Renal clearance of pancreatic and salivary amylase relative to creatinine in patients with chronic renal insufficiency

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SUMMARY Pancreatic and salivary amylase/creatinine clearance ratios in patients with various degrees of renal impairment were compared with those obtained for control subjects. In chronic renal insufficiency (mean GFR 30 ml/min $\pm$ 15 SD; n = 13) the clearance ratios for pancreatic (mean 3.5 $\pm$ 1.85 SD) and salivary (mean 2.3 $\pm$ 1.3 SD) amylase were significantly higher ($P < 0.05$) than those in controls. Corresponding control values (n = 26) were 2.64 $\pm$ 0.86 (pancreatic) and 1.64 $\pm$ 0.95 (salivary). Three patients showed values above the normal limit. In the diabetic group (mean GFR 41 ml/min $\pm$ 22 SD; n = 10) salivary amylase/creatinine clearance ratios (mean 2.36 $\pm$ 1.55 SD) were significantly higher than in controls ($P < 0.05$). Three patients showed raised values. Pancreatic amylase clearance was raised in only one of these patients. Three patients with terminal disease (mean GFR 10 ml/min) showed markedly raised (two- to threefold) clearance ratios for both salivary and pancreatic amylase. Of a total of 26 patients, eight had increased total amylase/creatinine clearance ratios. Pancreatic amylase/creatinine clearance was increased in seven patients, while nine patients showed raised salivary amylase/creatinine ratios. Patients with raised clearance ratios did not have clinical evidence of pancreatitis. We suggest that, in the presence of impaired renal function, a high amylase/creatinine clearance ratio need not be indicative of pancreatic disease.

The amylase (am)/creatinine (cr) clearance (C) ratio (C_{am}/C_{cr}) has been suggested as a useful aid in diagnosing acute pancreatitis in patients with renal insufficiency (Levitt *et al.*, 1969). Some authors have reported that the ratio C_{am}/C_{cr} remains normal in renal insufficiency (Blainey and Northam, 1967; Levitt *et al.*, 1969) and is increased in the presence of pancreatitis (Mulhausen *et al.*, 1969; Drieling *et al.*, 1974; Warshaw and Fuller, 1975). In contrast, recent studies (Morton *et al.*, 1976; Lankisch *et al.*, 1977) have found raised C_{am}/C_{cr} ratios in patients with chronic renal failure without accompanying pancreatitis. These studies measured the clearance of total (T) amylase. In investigating this problem we studied the clearance of both pancreatic (P) and salivary (S)-type amylase in 15 patients with chronic renal insufficiency (CRI) and 11 with diabetes mellitus (DM), all with impaired renal function.

Methods

PATIENTS

Twenty-six patients were divided into three groups as follows: (1) 13 patients with intrinsic renal disease. Their clinical diagnoses are outlined in Table 1. (2) Ten insulin dependent diabetic patients with chronic renal insufficiency. Details of this group are included in Table 2. (3) Three patients with terminal disease are shown in Table 3. Two of these had terminal renal failure one of whom was a diabetic; the third patient had terminal heart failure.

All patients in Tables 1 and 2 were clinically stable and had no clinical evidence of pancreatitis. The diabetic population were all controlled with mono-component insulins; one had ketoacidosis.

Control subjects (n = 26) comprised 12 males and 14 females (age range 19-70 years). These included 14 healthy volunteers and 12 hospital controls who showed no evidence of parotid, abdominal, or renal disease.

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Table 1 *Patients with chronic renal insufficiency*

