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Evaluation of gastric emptying in patients with chronic renal failure on continuous ambulatory peritoneal dialysis using ^{99m}Tc-solid meal

Alicja Hubalewska[1], Tomasz Stompór[2], Ewa Płaczkiewicz[1], Anna Staszczak[1], Bohdan Huszno[1], Władysław Sułowicz[2], Zbigniew Szybiński[1]

[1]Chair and Department of Endocrinology, Nuclear Medicine Unit, Jagiellonian University, Kraków, Poland
[2]Chair and Department of Nephrology, Kraków, Poland

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Abstract

BACKGROUND: Continuous ambulatory peritoneal dialysis (CAPD) is an alternative to the hemodialysis mode of terminal renal failure treatment. Nutritional status impairment is common among patients with end-stage renal disease, and its laboratory surrogates predict increased morbidity and mortality risk in patients on chronic haemodialysis or peritoneal dialyses. The aetiology of malnutrition is multifactorial and delayed gastric emptying is also considered to be a significant factor. The aim of this study was to estimate the direct influence of indwelled dialysate in the peritoneal cavity on gastric emptying in patients treated with CAPD.

MATERIAL AND METHODS: the study group included 20 patients (9 males, 11 females) aged 50,1 ± 11 years (range: 39––75 years) with chronic renal failure treated with CAPD for 18.4 ±14.7 months. All patients were non-diabetic and had no other than chronic uraemia co-morbidity known to influence autonomic nervous system function and gastric motility. The control group included 15 healthy volunteers matched by age, sex and body weight. Dialysis adequacy parameters were calculated based on 24-hour urine and dialysate collections. Gastric emptying was estimated with dynamic abdominal scintigraphy. We compared the results of gastric emptying tests performed in dialysed patients with and without dialysate liquid in the peritoneal cavity and related the values to those of the control subjects.

RESULTS: In the study group, weekly values of dialysis parameters were within the ranges considered satisfactory in terms of uraemia control. All parameters of gastric emptying were significantly delayed and prolonged in terminal renal failure patients, but the results have shown no significant differences between those with and without indwelling dialysate.

CONCLUSIONS: Based on the results we conclude that gastric emptying in subjects with chronic renal failure treated with CAPD is markedly delayed compared to healthy subjects. There was no significant effect of indwelling dialysate in the peritoneal cavity on gastric emptying rates found, based on the observation that its removal was not associated with any noticeable improvement of gastric emptying. The data strongly contraindicate the theory of peritoneal dialysate volume being the cause of this reversible disorder and indicate that the role of other possible factors leading to the development of gastropathy in those patients should be investigated.

Key words: peritoneal dialysis, gastric emptying, scintigraphy, ^{99m}Tc-solid meal

Correspondence to: Alicja Hubalewska, MD
Chair and Department of Endocrinology, Nuclear Medicine Unit, Jagiellonian University
ul. Kopernika 17; 31–501 Kraków, Poland
Tel: (+ 48) 12 424 75 00, fax: (+ 48) 12 421 40 54,
e-mail: alahuh@endo.cm-uj.krakow.pl

Introduction

Continuous ambulatory peritoneal dialysis (CAPD) is an alternative to the haemodialysis mode of terminal renal failure treatment. It is used in approximately 10–12% of dialysed patients in Poland and is preferred for treating older people. It is predicted,

that in a year 2010, 25–30% of patients with chronic renal failure will be treated with CAPD. The treatment requires 1.5–2 l dialysate liquid in the peritoneal cavity to be changed 4–5 times daily. Patients with chronic renal failure frequently suffer from nausea, vomiting, abdominal distension, early satiety and anorexia [1], but such symptoms do not certainly coexist with impaired gastric emptying. Nutritional status impairment is common among patients with end-stage renal disease, and its laboratory surrogates, including hypoalbuminaemia, predict increased morbidity and mortality risk in patients on chronic haemodialysis or peritoneal dialyses [2, 3]. The aetiology of malnutrition is multifactorial, mainly related to inadequate nutrient intake [4], although abnormal gastric myoelectrical activity and delayed gastric emptying are also considered to be important factors [5].

A few studies addressing the question of whether delayed gastric emptying in dialysis patients contributes to the above dyspeptic complaints have yielded conflicting results [3, 6–8]. However, disturbances in gastric emptying resulting possibly from the presence of dialysate liquid in the peritoneal cavity in patients on CAPD are described by some authors, but such disturbances might also result from autonomic neuropathy due to impaired control of uraemia or the direct influence of uraemic toxins.

