◎原 著

Age and Gender-Related Alterations of Six Serum Pancreatic Enzymes in Healthy Subjects

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Abstract : The serum levels of some pancreatic enzymes have been reported to be affected by age and gender. Currently, serum total amylase, pancreatic isoamylase (P-amylase), lipase, trypsin (ogen), pancreatic phospholipase A_2 (PLA₂), and elastase I are utilized in diagnosing pancreatic diseases. We here compared age and gender-related alterations of these six pancreatic enzymes in healthy subjects to delineate different properties among the enzymes.

Subjects were 155 males and 172 females between ages 20 and 79 years who were apparently healthy, and were stratified by age and sex. PLA_2 and elastase I were assayed by RIA, trypsin(ogen) by EIA and others by activity. The pancreatic enzymes, except PLA_2 , were significantly elevated with age, although they declined in males in the ≥ 60 age group. There were significantly higher in females than in males in the ≥ 60 age group, P-amylase in the 40-49 age group. Age should be considered in the valuation of serum enzymes except PLA_2 , sex differences should be considered in the valuation of amylase (total and P-amylase).

Keywords : pancreatic enzyme, amylase, phospholipase A2, aging, gender

Introduction

The serum levels of some pancreatic enzymes have been reported to be affected by age and gender¹⁻⁵⁾. Although the age and gender-related alterations are considered to be related to biochemical properties and renal or extrarenal handling of enzymes, the detail is not clear. Currently, serum total amylase, pancreatic isoamylase (P-amylase), lipase, trypsin(ogen), pancreatic phospholipase A_2 (PLA₂), and elastase I are utilized for the detection and/or diagnosis of pancreatic diseases⁶⁻¹¹.

In the present study, we compared age and gender-related changes of these six pancreatic enzymes in healthy subjects to delineate different properties among the enzymes.

Materials and Methods

SUBJECTS

The present study included healthy subjects (20-79 yr, 155 males, 172 females) undergoing routine annual check-up, who were judged as disease-free based on history, physical examination, complete blood count, blood chemistry, urine and stool examination, upper GI series, and abdominal ultrasonography. Blood samples were collected after an overnight fast, and aliquots of sera were stored at -35° C until assay of pancreatic enzymes. Informed consent was obtained from all subjects, and the procedures were in accordance with the Helsinki Declaration.

ENZYME ASSAY

Total amylase was assayed by a colorimetric method (α - amylase EPS, Boehringer Mannheim, Germany), P-amylase by an immunoinhibition method (Iso-amylase EPS, Boehringer Mannheim, Germany), lipase by a turbidimetric method (Lipase monotest, Boehringer Mannheim, Germany), trypsin(ogen) by an enzymeimmunoassay method (Kodazyme Trypsin M-EIA, Hoechst Marion Roussel, Osaka, Japan), PLA₂ by a radioimmunoassay method (Shionoria PLA₂, Shionogi, Osaka, Japan), and elastase I by a radioimmunoassay method (RIA Kit, Dainabot, Tokyo, Japan).

STATISTICAL PROCEDURES

Data were checked for normal or log-normal distribution. The significance of age and gender on the pancreatic enzyme levels was determined by two-way analysis of variance after performing Grubbs-Smirnov test. p < 0.05 was considered statistically significant.

Results

Total amylase, P-amylase, lipase, and trypsin

(ogen) levels were positively skewed and were logarithmically transformed. PLA_2 showed the normal distribution. Elastase I was between the normal and logarithmic normal distributions.

Medians of serum pancreatic enzyme levels for males and females in the various age groups are shown in Table 1. Serum pancreatic enzymes, except PLA₂, were significantly affected by age. These enzymes were elevated with age, although they declined in males older than 60 years. There were significant sex differences in total amylase and P-amylase levels : total amylase levels in female were significantly higher than those in males in the >60 age group (p<0.03), P-amylase levels in the 40-49 age group (p< 0.03).

Table 1.	Effect of Age and	Gender on Serum Le	evels of Six Pancreatic Enzymes
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Age(yr)	Sex	n	T-Amylase (IU/L)	P-ISO (IU/L)	Lipase (U/L)	Trypsin (ng/ml)	PLA2 (ng/di)	Elastase (ng/di)
20-39	м	33	128(70-224)	60(32-85)	67(18-167)	50(27-75)	253(130-439)	199(107-249)
	F	36	148(81-210)	65(39-112)	73(14-165)	45(19~66)	266(137-417)	181(123-289)
40-49	м	56	134(70~263)	67(37-119) ₁ *	86(30-207)	54(26-89)	280 (88-459)	213(106-390)
	F	62	146(72-295)	74(28-172)	84(17-201)	46(24-93)	260(130-496)	188(98-356)
50-59	м	49	158(77-343)	75(47-148)	98(20-195)	56(42-152)	290(148-560)	210(140-445)
	F	45	163(72-352)	71(36-138)	102(15-278)	53(30-118)	279(92-525)	225(126-393)
60~	м	17	140(102-189) +	68(44-116)	86(30-178)	53(24-91)	260(137-347)	173(129-360)
	F	29	182(84-321)	82(25-163)	93(44-260)	60(36-157)	312(119-586)	223(136-382)
				An	alysis of varian	C0		
Age								
M			0.03	0.002	0.02	0.03	NS	0.04
F			0.03	0.05	0.02	0.0006	NS	0.0001
Gender			0.04	0.02	NS	NS	NS	NS

