SHORT COMMUNICATION

Influence of Haemodialysis on Lipase Activity

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Summary: Our aim was to determine whether the increase in serum pancreatic lipase values, reported in patients with chronic renal failure maintained on haemodialysis, is the result of haemoconcentration by fluid removal during dialysis, or whether it is due to lipase stimulation by endothelial lipoprotein lipase, induced by the heparin used as an anticoagulant. We therefore compared the increases in serum lipase, when heparin was used, with those observed when this was replaced by the antithrombotic agent, defibrotide, which has no effect on lipoprotein lipase. In addition, in order to determine the effects of haemoconcentration, variations in total protein concentration and haematocrit values were determined on the same samples, both before and after dialysis. The results showed a statistically significant post-dialysis increase in lipase only when heparin was used (p < 0.03). There was also a mean percentage post-dialysis increase of 16.2% in total protein (p < 0.0001) and 15.5% in haematocrit (p < 0.0001), due to fluid removal. No significant correlation in percentage increases was found between lipase vs total protein or haematocrit values. These findings suggest that heparin-induced lipoprotein lipase stimulation is the principal cause of the post-dialysis increase in pancreatic lipase, and that fluid removal during dialysis makes only a minor contribution to this increase.

Introduction

Elevated serum values of pancreatic enzymes in chronic renal pathology have been frequently reported even without clinical signs of pancreatitis (1–6). These findings make laboratory diagnosis of acute pancreatitis difficult in uraemic patients with abdominal pain (7). Particularly high levels have been found in patients maintained on haemodialysis, both before and, especially after, dialysis (4, 6, 8). The enzyme most affected was lipase, and it has been suggested that this post-dialysis increase may be caused primarily by heparin-induced endothelial lipoprotein lipase activity, as heparin is routinely used during dialysis as an anticoagulant (8).

To verify this hypothesis we measured serum lipase activity in haemodialysis patients both before and after dialysis, using the conventional anticoagulant heparin during the first session, and substituting it with defibrotide, which does not affect lipoprotein lipase, one week later. Moreover, in order to determine whether the post-dialysis rise in lipase concentration is also due to haemoconcentration associated with ultrafiltration during dialysis, we compared the dialysis-induced percentage changes in haematocrit and total protein values with the percentage changes in lipase values.

Results and Discussion

Figure 1 shows mean ± SD pre- and post-dialysis values of serum lipase activity using heparin and its substitute defibrotide as anticoagulants. Predialysis values were elevated above normal limits in approximately 60% of patients, and values increased after dialysis. When heparin was used there was a 24.2% increase between pre- and post-dialysis values (238.7 ± 107.6 U/l vs 295.7 ± 107.7 U/l; t = 2.328; p < 0.03), while with defibrotide the increase was 9.1% (253.4 ± 99.8 U/l vs 276.0 ± 104.6 U/l; t = 0.951; p = 0.345). Mean pre-dialysis total protein values were 61 g/l, while after dialysis they were 71 g/l with a mean percentage increase of 16.2% (p < 0.0001). Haematocrit increased by 15.5% (33.3% pre- vs 38.5% post-dialysis; p < 0.0001).

Figure 2 shows the correlation of percentage increases between total protein and haematocrit values in the individual samples. The correlation was statistically significant (r = 0.40; p < 0.01). In contrast, the correlations of percentage increases between lipase vs total protein and lipase vs haematocrit values were not significant.

Opinions still differ today as to the cause of the increases in lipase and the other pancreatic enzymes in chronic renal pathology. In fact, some authors suggest that they may be due to the incapacity of the impaired kidneys to eliminate these enzymes from the blood.

Patients and Methods

Our study group included 37 patients (24 male, 13 female), mean age 54.2 years (range 25–76), suffering from chronic renal failure, on periodical haemodialysis. Mean duration of dialysis was 51.4 ± 43.5 months. The mean value of serum creatinine before dialysis was 990 ± 133 (range 804–1264) μmol/l. No patients in the study had clinical signs and symptoms of acute or chronic pancreatitis, either during or before the study period. Furthermore none of them was taking drugs that could affect serum levels of pancreatic enzymes. There were no alcoholics, and alcohol consumption was below 30 g/day. During the study period, the previous individual dialysis procedures and types of haemofilter used were not changed. All dialysers and haemofilters were made from cuprophane membrane. Treatment usually lasted between four and a half to five hours at blood flow rates ranging from 150 to 400 ml/min. The anticoagulant preparations used in the study were as follows:

- Eparina Vister, Parke-Davis 5000 units per dialysis;
- defibrotide, an extracted polydeoxyribonucleotide-type substance (Noravid, Roussel-Pharma) 400 mg per dialysis.

