The determination of insulin sensitivity in hemodialysis and continuous ambulatory peritoneal dialysis in nondiabetic patients with end-stage renal disease

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ABSTRACT

Objectives: To determine the beta-cell function and insulin sensitivity with homeostasis model assessment (HOMA) and area under curve (AUC) in nondiabetic uremic hemodialysis (HD) and continuous ambulatory peritoneal dialysis (CAPD) patients cross sectionally.

Methods: The study was performed between January to August 2001 in the Department of Nephrology, Dicle University School of Medicine, Diyarbakir, Turkey. Fifty-one HD patients, 45 CAPD patients, and 50 healthy control subjects were included in the study. Height, weight, waist and hip circumference, fat mass and percentage of body fat, and body mass index (BMI) were measured. The total high density lipoprotein (HDL) and low density lipoprotein (LDL)-cholesterol, triglyceride, urea, creatinine, insulin, potassium, parathyroid hormone (PTH) and 1,25 dihydroxycholecalciferol levels were measured. Oral glucose tolerance test (OGTT) was performed in the mid-week dialysis-free interval in HD patients, whereas after at least a night without dialysis exchanges in CAPD group. Area under curve both of insulin and glucose were calculated. The HOMA [insulin sensitivity (%S)] and AUC were used as indices of tissue insulin sensitivity.

Results: The LDL-cholesterol levels of patients with CAPD was higher than the HD group (p<0.001) and control group (p<0.0001). The baseline glucose levels of the 2 groups were not significantly different. Baseline insulin levels of CAPD group were higher than the HD group (p<0.001) and the control group (p<0.0001). Area under curve for glucose (AUC_{gluc}) and insulin (AUG_{ns}) value of CAPD patients were higher than the HD patients than the control group (p<0.0001). The HOMA [beta-cell function (%B)] values of CAPD group were higher than both HD (p<0.02) and control group (p<0.04). The HOMA [insulin sensitivity (%S)] levels of CAPD group was significantly lower than the HD patients (p<0.002) and the control group (p<0.001).

Conclusions: The CAPD treatment may lead to insulin insensitivity in non-diabetic end-stage renal disease patients and the high glucose content of CAPD solutions may be responsible for insulin resistance in CAPD patients.

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Patients with end-stage renal disease (ESRD) are known to have insulin resistance, and this resistance may be associated with atherosclerosis.[1] It is also well known that, glucose intolerance commonly appears due to insulin insensitivity of peripheral tissue in chronic renal failure (CRF).[2,3] Factors implicated in the pathogenesis of insulin resistance in CRF may be considered as uremic

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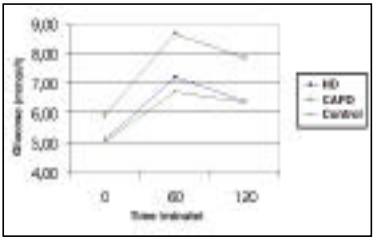

Figure 1 - Glucose behavior of the 3 groups during oral glucose tolerance test. HD - hemodialysis, CAPD - continuous ambulatory peritoneal dialysis.

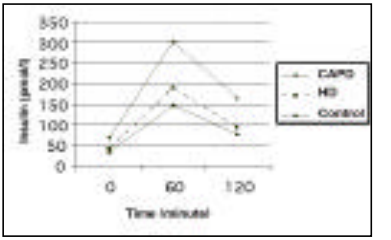

Figure 2 - Insulin behavior of the 3 groups during oral glucose tolerance test. HD - hemodialysis, CAPD - continuous ambulatory peritoneal dialysis.

toxins, exercise intolerance, metabolic acidosis, secondary hyperparathyroidism and vitamin D deficiency. However, the exact mechanism of insulin resistance in uremia is not yet clear.[4] Treatment of metabolic acidosis can increase insulin sensitivity in uremic patients. Insulin resistance can also be improved by initiation of hemodialysis (HD).[5,6] It was shown that thrice weekly HD for 10 weeks improved insulin resistance in ESRD.[6] Some authors demonstrated that the correction of anemia or treatment with 1,25 dihydroxycholecalciferol (1-25$(OH)_2D_3$) reversed insulin resistance,[7-10] but their results were not confirmed by other studies.[11-12] Despite numerous clinical studies regarding insulin sensitivity (%S) of patients undergoing HD therapy, there is a few data available concerning the effect of continuous ambulatory peritoneal dialysis (CAPD) therapy in the development of insulin resistance, particularly, in adult uremic patients. Glucose toxicity is an important factor in the development of insulin resistance.[13] In fact, CAPD solutions have high glucose content (1.36, 2.77, 3.86 g/dL), and absorption of glucose from peritoneal dialysis solution may cause a chronic stimulation of insulin secretion, hyperinsulinism and glucotoxicity.