Detection of delayed gastric emptying is difficult in the clinical setting because symptoms are notoriously non-specific and poorly predictive of the degree of gastric motor dysfunction, and many patients having this syndrome are asymptomatic. Currently, nuclear medicine provides very useful tools allowing functional studies of the gastrointestinal tract. A number of test meals can be used and the radioactive label may be incorporated into either the solid or liquid component for detecting abnormalities in gastric motility [9–13].

To estimate the direct influence of indwelled dialysate in the peritoneal cavity on gastric emptying in patients treated with peritoneal dialyses there was a need to compare gastric emptying rate in patients with dialysate and after its complete drainage and relate the results to healthy controls.

Material and methods

The study group included 20 patients (9 males, 11 females) aged 50,1 ± 11years (range: 39–75 years) with chronic renal failure treated with CAPD, on peritoneal dialyses for a mean period of 18.4 ± 14.7 months (range: 2–61 months). Mean body mass index (BMI) was 4.69 ± 3.03 kg/m^2 (range: 17.71–29.49 kg/m^2), while mean lean body mass (LBM) was 50.30 ± 8.56 kg (range: 38.85–63.26 kg). All patients involved in the study were non-diabetic and had nothing other than chronic uraemia co-morbidity which is known to influence the autonomic nervous system function and gastric motility. Patients receiving any medication affecting the gastric emptying rate were excluded from the study. The control group included 15 healthy volunteers matched by age, sex and body weight who were studied to establish normal ranges. Both groups are characterised in Table 1. The aetiology of terminal renal failure in patients of the study group was as follows: chronic glomerulopathy 10], interstitial nephropathy [2] and polycystic kidney disease [2]. It was impossible to establish the aetiology of underlying renal disease that led do end-stage renal failure for 6 patients, due to late referral to nephrologists.

Table 1. Characteristics of study patients and control group

	Patients	Controls
Number	20	15
Age (mean)	50.1 ± 11 years	48.2 ± 10 years
BMI (mean)	24.69 ± 3.03 kg/m^2	26.2 ± 4.8 kg/m^2
LBM (mean)	50.30 ± 8.56 kg	51.6 ± 9.82 kg
Urea (mean)	22.1 ± 4.99 mmol/l	6.4 ± 2.1 mmol/l
Creatinine (mean)	866.8 ± 199 umol/l	82.1 ± 13.6 umol/l
On peritoneal dialyses	18.4 ± 14.4 months	–

BMI — body max index; LBM — lean body max

Dialysis adequacy in peritoneal dialysis patients was tested using weekly fractional urea clearance normalised to distribution volume (Kt/V) and weekly creatinine clearance (wClCr), normalized to body surface area. Both above-mentioned parameters were calculated based on 24-hour urine and dialysate collections, as the sum of dialysis and residual clearances, and expressed as weekly values. The distribution volume for Kt/V was calculated using the Watson formula [14]. In addition, residual renal function (residual creatinine clearance; rClCr) was calculated and expressed in ml/min. Urine, dialysate and serum urea and creatinine concentrations for above calculations were measured using Hitachi 917 analyser (Hitachi, Tokyo, Japan). Adequacy parameters were calculated using commercially available software Nephron for Windows (DDPS, Kraków, Poland).

Gastric emptying was estimated with dynamic abdominal scintigraphy started immediately after the complete ingestion of a standardised 200 kcal solid meal containing ^{99m}Tc- labelled colloid, of 40 MBq activity. All patients were in a fasting state for at least 8 hours prior to the examination and the duration of complete meal ingestion was less than 10 minutes. Scintigraphy was performed at the rate of 23 images at 4-minute intervals for a total of 92 minutes. Patients were randomly allocated to either have the test with or without indwelling dialysate first. Two consecutive procedures — with and without dialysate liquid in the peritoneal cavity — were performed with a minimum seven day interval allowing complete elimination of colloid from the digestive tract after the previous examination. Gastric emptying curves were analysed with the computer programme of the gamma-camera ZLC Digitrac 7500 (Siemens, Erlangen, Germany) connected to acquisition station Mirage and processed by ICON computer programming. Mean gastric emptying half-time ($BPt_{1/2}$ — in patients with dialysate in peritoneal cavity and $BPt_{1/2}$ — without dialysate) and mean activity over the gastric area at 46 minutes and at 92 minutes of the procedure were analysed for dialysed patients both with dialysate in peritoneal cavity and after its complete drainage. The same parameters of gastric emptying function were assessed in healthy control subjects, who underwent the testing only once. We compared the results of the tests performed in dialysed patients with and without dialysate liquid in the peritoneal cavity and related the values to those of control subjects, known to have no pathological liquid in the peritoneal cavity and no uraemia.

