Peritoneal dialysis (PD) solutions with amino acids (AAs) were developed as an alternative to glucose-based PD solutions for chronic renal failure. Although AA solution has many theoretical advantages, the results reported in the literature are still not convincing.

Treatment of ARF is a complex problem. To tackle it, we investigated a PD solution based on a mixture of Nutrineal (Baxter Healthcare SA, Castlebar, Ireland) and Dianeal (Baxter Healthcare SA), mixed on the heating plate of the PAC Xtra cycler (Baxter Healthcare SA). The resulting solution was expected to lower the glucose load without affecting dialysis adequacy. We retrospectively analyzed data in children treated with the mixture, and evaluated safety, dialysis adequacy, acidosis, and nutritional state (albumin).

Glucose reabsorption and protein losses were significantly lower when mixed AA–glucose solution was used. Despite significant AA absorption in the patients, we observed no significant difference in plasma albumin levels. Reabsorption from the dialysate of AAs varied between 21% and 69%, resulting in 27% ± 12% of daily AA intake. Reabsorption of glucose from the dialysate was 32% – 72%.

In children in intensive care, who are often already very sensitive, an AA-containing mixture may help to control glycemia, subsequently reducing the need for insulin. Our data demonstrate that the calculated percentage reabsorption of glucose and AAs is high and that AA levels in plasma remain stable. Although our data do not demonstrate a potential influence on final outcome, they demonstrate the feasibility and safety of using combined AA–glucose solution, with a calculated resorption that lends nutritional support.

Key words
Acute renal failure, children, bicarbonate dialysis solution, low-sodium dialysis solution

Introduction
Peritoneal dialysis (PD) solutions with amino acids (AAs) were developed as an alternative for glucose-based PD solutions for chronic renal failure. Although AA solution has many theoretical advantages, the results reported in the literature are still not convincing. Also, data in children are limited, and, experts are very reluctant to endorse AA solution in dialysis guidelines (1,2).

The major indication for AA solution is nutritional support in malnourished adult patients (3). In children, however, support for malnutrition is a minor concern, because a gastrostomy is the treatment of choice (4). The major indication for AA solution in chronic dialysis in children is therefore probably preservation of the peritoneal membrane by reduction of the glucose load, especially when glucose solutions are used overnight in automated PD (APD). In acute renal failure (ARF), the situation may be different.

Treatment of ARF is a complex problem. Cardiorespiratory instability often forces a choice for APD, with frequent cycles and low fill volumes of hypertonic glucose solution. The hypertonic glucose often induces hyperglycemia in the intensive care patients, who often already have hyperglycemia (5,6). Not only is insulin treatment often required, but the high plasma glucose and osmolality also limit ultrafiltration efficiency.

To tackle this problem, we investigated a dialysis solution based on a mixture of Nutrineal (Baxter Healthcare SA, Castlebar, Ireland) and Dianeal (Baxter Healthcare SA), mixed on the heating plate of the PAC Xtra cycler (Baxter Healthcare SA). The resulting solution was expected to lower the glucose load without affecting dialysis adequacy.
Patients and methods

We retrospectively analyzed data in children treated with an AA-based PD solution (Nutrineal) mixed with Dianeal in a cycler. We evaluated safety, dialysis adequacy, acidosis, and nutritional state (albumin). We performed an AA analysis to evaluate whether the so-called NO-related AAs were increased in plasma, which could possibly lead to risk of shock and vasodilatation.

The study group consisted of 33 patients who were treated for ARF for at least 72 hours at our hospital during the period 1993 – 2000. The cycler was programmed for cycles of 10 minutes inflow, 100 minutes dwell time, and 10 minutes outflow. Glucose solution was used for the first 48 hours. From 48 hours to 72 hours, the solution combined 1 bag of Nutrineal 1.1% and 1 bag of Dianeal 3.86%.

We measured the dialysate and plasma AA concentrations (Figure 1), the plasma AA concentrations before and after Nutrineal (Figure 2), and dialysate parameters. We calculated peritoneal reabsorption (glucose and AAs) and determined blood urea nitrogen (BUN), creatinine, serum albumin, body parameters, and dialysis adequacy.

Results

We observed no significant differences in plasma creatinine, BUN, acidosis, or ultrafiltration rate before and after use of Nutrineal. Glucose reabsorption and protein losses were significantly lower when mixed AA–glucose solution was used. Despite significant AA absorption, we observed no significant difference in plasma albumin levels. Reabsorption from the dialysate of AAs varied between 21% and 69%, resulting in 27% ± 12% of daily AA intake. Reabsorption of glucose from the dialysate was 32% – 72%.