Name	Age (yr)	Sex	Diagnosis	Serum amylase (U/l)			GFR (ml/min)	C _{am} /C _{cr} (%)		
				T	S	P		T	S	P
M. F.	23	M	Chronic interstitial nephritis*	400	166	234	16.0	3.7	2.8	4.4
E. R.	47	M	Cirrhosis; CCF; COAD; HT;	170	81	89	21.0	5.0	4.07	5.4
			nephrotic syndrome*							
E. F.	67	M	Chronic pyelonephritis	470	100	370	20.4	1.18	0.88	1.26
M. R.	64	F	Chronic pyelonephritis, rheumatoid arthritis	360	146	214	7.8	3.25	2.92	3.5
K. D.	48	F	Chronic obstructive uropathy	640	131	509	12.3	2.9	0.97	3.35
T. H.	68	M	Coronary insufficiency; nephrosclerosis	310	200	110	22.0	1.44	1.2	1.9
E. B.	74	F	Hypernephroma*	168	88	80	30.2	2.34	1.7	2.04
F. S.	62	M	Gouty nephropathy; myxedema*	205	42	163	42.0	2.7	2.0	2.9
E. M.	67	M	Hypernephroma; haematuria	110	54	56	53.0	2.8	2.7	2.95
M. R.	84	M	Nephrosclerosis	155	24	131	56.0	2.95	1.56	3.0
T. L.	72	M	Tumour of kidney; Hypernephroma*	98	36	62	42.5	5.2	2.85	6.6
W. O'D.	57	M	Nephrotic syndrome; membranous nephritis*	275	86	189	32.6	6.3	5.1	6.9
K. D.	67	F	Rheumatic heart disease - CCF	140	39	101	33.4	1.18	0.98	1.26

CCF: congestive cardiac failure. COAD: chronic obstructive airways disease. HT: hypertension. *Histological diagnosis.

Table 2 *Diabetic patients with renal insufficiency*

Name	Age (yr)	Sex	Serum amylase (U/l)			GFR (ml/min)	C _{am} /C _{cr} (%)		
			T	S	P		T	S	P
M. D.	72	M	286	87	196	20.8	5.2	4.66	5.5
P. F.	77	M	480	235	245	23.9	2.6	0.96	3.95
P. D.	64	M	182	58	124	57	1.48	0.97	1.74
M. G.	55	M	133	62	71	47.6	2.2	2.07	2.4
F. M.	26	M	90	49	41	81	1.65	1.95	0.97
D. H.	35	M	180	77	103	15.45	3.85	3.88	3.82
C. K.	23	F	140	89	51	48	2.78	1.8	4.5
E. C.	67	F	120	44	76	17.5	1.48	1.34	1.56
J. H.	77	M	185	93	92	60	2.92	2.0	3.85
J. K.	21	M	47	28	19	36.8	4.0	4.0	3.65

Upper normal limits for C_{am}/C_{cr} (calculated as mean + 2 SD, n = 26; see Table 5) are C_T/C_{cr} = 3.8%, C_S/C_{cr} = 3.5%, and C_P/C_{cr} = 4.4%

Table 3 *Patients with terminal disease*

Name	Age (yr)	Sex	Diagnosis	Serum amylase (U/l)			GFR (ml/min)	C _{am} /C _{cr} (%)		
				T	S	P		T	S	P
W. L.	63	M	Chronic glomerulo-nephritis*	340	74	266	3.4	9.0	13.3	7.7
E. D.	22	M	Diabetic*	140	63	77	4.7	9.4	10.5	8.6
M. L.	46	M	Acute bacterial endocarditis†	165	31	134	21.5	9.5	14.2	8.4

* Terminal renal failure. † Terminal cardiac failure.

ANALYSES

A 24-hour urine sample was collected from all patients; blood was taken within this time interval. Each urine sample was measured for total volume and two 5 ml aliquots retained for amylase and creatinine determination. Albumin was added to the samples for amylase analysis (1 mg/ml urine). Serum and urine samples were stored at -20°C before analysis. Samples from control subjects were treated similarly. Storage times did not exceed five days for amylase and two weeks for creatinine. Pancreatic and salivary amylase were determined by the method of

O'Donnell *et al.* (1977) using an α -amylase inhibitor¹ prepared from wheat. The Phadebas blue starch method for amylase assay was standardised as described (O'Donnell *et al.*, 1977). Albumin (7.4 μ M) was incorporated in the reaction mixture in the case of all urine analyses. Creatinine estimations were carried out using the creatinine Rapid Stat Kit (Pierce, Rockford, Illinois). The amylase/creatinine clearance ratio was expressed as a percentage and calculated from the equation:

¹Patent applied for.

$$C_{am}/C_{cr} = \frac{\text{Urine amylase}}{\text{Serum amylase}} \times \frac{\text{Serum creatinine}}{\text{Urine creatinine}} \times 100$$

Values for serum and urinary pancreatic or salivary amylase were inserted in the equation to give the clearance of pancreatic (C_p/C_{cr}) or salivary (C_s/C_{cr}) amylase respectively.