We aimed to determine beta-cell function (%B) and %S in adult nondiabetic uremic patients treated with HD and CAPD using the homeostasis model assessment (HOMA) and area under curve (AUC) cross-sectionally.

Methods. A total of 51 HD patients (23 female, 28 male) aged 21-66 years (mean 43.3 ± 13.9 years), and a total of 45 CAPD patients (19 female, 26 male) aged 18-65 years (mean 39.6 ± 12 year), and 50 healthy control subjects (23 female, 27 male) aged 25-54 years (mean 38.2 ± 6.6 years) were included to the study. The study was performed between January to August 2001 in the Department of Nephrology, Dicle University School of Medicine, Diyarbakir, Turkey. All decisions in the dividing process of ESRD patients into HD or CAPD were decided by the Dialysis Center Fellows. Exclusion criteria from study were as follow: congestive heart failure, diabetes mellitus, invalidating illness (end stage pulmonary disease, cancer, mental retardation, and so forth). All patients were currently being treated with various ACE-inhibitors, 1,25$(OH)_2D_3$ (calcitriol at the dose of 0.25-1 mg/day) and calcium acetate(750 mg, 3 g per day). None of the patients were using corticosteroids, beta or alpha-blockers at least 3 months before the study. None of the controls had a history of any significant illness such as diabetes. Mean HD duration was 19 ± 13 months in HD group and mean CAPD duration was 20 ± 12 months in CAPD group. The daily CAPD regimen was comprised of 4 exchanges of 2 L of glucose solution with different glucose concentrations (glucose content was 1.36, 2.77, 3.86 g/dL). Hemodialysis was performed thrice weekly (a total 12-15 h/weeks) with a biocompatible membrane (polysulfone). In HD group, 28/51 patients were used erythropoietin and in CAPD group, 24/45 patients were used erythropoietin. The mean dose of erythropoietin in the patients was 145 ± 32 U/kg per week.

All of the patients height, weight and waist and hip circumference were measured and body mass index (BMI) was calculated. Body weights were measured without shoes and in light clothing, and were recorded to the nearest 0.5 kg. Body heights were measured without shoes or cap, and were recorded to the nearest centimeter. The BMI was expressed as weight (kilograms) per height (meters) squared. Waist circumference was taken as the maximum abdominal girth and recorded to the nearest centimeter. Hip circumference was taken as the maximum circumference at the level of the

greater trochanter and also recorded to the nearest centimeter. Fat mass and body fat percentage were determined by bioelectric impedance (Tanita body composition analyzer. TANITA Corporation 14-2, 1-chome, Maeno-cho, Itabashi-ku Tokyo, Japan). A trained hospital staff measured the blood pressure. Informed and written consent was obtained from all participants.

