYLASE	r	-0.833	
	P	0.000*	
S. LIPASE	r	-0.445	
	P	0.001*	

4. Discussion

Cigarette smoking is the most popular form of smoking and is one of the most prevalent social habits worldwide. Tobacco smoke contains multiple agents with cytotoxic or carcinogenic effects on the exocrine pancreas and studies have shown a close correlation between cigarette smoking and pancreatic dysfunction and /or cancer [(7)].

The study was carried on 50 non- alcoholic smokers and 20 age-matched non smokers.

Serum amylase was significantly decreased in smokers than non smokers ($p = 0.002$) and there was a significant difference between mild smokers and both moderate and heavy smokers as regards the same enzyme. There was a significant negative correlation between Pack.Year index and serum amylase level (r=-0.833).

Previous studies reported different facts. Dubick *et al.,* found that in smokers, basal serum amylase was 100% higher, than in the non-smokers [(8)]. Several explanations are possible, such as greater reflux of secretory pancreatic proteins into the blood. The exact mechanism behind this increased "leakiness" remains to be elucidated. Also, "subclinical" pancreatic cell injury caused by cytotoxic substances in the smoke or sustained increased intraductal pressure induced by the complex pharmacological actions of nicotine might be the cause [(9)].

Sliwińska-Mossoń *et al.,* found that it's mainly isoenzyme type II and III that increase. The latter was found only in acute pancreatitis [(10)].

Addition of nicotine at concentrations ranging from 10 μM to 30 mM caused dose-dependent increases in pH of acinar suspension with simultaneous amylase release. There was no increase in basal non-stimulated amylase release when acinar cells were incubated with nicotine adjusted to pH 7.40 [(11)].

On the other hand, Chowdhury *et al.,* said that amylase release in isolated acini was significantly decreased by nicotine, whereas the total cellular

amylase content was significantly increased indicating that a postreceptor mechanism is involved in the inhibition in stimulus-secretion coupling. The increase in total cellular amylase content and decreased enzyme secretion by nicotine may be implicated in the induction of pancreatic pathology [12]. Didilescu *et al.,* and Fujinami *et al.,* described a similar drop in salivary amylase too [3, 13].

Low serum amylase levels may reflect impaired exocrine-endocrine relationship in the pancreas. Insulin affects amylase secretion via the islet-acinar axis. Insulin binds to its receptor on acinar cells and stimulates amylase secretion [14-17]. Serum amylase levels are inversely associated with most cardiometabolic risk factors and may reflect metabolic abnormalities and abnormal glucose metabolism. Low serum amylase levels precede the overt metabolic abnormalities. The serum amylase level decreased significantly with increasing number of components of metabolic syndrome (MetS) [5].

Hayden *et al.,* suggested that a continuous interstitial matrix connection between endocrine and exocrine is lost in animal models and humans with type 2 diabetes, resulting in a dysfunctional insulino-acinar-ductal-incretin gut hormone axis [18]. Besides these mechanisms, there are multiple defects in insulin secretion and signaling in type 2 diabetes which might be associated with the low amylase secretion from the pancreas [5].

Blood insulin levels were not measured. Previous studies suggest that low circulating amylase may reflect low insulin secretion. However, obese people with MetS and type 2 diabetes tend to show hyperinsulinemia to compensate for insulin resistance. Therefore, whether low serum amylase levels are truly associated with hypoinsulinemia or hyperinsulinemia is unclear [5].

Serum lipase was significantly decreased in smokers than non smokers (p = 0.000) and there was a significant difference between mild smokers and both moderate and heavy smokers as regards the same enzyme. There was a significant negative correlation between Pack.Year index and serum lipase level (r=-0.445).

There are several types of lipase enzymes, out of which pancreatic lipase is the most common lipase found in the human digestive system. Lipase is also produced by the stomach and the liver. Some related enzymes can be found in the human body such as, lipoprotein lipase and endothelial lipase. Deficiency of this enzyme can lead to increase in the levels of cholesterol and triglycerides in the body, to glycosuria in spite of normal blood glucose level and can lead to decreased cell permeability so that nutrients cannot easily enter the cell, while the waste materials cannot easily get out. Lipase deficient individuals often encounter problems in losing weight and are also more likely to develop varicose vein problems. Plasma lipase is an important regulator of plasma lipoprotein concentration. TGL rich lipoprotein is hydrolyzed by the catalyst lipoprotein lipase and thus, enables clearance of TGL from blood [6]. .

Mechanisms for the altered lipid profile among smokers were proposed: Nicotine stimulates catecholamines resulting in lipolysis and increased concentration of plasma free fatty acids (FFAs) which further results in increased secretion of hepatic FFAs and triglycerides along with very low density lipoprotein cholesterol (VLDL-c) in blood [19-21]. Fall in estrogen due to smoking leads to decreased HDL while hyperinsulinaemia in smokers leads to increased cholesterol, LDL-c, VLDL-c and TG due to decreased activity of lipoprotein lipase [22].

Adiponectin was described as a mechanism linking adiponectin to endocrine pancreatic function since its receptors AdipoR1 and AdipoR2 are expressed in human pancreatic b cells. Higher adiponectin concentrations increase insulin sensitivity, decreasing insulin concentrations and facilitating glucose control. Alternatively, cigarette smoke reduce adiponectin concentrations. In addition to the lipolytic effect of nicotine on adipose tissue, mediated via catecholamine release [9].

Kong C et al hypothesized that smoking is associated with increased hepatic lipase activity, insulin resistance, dyslipidaemia and early atherosclerosis in Type 2 diabetes [23]. Since hepatic lipase converts VLDL to LDL].This may be one mechanism whereby smoking further increases the risk of cardiovascular disease in Type 2 diabetes.

On the other hand, Chajek-Shaul T et al reported that smoking depresses adipose lipoprotein lipase response to oral glucose. LPL helps unloading plasma triglycerides in peripheral tissues. The greater the insulin release, the less the decrease in lipoprotein lipase activity. The lower body weight in smokers can be related to the paradoxical response of adipose tissue lipoprotein lipase to carbohydrate and that the reversal of this behavior contributes to the weight gain often observed after cessation of smoking [24].

Sentí M et al proved that this response is genetically determined (H+H+ genotype has a deleterious effect on lipid profile) and is modulated by physical activity so that the expenditure of more than 291 kcal/day in physical activity improves lipase response to oral glucose and modulates the combined effect of a common variant of the lipoprotein lipase gene and smoking on serum triglyceride levels and high-density lipoprotein cholesterol in men [25].

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