NORMAL VALUES

The normal limits for serum amylase (total, pancreatic, and salivary) were calculated from the data on 69 female and 72 male control sera (O'Donnell *et al.*, 1977). The values which represent 95% confidence limits and were calculated after logarithmic transformation are as follows:

Serum amylase (u/l)	Males	Females
Total	56-270	75-277
Pancreatic	37-162	52-175
Salivary	9-172	9-196

The amylase/creatinine clearance values for the control subjects showed no statistical difference between 12 males and 14 females and were grouped together for comparison purposes. The normal limits were taken as mean $\pm$ 2 SD ($n = 26$). Statistical analyses were performed using the non-paired Student's *t* test.

Results

Differential serum amylase values for the 13 patients with chronic renal insufficiency are shown in Table 1 together with the amylase/creatinine clearance values

for total, salivary, and pancreatic amylase. The glomerular filtration rates (GFR) as measured by creatinine clearance are also given. These range from 7.8 ml/min to 56 ml/min (mean 30 ml/min $\pm$ 15 SD). Six patients had total serum amylase values above our upper limit. Five of these patients had raised serum pancreatic amylase values with normal salivary levels. The sixth patient showed a raised serum salivary amylase. When this group of 13 patients was compared with 69 control subjects the serum salivary and pancreatic amylase levels were both significantly higher in the patients with chronic renal insufficiency (Table 4). Three of the 13 patients in Table 1 had abnormal total amylase/creatinine clearance ratios—that is, $> 3.8\%$. Salivary amylase clearance was increased—that is, $> 3.5\%$ —in two and pancreatic amylase clearance was increased—that is, $> 4.4\%$ —in all three patients. Taken as a group, the mean total amylase/creatinine clearance ratio was significantly higher in these 13 patients when compared with controls ($P < 0.025$) (Table 5). This was due to an increased clearance of both salivary and pancreatic components.

Data related to the diabetic population are shown in Table 2. The GFR ranged from 15 to 81 ml/min (mean 41 ml/min $\pm$ 22 SD). Hyperamylasaemia was present in two of the 10 patients; in one case (M. D.) this was due to pancreatic amylase only, while in the other (P. F.) both pancreatic and salivary amylase levels were elevated. When compared with the control group serum salivary levels were significantly higher ($P < 0.01$) in the diabetic patients (Table 4).

Table 4 Serum amylase and creatinine levels in patients with renal insufficiency compared with controls

Subjects	No.	Serum amylase (U/l)			Serum creatinine† (mg %)
		Total	Salivary Mean $\pm$ SD	Pancreatic	
Controls	69	151.7 $\pm$ 47.7	52.4 $\pm$ 31.7	99.5 $\pm$ 29.8	0.85 $\pm$ 0.21*
CRI + DM	10	184.3 $\pm$ 122.1	82.2 $\pm$ 57.8	101.8 $\pm$ 70.5	1.93 $\pm$ 1.27
		NS	$P < 0.01$	NS	$P < 0.0005$
CRI	13	269.3 $\pm$ 161.6	91.8 $\pm$ 55.0	177.5 $\pm$ 132.2	2.55 $\pm$ 1.31
		$P < 0.0005$	$P < 0.0005$	$P < 0.0005$	$P < 0.0005$

NS: not significant. *Creatinine values in patients are compared with 26 control sera. †For SI units multiply by 88.4. Terminal patients not included in statistics.