Total cholesterol (HDL, LDL and very low-density lipoprotein (VLDL) cholesterol) and triglyceride levels were determined using the Abbott Aeroset autoanalyzer after 12 hours fasting period at 08:00 am. The LDL cholesterol was calculated by Friedwald equation (LDL cholesterol = total cholesterol - (HDL + TG/5)). World Health Organization criteria (1999) based on a standard 75 g oral glucose tolerance test was performed at 08:00-08:30 am in the mid-week dialysis-free interval in HD patients, whereas after at least a night without dialysis exchanges in CAPD group. Blood samples for measurement of insulin and glucose were obtained at baseline, 60th minute and 120th minute of oral glucose loading. After separation and centrifugation, serum samples were stored at -40^{o}C until assayed. Serum iron and total iron binding capacity (TIBC) were measured by spectrophotometric methods (Aeroset, Japan). The parathyroid hormone levels (PTH) were measured by chemiluminescence assay (Immulite 2000 EPC Diagnostic product Corp, USA). Serum 1,25 $(OH)_2D_3$ were measured by radioimmunoassay (Immunodiagnostic system, USA). Serum insulin levels were measured by radioimmunoassay (RIA, Diagnostic System Laboratories, Webster, Texas, USA, Berthold LB 2111). The intraassay coefficient variation (CV) were 8.2% at serum concentration of 4.75 µU/ml, 4.8% at serum concentrations 17.62 µU/ml and 6.3% at serum concentrations of 54.60 µU/ml. The interassay CV was 11.2% at serum concentrations of 4.92 µU/ml, 7.5% at serum concentrations of 16.23 µU/ml and 4.7% at serum concentrations of 52.92 µU/ml. We calculated Kt/V ratio (ureakinetic model for establishing dialysis adequacy) of all subjects with HD and CAPD according to The National Kidney Foundation Dialysis Outcomes Quality Initiative (NKF-DOQI) recommendation.[14] The HOMA and AUC were used in determining the %S and %B function. Since the measurement of insulin sensitivity in vivo involves techniques that are not readily available to most investigators and requires significant amount of both physician and patient time, Turner et al[16] developed a mathematical model that predicted %S from simple measurement of fasting plasma glucose and insulin concentrations.[15] This approach was called HOMA. If the simultaneous fasting plasma glucose and insulin levels are known, the model will generate estimates of the β-cell secretory capacity and %S required to produce the measured glucose and insulin concentrations. The euglycemic insulin clamp technique provides the most direct measure of tissue sensitivity to insulin and has become the gold standard for measuring insulin action in vivo.[17] Authors found that assessment of insulin by HOMA sensitivity correlated well with that determined by the euglycemic insulin clamp technique ($r = 0.88$, $p<0.0001$). In our study, mathematical modelling of the fasting glucose and insulin pairs, HOMA was used as an indexes of pancreatic beta cell function [HOMA-(%B)] and tissue insulin sensitivity [HOMA-(%S)]. The HOMA-%S and HOMA-%B were determined by using HOMA computer program application. The integrated AUC analysis for glucose and insulin were determined according to the formula of Tai et al.[18]

Results were shown as mean ± standard deviation. Quantitative data were compared by analysis of variance (ANOVA). When ANOVA was significant, Tukey test was used in comparison between groups. Independent t-test was used in comparison of HD and CAPD patients viewpoint of biochemical parameters related with ESRD. The values $p<0.05$ were accepted as statistically meaningful.

Results. The HDL-cholesterol levels of patients with CAPD and HD were significantly lower than control group ($p<0.001$). The LDL-cholesterol levels of patients with CAPD were higher than the HD group ($p<0.001$) and the control groups ($p<0.0001$). Triglyceride levels of CAPD ($p<0.004$) and HD groups ($p<0.0001$) were higher than control group, but mean triglyceride level was not significantly different between CAPD and HD groups. While systolic and diastolic blood pressures of CAPD and HD groups were not significantly different from each other, they were significantly higher than the control group ($p<0.0001$). Mean age, body height, body weight, BMI, waist circumference, hip circumference, fat percentage, fat mass, urea, creatinine, calcium, phosphate, potassium, total-protein, albumin, TIBC and PTH levels of the 2 groups were not significantly different.

The mean baseline (0th minute) glucose level of the 3 groups was not different from each other [CAPD group: 5.5±1.2(mmol/l), HD group: 5.3±1.9(mmol/l), and control group: 4.9±0.7 (mmol/l)], but first and 2nd hour glucose levels of CAPD (8.6±1.1 mmol/l, 7.8±2.3 mmol/l) patients were higher than HD (7.2±1.2 mmol/l, 6.4±1.5mmol/l) and control group (6.7±0.8 mmol/l, 6.3± 0.5 mmol/l, $p<0.0001$). The AUC_{gluc} of CAPD patients were higher than the HD patients (15.5±2.7 mmol/l.h, $p<0.0001$) and control group (12.4±1.4 mmol/l.h, $p<0.0001$). The mean baseline insulin levels of the CAPD group was higher than

the HD group (70.3±38.7 pmol/l, $p<0.001$) and control group (41.6±17.2 pmol/l, 34.4±16.5 pmol/l, $p<0.0001$). Mean of first and 2nd hour insulin levels of CAPD patients (302±161.0 pmol/l, 164.6±107.3 pmol/l) were higher than HD patients (118.6±112.8 pmol/l, 92.5±75.2 pmol/l and control group (148.7±46.6 pmol/l, 77.1±31.1pmol/l $p<0.0001$). On the contrary, mean insulin level of HD group was not significantly different from control group. AUC_{ins} value of CAPD patients (418±241pmol/l per hour) were higher than the HD patients (255±169 pmol/l per hour) and control group (203±41 pmol/l per hour, $p<0.0001$).