Informed consent for the study was obtained from all patients.

Blood samples were taken after an overnight fast before and after each dialysis procedure, starting with heparin as an anticoagulant and substituting this one week later with defibrotide. After centrifugation, pancreatic lipase was assayed within 2 hours using the turbidimetric method (Lipase monostest, Boehringer-Mannheim, Germany, reference value < 190 U/l). Total protein was measured using a biuret direct colorimetric method (Enzycolor TP; Poli Diagnostici, Milan, I). Haematocrit was measured in an ALT 4223 centrifuge.

Data are expressed as mean ± standard deviation (SD). Statistical analysis was performed using Student's t test and Pearson's simple linear correlation coefficient r.
Fig. 1 Pre-(■) and post- (▲) dialysis mean ± SD of serum lipase activity using heparin or defibrotide.

(1—6) while others hypothesize the presence of subclinical foci of pancreatitis which are not detectable clinically but have been confirmed by a number of autopsy studies (9, 10). Even dyslipaemic disease could be responsible for the pancreatic foci, and it is important to underline that chronic nephrotics, in particular haemodialysis patients, frequently have hypertriglyceridaemia (11, 12).

Another suggested cause of the post-dialysis increase in lipase is lipoprotein lipase stimulation (8, 13). To verify this hypothesis we compared the effects of two anticoagulants: heparin, which is an activator of endothelial lipoprotein lipase, and defibrotide, which does not activate lipoprotein lipase. Our results showed a mean post-dialysis increase in total lipase concentration of 9.1% when defibrotide was used, which is unexpectedly lower than the mean increase in total proteins and haematocrit levels.

This discrepancy can be due to technical problems (adhesiveness of lipase to the dialysis membrane or analytical interference of defibrotide) or other unknown factors. In contrast, when heparin was used, the mean increase recorded was 24%. On the basis of these results, it is concluded that the post-dialysis increase in lipase is probably mainly caused by heparin-induced lipoprotein lipase activity, with a minor contribution from the haemoconcentration resulting from fluid removal.

The positive correlation between the percentage increase in total protein vs haematocrit values can be explained by the same parallel percentage increase observed in these two quantities. The increase in lipase, however, was greater because it was further stimulated by lipoprotein lipase, and this may explain the lack of correlation with the other two quantities. Knowledge of these phenomena is of practical importance because uraemic patients frequently have episodes of pancreatitis (9). It is therefore important, when evaluating a subject on haemodialysis with suspected acute pancreatitis, to use pre-dialysis values.

Fig. 2 Correlations between increases in total protein concentration and haematocrit values during dialysis.

References

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SHORT COMMUNICATION

Variations in Serum Cholinesterase Activity in Different Age and Sex Groups

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Summary: Measurements of serum cholinesterase activity has been used to assess liver function, predict susceptibility to prolonged apnoea after administration of the muscle relaxant succinylcholine and monitor excessive exposure to the anti-cholinesterase organophosphorus insecticides (1, 2). Serum cholinesterase activity can be affected by many physiological and pathological conditions such as age, pregnancy, puerperium, obesity, some drug therapy, and liver diseases. Additionally, congenital cholinesterase deficiency, which is due to several genetic variants of the enzyme, has also been reported (3, 4). Since the enzyme activity is altered by many factors, we aimed to show the distribution of serum cholinesterase activity levels in different age and sex groups, in order to establish the reference limits in our population.