Table 5 Data on amylase and creatinine excretion

Subjects	No.	C_{am}/C_{cr} (mean $\pm$ SD (%))			Urine Am/Urine Cr (mean $\pm$ SD (U/mg))*		
		T	S	P	T	S	P
Controls	26	2.31 $\pm$ 0.74	1.64 $\pm$ 0.95	2.64 $\pm$ 0.86	0.37 $\pm$ 0.23	0.085 $\pm$ 0.06	0.28 $\pm$ 0.20
CRI + DM	10	2.81 $\pm$ 1.23	2.36 $\pm$ 1.33	3.19 $\pm$ 1.44	0.35 $\pm$ 0.30	0.11 $\pm$ 0.05	0.24 $\pm$ 0.26
		NS	$P < 0.05$	NS	NS	NS	NS
CRI	13	3.15 $\pm$ 1.57	2.29 $\pm$ 1.28	3.5 $\pm$ 1.85	0.31 $\pm$ 0.16	0.08 $\pm$ 0.05	0.23 $\pm$ 0.13
		$P < 0.025$	$P < 0.05$	$P < 0.05$	NS	NS	NS

NS: not significant. *For SI units (U/mmol) multiply by 0.1131. Terminal patients not included in statistics.

Serum pancreatic amylase levels were not significantly different from controls. The salivary and pancreatic amylase/creatinine clearance ratios were raised in one patient (M. D.). Two additional patients (D. H. and J. K.) showed a marginal rise in salivary amylase/creatinine clearance. The mean total amylase/creatinine clearance ratio of the diabetic population was not significantly different from controls (Table 5). Examination of differential amylase clearance values in this same group shows the salivary amylase/creatinine clearance ratio to be significantly higher ($P < 0.05$) compared with controls (Table 5). Mean pancreatic amylase/creatinine clearance ratios did not reach a level of significance. The quotient urinary amylase/urinary creatinine for both patient populations are also shown in Table 5 and compared with controls. No significant difference was noted.

Patients with terminal disease are summarised in Table 3. While only one patient showed hyperamylasaemia all three patients had markedly increased clearance of both salivary and pancreatic amylase.

The significantly increased rate of pancreatic amylase clearance relative to salivary amylase clearance ($P < 0.0005$) in control subjects has already been reported (Hegarty *et al.*, 1978). This degree of preferential clearance of pancreatic relative to salivary amylase is markedly reduced in patients with renal insufficiency (Tables 3 and 6).

Discussion

This present study has demonstrated that, of 15 patients with chronic renal insufficiency, 10 showed normal clearance ratios for both salivary and pancreatic amylase. Of the remaining five patients, two had terminal disease and two had nephrotic syndrome, all with increased salivary and pancreatic amylase/creatinine clearance ratios. The fifth patient had hypernephroma and showed a high clearance ratio for pancreatic amylase only. It would appear that in terminal disease associated with renal failure a high amylase/creatinine clearance ratio need not indicate pancreatic disease. Post-mortem studies in two terminal patients failed to show evidence of pancreatitis. The two patients with nephrotic

syndrome are of definite interest, as their high clearance values may well be related to the heavy proteinuria present. The reason for the high pancreatic amylase clearance ratio in the hypernephroma patient is unclear; the capacity of certain tumours to produce amylase has been described (Ammann *et al.*, 1973; Berk and Fridhandler, 1975).

Eight of the 11 diabetic patients showed normal clearance values. Of the remaining three, one had terminal renal failure (GFR 5 ml/min) with increased clearance ratio of both salivary and pancreatic amylase. One patient was mildly ketoacidotic and showed a raised clearance ratio for salivary amylase only. The explanation for the increased salivary amylase clearance ratio in the third patient is not clear.