After standard OGTT; diabetes mellitus (120th blood glucose ≥ 11 mmol/l) was found in only one subject from the HD group, on the other hand 5 subjects were from CAPD group. Impaired glucose tolerance (120th blood glucose 7.7-11 mmol/l) were determined in 2 subjects in HD group, and 6 subjects in CAPD group. All comparisons of CAPD and HD groups were shown in **Table 1**. The mean Kt/V per session for HD group was 1.36 ± 0.3 and the mean weekly Kt/V for CAPD group was 2.1 ± 0.4. The NKF-DOQI recommendation of a single-pool Kt/V of 1.2 for HD, corresponds to a weekly Kt/V of 1.9 for CAPD.[14] Therefore, dialysis depuration in our patients was accepted as sufficient.

The HOMA-%B values of CAPD group (125 ± 71%) were higher than both HD (91 ± 62%, $p<0.02$) and control group (93 ± 49%, $p<0.04$). The HOMA-%B level of hemodialysis group was not significantly different from the control group. The HOMA-%S levels of CAPD group (70 ± 44%) was significantly lower than the HD (109 ± 67, $p<0.002$) and control group (114 ± 50%, $p<0.001$). There was no difference for HOMA-%S levels between HD and control group.

Table 1 - The comparison of HD and CAPD patients viewpoint of biochemical data related with ESRD conditions.

Biochemical parameters	HD (n=51)	CAPD (n=45)	*P*-value
Potassium (mmol/l)	4.67 ± 0.9	4.63 ± 0.9	NS
Total calcium (mmol/l)	2.12 ± 0.37	2.09 ± 0.37	NS
Hematocrit (%)	28.9± 4.9	28.1 ± 6.4	NS
Urea (mmol/l)	46.4 ± 18.9	41.9 ± 10.7	NS
Creatinine (mmol/l)	879.5 ± 256.3	937.0 ± 265.2	NS
PO4 (mmol/l)	1.76 ± 0.51	1.77 ± 0.45	NS
Total protein (g/l)	69 ± 7.3	68.4 ± 10.3	NS
Albumin (g/l)	33 ± 3	32 ± 6	NS
Serum iron(mmol/l)	18.6 ± 10.7	17.1 ± 7.5	NS
Total IBC (mmol/l)	54.5 ± 12.7	51.9 ± 15.9	NS
Parathyroid hormone (ng/l)	541 ± 174	532 ± 183	NS
Arterial pH	7.38 ± 0.1	7.36 ± 0.2	NS
HCO_3(mmol/l)	22 ±2	22 ± 3	NS
1-25 $(OH)_2D_3$ (pmol/l)	50.4 ± 4.8	48 ± 7.2	NS

NS - non-significant, IBC - iron binding capacity, HD - hemodialysis, CAPD - continuous ambulatory peritoneal dialysis, ESRD - end-stage renal disease

Discussion. The main remarkable findings of the present study were as follows; 1) Insulin sensitivity index (HOMA-%S) of CAPD group was lower than control and HD group. 2) The AUC_{ins} and AUC_{gluc} of CAPD patients were higher than HD patients and control subjects. These results indicate that CAPD patients were more resistant to insulin than HD and control subjects

Insulin sensitivity may reduce in various conditions. Obesity, especially abdominal obesity, is the most known condition that causes insulin resistance.[19] In terms of age, body weight and height, BMI, waist and hip circumference, percentage of fat and mass of all groups did not show any statistical difference. Therefore, this insulin resistance in CAPD patients should not be a result of obesity and its related conditions. We can say that insulin resistance in patients with CAPD may be a result of CAPD procedure itself or other uremic consequences.