Serum samples were obtained from patients admitted to the International Hospital, Istanbul, for surgery, where serum cholinesterase activity is studied as a routine preanaesthesia screening test. The types of surgery performed on the subjects were as follows: adenoidectomy, appendectomy, herniectomy, myomectomy, transurethral resection due to prostatic hypertrophy. Any surgical operation related to a systemic disorder was excluded. Pregnant women were also excluded. The subjects were divided into six groups according to their ages, and each group subdivided according to sex. The serum cholinesterase activity of 1967 patients was analysed on a BM/Hitachi 911 analyzer at 37 °C, using a reagent kit (Boehringer Mannheim) based on the method of Knedel & Böttger (5). Interassay coefficient of variation for this method in our laboratory is 4.8%.

For the statistical analysis of data, Student's t test and Levene F test were used. Mean values and standard deviation of serum pseudocholinesterase activities in different sex and age groups are shown in table 1. Percentiles (2.5, 50 and 97.5%) are also presented. Frequency histograms of cholinesterase activity are shown in figure 1. When the mean values for the adults of each sex (groups III and IV) were compared with those of the corresponding sex in other age groups, significant differences were found (tab. 1). Adult women in groups III and IV showed much lower values than younger females in groups I and II (p < 0.001), whereas the values for older women in group V were higher than those for groups III and IV (p < 0.01). On the other hand, the mean values for men were lowest in the elderly (61—93 years) and highest at 0—5 years, showing a decline throughout the life span. The decrements ob-

Tab. 1 Serum cholinesterase activities in men and women in different age groups, significant in comparison (a) with group III; (b) with group IV; (c) with group V; (d) with group VI.

<table>
<thead>
<tr>
<th>Age groups (years)</th>
<th>n</th>
<th>Cholinesterase (kU/l, x ± SD)</th>
<th>Cholinesterase (kU/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men</td>
<td>Women</td>
<td>Men</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>a, b, c, d</td>
</tr>
<tr>
<td>I (0—5)</td>
<td>61</td>
<td>17</td>
<td>10.75 ± 3.00</td>
</tr>
<tr>
<td>III (16—25)</td>
<td>64</td>
<td>143</td>
<td>9.67 ± 2.79</td>
</tr>
<tr>
<td>IV (26—50)</td>
<td>287</td>
<td>765</td>
<td>9.54 ± 2.72</td>
</tr>
<tr>
<td>V (51—60)</td>
<td>139</td>
<td>106</td>
<td>8.65 ± 2.73</td>
</tr>
<tr>
<td>VI (61—93)</td>
<td>171</td>
<td>111</td>
<td>8.16 ± 3.19</td>
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* p < 0.001, in comparison with women of the same age.
served in both groups V and VI were significant when compared with all other groups, giving the highest significance with group I ($p < 0.001$). On the other hand, the mean value for group IV (adult men) is significantly lower than that of group I ($p < 0.01$), and higher than those of groups V and VI ($p < 0.001$), indicating that the decline is more prominent in the elderly.

When the mean values for both sexes were compared with each other, no significant difference was observed except in the third and fourth groups which consisted of adults. In women in the age range 16–50 years, enzyme activity was significantly lower than in men ($p < 0.001$; tab. 1).

The mean value for enzymatic activity in the first five years of life was significantly high in both sexes when compared with that in adults. The reference values obtained in this study are similar to those reported previously. In the adult age group, women exhibited significantly low values when compared with men as well as with women in other age groups. This finding, which is in good agreement with a previous study (6), cannot be explained by the reported physiological decrease in enzymatic activity during pregnancy (7), since cases with pregnancy were excluded. It is known that various physiological and pathological conditions may affect the activity of the enzyme. Factors such as nutritional status, anaemia and use of oral contraceptives may – at least partly – be responsible for the low levels of enzyme activity in adult women. However, a marked effect of hormonal status is apparent, since cholinesterase activity decreases following menarche, and tends to increase after menopause (6).

It has been recommended that succinylcholine should not be used for relaxation if the serum cholinesterase activity is less than 4000 U/l (8). In our study, of 1967 cases, the enzymatic activity was found to be lower than 4000 U/l in 81 cases (4.1%). In a study carried out using propionyl-thiocholine as substrate, this frequency was reported to be 6.2% for 2756 cases studied in a North American population (8).

Inhibition tests using dibucaine or fluoride will be used in further studies to determine genetic variants of the pseudocholinesterase. Meanwhile, the preoperative determination of serum cholinesterase activity helps to decrease the possible side effect of anaesthesia and contributes to the successful outcome of surgery.

**References**


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