Statistical analysis of the data was performed using Statistica 5.1 software (StatSoft, Tulsa, OK, USA). All variables except the duration of dialysis were distributed normally and so are presented as mean values ± SD. With normal distribution it was possible to use Student's *t*-test for comparisons between groups and Pear-

son's test to determine possible correlations between tested variables. Calculated p values less than 0.05 were considered statistically significant.

Results

In the study group that included 20 patients with chronic renal failure on continuous ambulatory peritoneal dialyses, weekly fractional urea clearance normalised to distribution volume (Kt/V) was 2,17, weekly creatinine clearance (wClCr) was 68.04 L/week/1.73 m^2 and residual renal creatinine clearance (rClCr) — 2,8 ml/min; weekly values of tested parameters were found to be within the ranges currently accepted as satisfactory in terms of uraemia control. Mean urea serum level was 22,1 ± 4,99 mmol/L (range: 12.1––29.8 mmol/L) and mean creatinine was 866.8 ± 230 μmol/L (range: 470–1280 μmol/L).

Two examples of gastric emptying measurements are presented in Figure 1 and Figure 2.

As shown in Figure 3 mean gastric emptying half-time was 64 minutes in patients without dialysate in the peritoneal cavity ($BPt_{1/2}$) and 60.1 minutes in those with dialysate in the peritoneal cavity ($Pt_{1/2}$), while the normal value established in healthy individuals was only 39 min. The mean values of activity over the gastric area after 46 minutes of the test were found to be 59% ($BP\%_{46min}$), 57% ($P\%_{46min}$) and 45% respectively. Further mean values of activity over the gastric area after 92 minutes in the groups studied were 33.9% ($BP\%_{92min}$), 33.8 ($P\%_{46min}$) and below 15% in healthy subjects. Table 2 presents the gastric emptying rates for patients with terminal renal failure as well as for healthy subjects, that were found to be normal. All parameters of gastric emptying were significantly delayed and prolonged in terminal renal failure patients treated with CAPD, but the results have shown no significant differences between those with and without indwelling dialysate.

Conclusions

Gastric emptying in subjects with chronic renal failure treated with continuous ambulatory peritoneal dialyses is markedly delayed compared to healthy subjects in control group. There was no significant effect of indwelling dialysate in peritoneal cavity on gastric emptying rate found, based on the observation that its removal was not associated with any noticeable improvement in gastric emptying.

Discussion

A delay in the gastric emptying rate has previously been reported in peritoneal dialysis patients [5–8, 15], but in some studies it was found to become normal after the dialysate evacuation [16], which we failed to demonstrate. Conflicting results may partly be due to different modes of gastric motility assessment employed in those studies as a number of test meals can be used and a radioactive label may be incorporated into either the solid or liquid component [9–11]. Another reason for differences between the studies may be caused by the relatively small number of patients studied and different levels of care and uraemia control between the groups as well as significant differences in disease duration and hence varying exposure to risk factors.

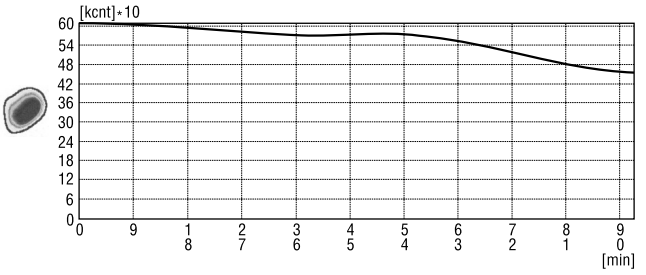

Figure 1. Delayed gastric emptying — example of test results.