Effects of dialysis modality on insulin resistance were studied previously, but results are not conciliatory. In a study made by Delarue et al[20] showed that CAPD might cause an insulin-resistance in patients with ESRD. On the contrary, Mak[21] evaluated insulin sensitivity in HD and continuous cycling peritoneal dialysis (CCPD) patients before and after renal replacement treatment, and he found that insulin sensitivity was significantly higher in the CCPD group than in the HD group after 3 monthly treatment. Raised blood glucose levels may impair tissue insulin sensitivity, and this concept is termed as the glucotoxicity theory.[13] The CAPD solutions contain more glucose (1.36, 2.77 and 3.86 g/dL) than HD dialysis solutions. It was claimed that glucose absorption from peritoneal dialysis solutions may lead to chronic stimulation of insulin secretion and cause hyperinsulinism.[22] As AUC_{gluc} and AUC_{ins} of CAPD patients were higher than HD subjects, probable glucose absorption from peritoneal dialysis solutions may cause a chronic stimulation of insulin secretion, hyperinsulinism and glucotoxicity in CAPD patients in our study. This result indicates that peritoneal absorption of glucose in CAPD solution may increase serum glucose level and this high glucose level may affect insulin sensitivity by glucotoxicity. It is well known that glucotoxicity is a more important condition, which leads to insulin resistance and metabolic syndrome.[13] Long-term glucose loading via CAPD solution may be responsible from impairment of insulin sensitivity. In fact Delarue et al[23] claimed that oral glucose in

CAPD patients induces a higher glycemic and insulinemic response and insulin resistance in CAPD patients even after months of renal replacement therapy.

In the HD therapy group, AUC_{ins}, AUC_{gluc} and HOMA-%B and HOMA-%S values were not significantly different from the control group. Anthropometric and uremic parameters between CAPD and HD patients were similar apart from dialysis modality and glucose contents of dialysate. Therefore, glucose content of CAPD solution may play a role in the development of insulin resistance. Amici et al[22] showed that daily glucose load was lower in subjects treated with icodextrin when compared to subjects treated with standard glucose solutions. When compared to HD subjects, oral glucose load in CAPD patients induces a higher glycemic and insulinemic response. As the osmotic agents currently used for peritoneal dialysis, namely, glucose or amino acids, are also substrates, a metabolic transfer occurs during their peritoneal absorption, glucose content of CAPD solutions in selection of dialysis modality in ESRD patients should be taken into account for a probability of insulin resistance.

An excess of PTH or a deficiency in $1,25(OH)_2D_3$ has also been implicated in the pathogenesis of insulin abnormalities in uremia.[8] However, in the present study, serum albumin and PTH levels of HD and CAPD patients were not significantly different from each other. Therefore, it is unlikely that PTH levels and hypoalbuminemia play important role in insulin sensitivity of ESRD patients. Serum $1,25(OH)_2D_3$ level may be an important contributing factor to insulin resistance in uremic patients.[8] We measured and compared serum $1,25(OH)_2D_3$ levels both in HD and CAPD patients however, we did not find any statistical difference in the viewpoint of serum $1,25(OH)_2D_3$ levels. As almost all patients were taking active vitamin D (calcitriol), we considered that the insulin resistance cannot be related to serum $1,25(OH)_2D_3$ levels in CAPD patients.

Metabolic acidosis is a common complication of uremia, and it may also contribute to the pathogenesis of insulin resistance. Previous studies using the glucose clamp technique by DeFronzo et al[2,24] have demonstrated that peripheral tissue insensitivity to insulin as the primary cause of glucose intolerance in patients with ESRD. Mean serum pH values of CAPD and HD patients did not show statistical difference in our study. For this reason, we could not say that insulin resistance in our CAPD patients is a result of metabolic acidosis.

In conclusion, the CAPD treatment seems to be a cause of insulin insensitivity in non-diabetic ESRD patients. In addition, the high glucose content of CAPD solutions may be responsible from insulin resistance in CAPD patients.