Data expressed as median (and range). NS: p > 0.05, p < 0.03 for sex difference

Discussion

In the present study, serum pancreatic enzymes, except PLA_2 , showed significant age-related changes. It has been reported that serum levels of some pancreatic enzymes increase with age, although their results were not always consistent^{1.6)}. There are four possible mechanisms for the increase of pancreatic enzymes with aging : 1) the decrease of pancreatic enzyme clearance due to the decrease of renal function. 2) the increased release of pancreatic enzymes into blood due to the increased fragility of pancreas. 3) the decrease in uptake and degradation of pancreatic enzymes by a variety of body

tissues. 4) the increased release of pancreatic enzymes from extrapancreatic sources. However, it is generally accepted that age-related increase of serum pancreatic enzymes is due to a decline of renal function¹⁺³. The previous study showed that total amylase, P-amylase, trypsin(ogen), PLA₂ were vulnerable to impaired renal function¹². Why PLA_2 is not influenced by age is not clear. Most of PLA₂ in blood seem to be derived from the pancreas since PLA₂ is present only a little in organs other than the pancreas¹³⁾. Moreover, the previous studies suggested that the pancreatic enzyme content of pancreas decreased with age^{14,15)}, and that the extent of decrease of the enzymes was different¹⁵⁾. Therefore, a possible explanation for why PLA₂ is not influenced by age is that the release of PLA_2 from the pancreas may decrease with age more severely than that of the other pancreatic enzymes. Thus, PLA_2 may not be elevated in blood with age. Serum elastase I levels also increased with age. Elastase I in the blood stream is present as complex forms with inhibitor proteins, such as α_1 - antitrypsin and α_2 - macroglobulin^{16,17}, which can hardly pass through glomeruli and are mainly cleared by extrarenal metabolic pathways^{18, 19}. Some studies have shown that serum elastase I levels are less affected by renal dysfunction, suggesting that it is cleared mainly by extrarenal metabolic pathway such as the reticuloendothelial system^{12, 20, 21)}. We previously reported that serum elastase I was significantly elevated only in patients with severe renal dysfunction (creatinine clearance $\leq 10 \text{ ml/min}$)¹²⁾. Subjects with moderate to severe renal dysfunction were excluded in this study. Therefore, extrarenal metabolic pathway, such as the reticuloendothelial system, also seems to be involved in the increase of serum levels with age. However, we cannot completely exclude the possibility that the sources of elastase I other than the pancreas may

contribute to the significant age-related changes in serum levels because the enzyme is still detectable in pancreatectomized patients¹⁹⁾, and it often increases in nonpancreatic diseases such as ileum-colon disease¹⁹⁾.

The present study showed that total amylase and P-amylase levels only were affected by gender. Although Moller-Petersen and Pedersen¹⁾ reported that trypsin (ogen) was affected by gender, we did not confirm their results in this study. It is not clear why amylase is apt to be affected by gender. Kasperczyk et al²²⁾ reported the significant change of amylase activity in the ovary of rats during sex cycle, suggesting the involvement of sex hormone. The difference in amylase levels between male and female could not be explained only by the differences in renal function between male and female, because trypsin (ogen) and PLA_2 , which are vulnerable to renal dysfunction, were not affected by gender. The sex difference of P-amylase in the 40-49 age group may be related to menopause. The etiology of the sex difference of total amylase in the ≥ 60 age group is not clear.

Finally, no studies on the gender-related difference in extrarenal metabolic function have been undertaken. The present study did not demonstrate the gender-related difference, since there was not any significant difference in serum elastase I levels between male and female.

In conclusion, PLA_2 and amylase (total and P-amylase) proved to have particular properties among the six pancreatic enzymes. PLA_2 only did not show age-related change. The age-related changes of the other enzymes may reflect a decline of renal and extrarenal clearance of enzymes with age. Amylase (total and P-amylase) only was significantly affected by gender. The etiology of the sex difference of amylase requires further investigation.

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6 種類の血中膵酵素値に及ぼす加齢および性の影 響

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ある種の血中膵酵素値は加齢や性により影響を 受けることが知られている。現在膵疾患の診断に 利用されている6種類の膵酵素、アミラーゼ、P-アミラーゼ、リパーゼ、トリプシン、フォスフォ リパーゼA2(PLA2)、そしてエラスターゼ I の血 中値に及ぼす加齢および性の影響を比較検討した。 Minerva Gastroenterol Dietol 40 : 113-117, 1994.

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- 健常者327名(男性:155名,女性:172名,年齢: 20-79歳)を対象として,年齢および性により層 別化して検討した。PLA₂とエラスターゼ I はRIA, トリプシンはEIA,そして他の酵素は活性を測定 した。PLA₂以外の血中膵酵素値は加齢とともに 有意に上昇した。しかし男性では60代以降低下し た。性差はアミラーゼとP-アミラーゼとに有意 差が認められた。すなわち,アミラーゼとに有意 差が認められた。すなわち,アミラーゼは60代以 降に,P-アミラーゼは40-49歳群でそれぞれ男 性より女性において有意の高値を示した。PLA₂ 以外の血中膵酵素値を評価する際には加齢による 影響を考慮すべきであり,アミラーゼおよびP-アミラーゼの血中値を評価する際には性を考慮す べきである。

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