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WORSENING OF MALNUTRITION-INFLAMMATION SCORE IS ASSOCIATED WITH HIGH RATIO OF EXTRACELLULAR TO TOTAL BODY WATER IN HEMODIALYSIS PATIENTS

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The Malnutrition-Inflammation Score (MIS) has been reported to be associated with mortality in hemodialysis (HD) patients. Bioelectrical impedance analysis is useful for assessing the body fluid components. The purpose of this study is to evaluate the association between change in MIS and fluid components in HD patients. A total of 76 patients who were receiving a 5-hour HD, 3 times weekly, were enrolled in this study. MIS was performed every 6 months. Using IN BODY 720, body fluid components were estimated once a year, including intracellular water (ICW), extracellular water (ECW), total body water (TBW), total body fat, body fat percentage and ECW/TBW ratio. In univariate analysis, worsening of MIS was correlated positively with age and ECW/TBW ratio. In multivariate analysis, worsening of MIS was significantly associated with higher ECW/TBW ratio. Higher ECW/TBW ratio remained significantly correlated with worsening of MIS in non-obese HD patients, but not in obese patients. In conclusion, non-obese HD patients who has higher ECW/TBW ratio should be considered to be a risk group for malnutrition.

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BENEFICIAL EFFECT OF KETO AMINO ACIDS FOR DIALYSIS PATIENTS

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Nutritional status is an important predictor of clinical outcome in dialysed patients. Beside decreased serum protein/albumin,lower BMI with decreased muscle mass is the most significant predictor of morbidity and mortality. Keto amino acids (KA) represent an additional source for protein anabolism influencing indirectly also carbohydrate and lipid metabolism,Ca-P and acid base balance.Additionaly,by concominant metabolic and hemodynamic effect on residual nefrons, KA can help to slow progression of residual renal function (RRF) mainly in peritoneal dialysis patients. We conducted a long-term prospective randomized placebo controlled trial to test whether a modified low-protein diet (LPD) with or without keto acids (KA) would be safe ,well tolerated and associated with an increase of metabolic status and preservation of RRF in peritoneal dialysis (PD). We evaluated a total of 62 PD patients (32M/30F) aged 26-72 yrs with creatinine clearance (Ccr) 7.9-5.7 mL/min/1.73m^2 for a period of 12 months. All patients were on modified LPD containing 0.8 protein/kg/IBW/day and 135/kJ/kg/IBW/day. LPD was randomly supplemented with KA at dosage of 100 mg/kg/IBW/day (30 patients, Group I) while 30 patients (Group II) received placebo. We analysed also muscle and fat metabolism by MR spectroscopy (MRS, m.tibialis anterior)) and imagining (MRI,visceral fat).Patients from Group I were before enrolment on conservative management using LPD + KA (0.6g P + 0.1g KA/kg/IBW/day) for longer time (18-48 months, median 28) with good compliance (SGA). Patients from group II were never treated with LPD and KA.All patients were monitored at the beginning of PD and at every 3 months for 12 months.;A neutral or positive long- term nitrogen balance (nPCR in g/kg IBW/day) was achieved in Group I ($p < 0.05$).RRF measured as Ccr remained stable in Group I (6.5 ± 2.18 to 5.9 ± 2.54 ml/min, p=NS),while it decreased in Group II (6.7 ± 2.22 to 3.2 ± 1.44 ml/min, $p < 0.02$).There were no differences in Dialysate clearance (DCcr(L/week/1.73 m^2).At the end of the study,there were significant differences in Total clearance per week expressed as Dialysate clearance + Residual creatinine clearance (TCcr=DCcr + RCcr), P< 0.01 and Total Kt/Vurea/week,P< 0.01.Serum albumin increased significantly (from 29.5 ± 2,5 to 35.4 ± 3.4 g/L, P< 0.01) in Group I comparing to Group II (30.4 ± 3.4 to 31.8 ± 3.5 g/L, P =NS).Also urine output was sigificantly higher in Group I (1226 ± 449 mL/day) than in Group II (678 ± 327 mL/day, P< 0.01), respectively).Fat in muscle measured by MR spectroscopy (MRS, m.tibialis anterior) significantly decreased in Group I and was linked to reduced volume of visceral fat measured by MRI ($p < 0.02$). In conclusion, comparing to control Group II, long-term administration of modified LPD+KA was associated in Group I with better metabolic status and residual renal function.(RRF ,diuresis,Total clearance,Total Kt/V $_{(urea)_w}$.S-albumin and nPCR).We confirmed positive changes in muscle mass and fat metabolism measured by MRS and MRI. Long-term administration of KA supplemented diet in dialysed patients was safe and well tolerated.Thus,this regimen may ramarkable increase nutritional status and clinical outcome of dialysed patients.