References

1. Shinohara K, Shoji T, Emoto M, Tahara H, Koyama H, Ishimura E, et al. Insulin resistance as an independent predictor of cardiovascular mortality inpatients with end-stage renal disease. ***J Am Soc Nephrol*** 2000; 13: 1894-1900.
2. De Fronzo RA, Alvestrand A, Smith D, Hendler R, Hendler E, Wahren J. Insulin resistance in uremia. ***J Clin Invest*** 1981; 67: 563-568.
3. Hager SR: Insulin resistance of uremia. ***Am J Kidney Dis*** 1989; 14: 272-276.
4. Rasic-Milutinovic Z, Perunicic-Pekovic G, Pljesa S. Clinical significance and pathogenic mechanisms of insulin resistance in chronic renal insufficiency (part II): pathogenic factors of insulin resistance in chronic renal insufficiency. ***Med Pregl*** 2000; 53: 159-163.
5. Mak RHK. Effect of metabolic acidosis on insulin action and secretion in uremia. ***Kidney Int*** 2000; 54: 603-607.
6. Oshida Y, Sato Y, Shiraishi S, Sakamoto N. Studies on glucose intolerance in chronic renal failure: Estimation of insulin sensitivity before and after initiation of hemodialysis. ***Clin Nephrol*** 1987; 28:35-38.
7. Mak RHK. Correction of anemia by erythropoietin reverses insulin resistance and hyperinsulinemia in uremia. ***Am J Physiol*** 1996; 270: 839–894.
8. Mak RHK. 1,25 dihydroxycholecalciferol corrects glucose intolerance in hemodialysis patients. ***Kidney Int*** 1992; 41: 1048–1054.
9. Borissova AM, Djambazova A, Todorov K, Dakovska L, Tankova T, Kirilov G. Effect of erythropoietin on the metabolic state and peripheral insulin sensitivity in diabetic patients on hemodialysis. ***Nephrol Dial Transplant*** 1993; 8: 93–95.
10. Kokot F, Wiecek A, Grzeszczak W. Influence of erythropoietin treatment on endocrine abnormalities in hemodialyzed patients. In: Baldamus CA, Koch KM, Scigalla P, Wieczorek L, editors. Erythroprotein: From Molecular Structure to Clinical Application, Basel (COUNTRY): Karger; 1990. p. 257–72.
11. Chagnac A, Korzets A, Zevin D, Korzets A, Hirsh J, Gafter U, et al. Effect of erythropoietin on glucose tolerance in hemodialysis patients. ***Clin Nephrol*** 1994; 42: 398–400.
12. Allegra V, Mengozzi G, D'Achille F. Glucose-induced insulin secretion in uremia: role of anemia. ***Nephron*** 1992; 62: 246–247.
13. Yki-Jarvinen H, Glucose toxicity. ***Endocr Rev*** 1992; 13: 415-431.
14. National Kidney Foundation-Dialysis Outcomes Quality Initiative: Clinical practice guidelines for peritoneal dialysis adequacy. ***Am J Kidney Dis*** 1997; 30 (Suppl 2): 70–73.
15. Matthews DR, Hosker JP, Rudenski AS, Burnett MA, Darling P, et al. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. ***Diabetologia*** 1985; 28: 412-419.
16. Turner RC, Holman RR, Matthews D. Insulin deficiency and insulin resistance interaction in diabetes: estimation of their relative contribution by feedback analysis from basal plasma insulin and glucose concentrations. ***Metabolism*** 1979; 28: 1086-1096.
17. DeFronzo RA, Tobin JD, Andres R. Glucose clamp technique: a method for quantifying insulin secretion and resistance. ***Am J physiol*** 1997; 237: 214-223.
18. Tai MM. A mathematical model for the determination of total area under glucose tolerance and other metabolic curves. ***Diabetes Care*** 1994; 17: 152–154.

19. Beck-Nielsen H. Insulin resistance: Organ manifestations and cellular mechanisms. ***Ugeskr Laeger*** 2002; 164: 2130-2135
20. Delarue J, Maingourd C, Couet C, Vidal S, Begros P, Lamisse F. Effect of oral glucose on intermediary metabolism in continuous ambulatory peritoneal dialysis patients versus healthy subjects. ***Peritoneal Dial Int*** 1998; 18: 505-511.
21. Mak RHK. Insulin resistance in uremia: effect of dialysis modality. ***Pediatr Res*** 1995; 40: 304-308.
22. Amici G, Orrasch M, Da Rin G, Bocci C. Hyperinsulinism reduction associated with icodextrin treatment in continuous ambulatory peritoneal dialysis patients. ***Adv Perit Dial*** 2001; 17: 80-83.
23. Delarue J, Maingourd C. Acute metabolic effects of dialysis fluids during CAPD. ***Am J Kidney Dis*** 2001; 37: 103-107.
24. DeFronzo RA, Tobin JD, Rowe JW, Andres R. Glucose intolerance in uremia. Quantification of pancreatic beta cell sensitivity to glucose and tissue sensitivity to insulin. ***J Clin Invest*** 1978; 63: 425–435.