The precise mechanisms of amylase transfer within the kidney have not yet been clarified. It was earlier concluded that amylase clearance was essentially a function of glomerular filtration without significant tubular reabsorption (McGeachin and Hargan, 1956; 1957; Duane *et al.*, 1971). Recent work by Johnson *et al.* (1976) provides strong evidence in favour of tubular reabsorption of amylase in man. This has also been shown experimentally in the rat (Noda, 1972; Fredriksson and Jacobson, 1974). The more rapid clearance of pancreatic amylase relative to salivary amylase (Duane *et al.*, 1972; Takeuchi *et al.*, 1974; Fridhandler *et al.*, 1972; Long and Grider, 1976; Hegarty *et al.*, 1978) may be related to a more active reabsorption of salivary amylase by the proximal or distal tubule. Loss of this preferential clearance of pancreatic amylase relative to salivary amylase is evident in renal insufficiency (Tables 3 and 6) and is undoubtedly related to the accompanying renal tubular atrophy. Loss of tubular function would also explain why both salivary and pancreatic amylase/creatinine clearance ratios are sometimes raised in renal disease. Acute pancreatitis, which is accompanied by renal tubular dysfunction, also leads to increased clearance ratios for both salivary and pancreatic amylase (Johnson *et al.*, 1976). Interestingly, in chronic pancreatitis, where tubular function is not impaired, as evidenced by normal clearance of β_2 -microglobulin, C_p/C_{cr} only is raised (Hegarty *et al.*, 1978).

Table 6 Renal clearance of pancreatic amylase compared with salivary amylase in renal insufficiency

Subjects	No.	C_s/C_{cr}	C_p/C_{cr}	C_p compared with C_s^*
		Mean $\pm$ SD (%)		
Controls	26	1.64 $\pm$ 0.95	2.64 $\pm$ 0.86	$P < 0.0005$
CRI + DM	10	2.36 $\pm$ 1.33	3.19 $\pm$ 1.44	$P < 0.15$
CRI	13	2.29 $\pm$ 1.28	3.5 $\pm$ 1.85	$P < 0.05$

*t test. Terminal patients not included.

Our study demonstrates a rise of both salivary and pancreatic amylase in the serum of patients with chronic renal insufficiency compared with controls. This increase (~ two fold) is less than the corresponding rise in serum creatinine (~ three fold) (Table 4). Since the quotient urinary amylase/urinary creatinine is not significantly higher in patients with chronic renal insufficiency relative to controls (Table 5), the increased C_{am}/C_{cr} ratio must also be related to the greater rise in serum creatinine than in serum amylase (see clearance equation).

This finding of an increased amylase/creatinine clearance ratio in some patients with chronic renal insufficiency agrees with the results of Morton *et al.* (1976) and Lankisch *et al.* (1977). A high amylase/creatinine clearance ratio has also been reported in severe renal failure (GFR less than 25 ml/min) by Pedersen *et al.* (1976). The severity of renal insufficiency may explain why the results differ from those previously reported (Blainey and Northam, 1967; Levitt *et al.*, 1969).

The majority of our patients with chronic renal insufficiency had normal amylase/creatinine clearance ratios. Warshaw (1976) has suggested that perhaps the most assured use of the amylase/creatinine clearance ratio will be when it is not raised, thereby excluding pancreatitis. The validity of this suggestion appears doubtful in view of the recent report (Dürr *et al.*, 1977) that some patients with acute pancreatitis have normal C_{am}/C_{cr} ratios.

Our results show that the increased amylase/creatinine clearance ratio in chronic renal insufficiency could be due to both salivary and pancreatic amylase. The clearance ratio should therefore be interpreted with caution in the presence of severe renal insufficiency. A high ratio need not be indicative of pancreatitis, since our patients had no clinical evidence of exocrine pancreatic disease and were not on drugs which could cause hyperamylasaemia.