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EFFECT OF KETO AMINO ACIDS ON ASYMMETRIC DIMETHYL ARGININE, MUSCLE AND FAT TISSUE IN CHRONIC KIDNEY DISEASE

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Levels of endogenous nitric oxide synthase inhibitor asymmetric dimethylarginine (ADMA) are elevated in chronic kidney disease (CKD) and may contribute to vascular complications. In this study we tested the hypothesis that elevated ADMA can be reduced in CKD patients by long-term administration of low-protein diet (LPD) supplemented with keto amino acids (KA). In a long-term prospective double blind placebo controlled randomized trial, we evaluated a total of 120 CKD patients (62/58F) aged 22-76 yrs with creatinine clearance 22-40mL/min/1.73m^2 for a period of 36 months. All patients were on low-protein diet containing 0.6 protein/kg/IBW/day and 120-125/kJ/kg/IBW/day. LPD was randomly supplemented with KA at dosage of 100 mg/kg/IBW/day (61 patients, Group I) while 59 patients (Group II) received placebo. During the study period, glomerular filtration rate (GFR) slightly decreased (C_{cr} from 34.2 ± 11.6 to 29.9 ± 9.2 mL/min and 33.5 ± 11.6 to 22.2 ± 10.4 mL/min in Group I and II, respectively); this however was more marked in Group II ($p < 0.01$). Fat in muscle measured by MR spectroscopy (MRS, m.tibialis anterior) significantly decreased in Group I and was linked to reduced volume of visceral fat measured by MRI ($p < 0.01$). Reduction of fat in Group II was not significant. In Group I, there was a significant decrease in the plasma level of ADMA (from 2.4 ± 0.4 to 1.2 ± 0.3 μmol/L, $p < 0.01$), but ADMA remained unchanged in Group II. A further remarkable finding was reduction in the plasma concentration of pentosidine (from 486 ± 168 to 325 ± 127 μg/L, $p < 0.01$) and decrease of proteinuria (from 3.7 ± 2.20 to 1.6 ± 1.2 g/24hrs, $p < 0.01$) in Group I. Plasma adiponectin (ADPN) in Group I rose ($p < 0.01$). Analysis of lipid spectrum revealed a mild yet significant decrease in total cholesterol and LPD-cholesterol ($p < 0.01$), more pronounced in Group I. In Group I, there was a decrease in plasma triglycerides (from 3.8 ± 1.5 down to 2.3 ± 0.5 mmol/L, $p < 0.01$), whereas glycated hemoglobin (HbAc1) decreased from 7.0 ± 1.3 to 4.1 ± 0.9 %, ($p < 0.01$) nIn conclusion,comparing to placebo group long term co-administration of LPD and KA in CKD patients led to decrease of ADMA,fat in muscle and visceral body fat, and proteinuria. Concomitant decreases of glycated haemoglobin, LDL-c and pentosidine may also contribute to the delay in progression of renal failure and decrease of cardiovascular risk factors..The study was supported by Research Project MZO 00023001 awarded by Ministry of Health of the Czech Republic

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PIOGLITAZONE IMPROVES INSULIN SENSITIVITY, REDUCES VISCERAL FAT AND STIMULATES LIPOLYSIS IN NON DIABETIC DIALYZED PATIENTS

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Insulin resistance is common in dialyzed patients and is associated with increased mortality and protein-energy wasting. The aim of this study was to investigate the effect of pioglitazone (PIO), a powerful insulin sensitizer, on insulin sensitivity, body composition and adipose tissue metabolism, in dialyzed patients. A double blind randomized cross-over study was performed in non diabetic dialysis patients. Each patient followed 2 treatment phases of 16 weeks, starting either with oral PIO 45 mg/d or placebo (PL), and then switched to the other phase. At the end of each phase, patients underwent hyperinsulinemic euglycemic clamps, dual energy X-ray absorptiometry, an abdominal CT, and extensive plasma biochemical analysis. Twelve patients including 8 HD (59.6 ± 4.4 y) and 4 PD patients (43.5 ± 3.6 y) were recruited. Nine patients completed both phases and 3 patients dropped out (renal transplantation/2 HD and peritonitis/1 PD). PIO was safe and well tolerated.