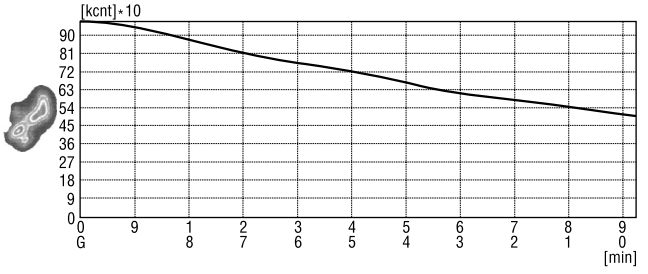

Figure. 2. Normal gastric emptying — example of test results.

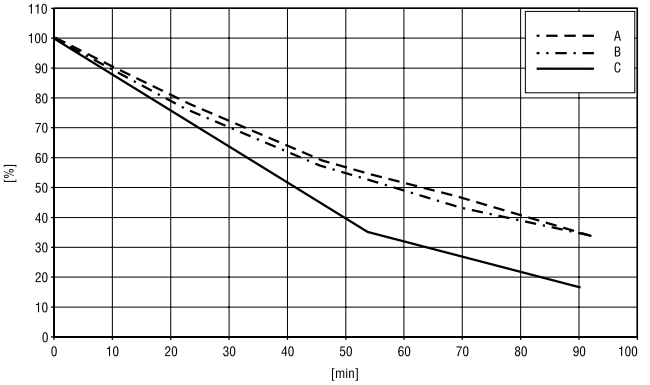

Figure 3. Gastric emptying curves: A — in healthy subjects; B — in CAPD patients without dialysate in the peritoneal cavity; and C — in patients with indwelling dialysate in the peritoneal cavity.

Table 2. Gastric emptying rates for patients with terminal renal failure treated with peritoneal dialyses and for healthy control subjects

	$P\ t_{1/2}$	$BP\ t_{1/2}$ [min]	$P\%_{46min}$	$BP\%_{46min}$ [%]	$P\%_{92min}$ [%]	$BP\%_{92min}$
Minimal	22	8	20.2	15.9	0	0
maximal	92	92	86.9	94.2	68.1	65.2
mean	60.54	63.9	57.09	59.13	33.77	33.91
SD	± 25.03	±2 8.28	± 17.59	± 23.94	± 20.97	± 24.34
Control		39 ± 9		45		<15

The existing evidence allows one to assume a multifactorial pathogenesis of gastropathy in dialysed patients, but exact mechanisms remain unknown. Metabolic disturbances seen in urae-

mic patients are strong candidates in the development of impaired gastric motility. Delayed gastric emptying may be a result of direct action of uraemic toxins on the stomach wall and its consequent reduced compliance due to suppressed smooth muscle contractility, but reported impaired gastric myoelectrical activity may also reflect the involvement of the autonomic nervous system, similar to that seen in diabetic non-obstructive impairment of gastric propulsive activity.

In a study comparing gastric emptying of solids in peritoneal dialysis patients with a cirrhotic model (in which gastric emptying was studied before and after a large volume paracentesis) it was confirmed not to be only the effect of the increased intraperitoneal volume [15]. In peritoneal dialysis patients gastric emptying was delayed when "full" and normalised after drainage of the dialysate, unlike in alcoholic cirrhotic patients, in which it was delayed independently of the volume of ascites.

The volume of dialysate was found to play a role in a few studies, but especially in patients with a small body surface area, who should rather be considered as candidates for an intermittent nocturnal peritoneal dialysis scheme [7]. But in general what seems to matter is not the very presence of fluid in the peritoneal cavity but its content. Instead of suspected pressure or volume effect, it is rather the absorption of substrate substances with caloric or metabolic action that play a greater role in impaired gastric emptying in peritoneal dialysed patients [8]. Impaired gastric motility in patients with renal failure not improving after complete drainage of the dialysate as found in our study, also contraindicates the theory of peritoneal dialysate volume being the cause of this reversible disorder.

While the methods of gastric emptying assessment vary between studies, their comparison as well as pooling the data for more powerful statistical analysis are not justified. But existing evidence, including our study, is sufficient to conclude that impaired gastric emptying in patients treated with CAPD is not necessary related to indwelled dialysate and that there are other possible causes that may play a role in the development of gastropathy in those patients.

A greater number of patients would possibly allow one to analyse the influence of disease duration on the development of gastropathy in patients with chronic renal failure, while longitudinal prospective studies could help to elucidate the role of uraemic metabolic disturbances in the development of the condition.

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