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References

- Ammann, R. W., Berk, J. E., Fridhandler, L., Ueda, M., and Wegmann, W. (1973). Hyperamylasemia with carcinoma of the lung. *Annals of Internal Medicine*, **78**, 521-525.
- Berk, J. E., and Fridhandler, L. (1975). Clinical application of amylase isoenzyme analysis. *American Journal of Gastroenterology*, **63**, 457-463.
- Blainey, J. D., and Northam, B. E. (1967). Amylase excretion by the human kidney. *Clinical Science*, **32**, 377-383.
- Dreiling, D. A., Leichtling, J. J., and Janowitz, H. D. (1974). The amylase/creatinine clearance ratio: Diagnostic parameter or physiologic phenomenon? *American Journal of Gastroenterology*, **61**, 290-296.
- Duane, W. C., Frerichs, R., and Levitt, M. D. (1971). Distribution, turnover, and mechanism of renal excretion of amylase in the baboon. *Journal of Clinical Investigation*, **50**, 156-165.
- Duane, W. C., Frerichs, R., and Levitt, M. D. (1972). Simultaneous study of the metabolic turnover and renal excretion of salivary amylase - ^{125}I and pancreatic amylase - ^{131}I in the baboon. *Journal of Clinical Investigation*, **51**, 1504-1513.
- Dürr, H. K., Bode, J. C., Lankisch, P. G., and Koop, H. (1977). Amylase-creatinine clearance ratio in pancreatitis (Letter). *New England Journal of Medicine*, **296**, 635.
- Fredriksson, A., and Jacobson, G. (1974). Influence of renal function on the urinary excretion of amylase: An experimental study in the rat. *Scandinavian Journal of Clinical Laboratory Investigation*, **33**, 313-321.
- Fridhandler, L., Berk, J. E., and Ueda, M. (1972). Isolation and measurement of pancreatic amylase in human serum and urine. *Clinical Chemistry*, **18**, 1493-1497.
- Hegarty, J. E., O'Donnell, M. D., McGeeney, K. F., and FitzGerald, O. (1978). Pancreatic and salivary amylase/creatinine clearance ratios in normal subjects and in patients with chronic pancreatitis. *Gut*, **19**, 350-354.
- Johnson, S. G., Ellis, C. J., and Levitt, M. D. (1976). Mechanism of increased renal clearance of amylase/creatinine in acute pancreatitis. *New England Journal of Medicine*, **295**, 1214-1217.
- Lankisch, P. G., Wolfrum, D. I., Koop, H., and Winckler, K. (1977). Amylase/creatinine clearance ratio (C_{am}/C_{cr}) and renal tubular function in acute pancreatitis (AP): Lack of specificity. *Irish Journal of Medical Science*, **146**, Suppl. 1, 28.
- Levitt, M. D., Rapoport, M., and Cooperband, S. R. (1969). The renal clearance of amylase in renal insufficiency, acute pancreatitis, and macroamylasemia. *Annals of Internal Medicine*, **71**, 919-925.
- Long, W. B., and Grider, J. R., (1976). Amylase isoenzyme clearances in normal subjects and in patients with acute pancreatitis. *Gastroenterology*, **71**, 589-593.
- McGeachin, R. L., and Hargan, L. A. (1956). Renal clearance of amylase in man. *Journal of Applied Physiology*, **9**, 129-131.
- McGeachin, R. L., and Hargan, L. A. (1957). Amylase clearance and excretion during water diuresis. *Proceedings of the Society of Experimental Biology and Medicine*, **95**, 341-343.
- Morton, W. J., Tedesco, F. J., Harter, H. R., and Alpers, D. H. (1976). Serum amylase determinations and amylase to creatinine clearance ratios in patients with chronic renal insufficiency. *Gastroenterology*, **71**, 594-598.
- Mulhausen, R., Brown, D. C., and Onstad, G. (1969). Renal clearance of amylase during pancreatitis. *Metabolism*, **18**, 669-674.
- Noda, A. (1972). Renal handling of amylase: Evidence for reabsorption by stop-flow analysis. *Metabolism*, **21**, 351-355.
- O'Donnell, M. D., FitzGerald, O., and McGeeney, K. F. (1977). Differential serum amylase determination by use of an inhibitor, and design of a routine procedure. *Clinical Chemistry*, **23**, 560-566.
- Pedersen, E. B., Brock, A., and Kornerup, H. J. (1976). Serum amylase activity and renal amylase clearance in patients with severely impaired renal function and in patients treated with renal allotransplantation. *Scandinavian Journal of Clinical Laboratory Investigation*, **36**, 137-140.
- Takeuchi, T., Matsushima, T., Sugimara, T., Kozu, T., Takeuchi, T., and Takemoto, T. (1974). A rapid new method for quantitative analysis of human amylase isozymes.

Clinica Chimica Acta, **54**, 137-144.
 Warsaw, A. L. (1976). The kidney and changes in amylase clearance. *Gastroenterology*, **71**, 702-704.
 Warsaw, A. L., and Fuller, A. F., Jr. (1975). Specificity of

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