Figure 1 shows that the relative concentrations of several AAs were different in dialysate and plasma. The large standard deviations for the measured dialysate concentrations may be surprising, but they do not suggest a manufacturing problem. Rather, they are related to the different size and format of the Nutrineal and Dianeal bags, which produce a slight disequilibrium as the 2 bags pump up to the heating plate.

Figure 2 shows that, after 48 – 72 hours, plasma AA levels were not significantly changed (especially arginine concentration).
Discussion

The introduction of APD into clinical practice in an intensive care unit raises several metabolic problems and affects the nutrition status and the acid, electrolyte, and fluid balance of the patients (7). The option of continuous renal replacement therapy therefore offers the ability to ultrafilter and to dialyze to the desired level and to deliver high nutritional support (1,8–10). But what is often forgotten is that more ultrafiltration requires more substitution and that “more” has not always been proven to be “better.” There may be a place to optimize softer types of renal replacement therapy such as PD. The present study demonstrates that modifying conventional PD may result in significant nutritional support, better metabolic homeostasis, and fewer side effects (hyperglycemia, need for insulin).

The possibility of using PD itself as a source of nutrients in the treatment of malnutrition is an intriguing concept (11). Unfortunately, it is not possible to produce dialysis solution that contains both glucose and AAs because of technical problems of preservation (such as crystallization and caramelization) unless a multiple-compartment system such as that currently used for bicarbonate-buffered solution is developed. Hence, the simultaneous infusion of glucose and AAs is not possible in continuous ambulatory PD in adults (11,12). Automated PD (APD), which is based on the use of a cycler, permits different solutions to be simultaneously pumped from reservoir bags into an empty bag on the heating plate, thereby producing a reasonably homogeneous mixture. In theory, 1 glucose bag can be mixed with 1 AA bag to obtain 50% of each, or 2 glucose bags could be mixed with 1 AA bag for patients who need a reduced AA load. Various options are possible.

In APD, a combined AA and glucose solution rather than the traditional single daily bag of Nutrineal is potentially superior for reaching anabolic goals, for these reasons:

- An optimal anabolic effect requires AAs and glucose to be delivered together.
- Large glucose-induced changes in insulin are avoided.
- Loss of AAs in glucose dwells (3 of 4) is avoided.
Soon after the introduction of Nutrineal, those theoretical considerations were already documented in clinical practice. Indeed, in almost all of the studies on the use of intraperitoneal AAs, a significant increase in serum levels of urea were reported, suggesting unsatisfactory utilization of the infused AAs (11,12). Moreover, it is well known that, without an energy source, nitrogen will not be effectively incorporated into proteins.

In parenteral nutrition, the combined infusion of non protein calories and AAs has been a key factor in ensuring the optimal utilization of the AAs. Total parenteral nutrition (TPN) solutions with a ratio of 150:1 (non protein calories to nitrogen) are considered appropriate for most patients to incorporate delivered AAs into new proteins. A mixture of Nutrineal and Dianeal simultaneously achieves three conditions favorable for protein synthesis: hyperinsulinemia, hyperaminoacidemia, and an adequate ratio of non protein calories to nitrogen (absorbed glucose to AAs).

These considerations are of even more importance in intensive care units, where most patients are catabolic, lack enteral nutrition, and require ultrafiltration for every parenteral milliliter administered. The use of combined glucose–AA solutions in a peritoneum with hyperemic dilated vessels will result in significant peritoneal resorption. That resorption may meet a significant percentage of the patient’s nutritional needs (AAs and glucose), limiting the need for intravenous administration of TPN. Limiting intravenous fluid administration helps to eliminate the need for ultrafiltration by dialysis.

In children in intensive care, who are often already very sensitive, an AA-containing mixture may help to control glycemia, subsequently reducing the need for insulin. Our data demonstrate that the calculated percentage reabsorption of glucose and AAs is high and that plasma AA levels remain stable. The reabsorption data are comparable with data reported by Canepa et al. and Qamar et al. (13–17).

Adequate protein and energy intake are essential to the maintenance of nitrogen balance and the prevention of malnutrition in intensive care. Treatment with oral calorie and protein supplements is often impossible, but intravenous administration of TPN is often limited by the excessive fluid load imposed on a patient in anuria by the need to reach a given nutritional target. The use of AA-based dialysis fluid combined with glucose may provide opportunities to compensate for dialytic losses of protein and AAs and to supplement inadequate dietary protein intake, with subsequent improvement in nutritional status, because of the resulting anabolic benefit and limitation of unnecessary AA metabolism.

**Conclusions**

Although our data do not demonstrate a potential influence on final outcome, they demonstrate the feasibility and safety of using combined AA–glucose solution, with a calculated resorption that lends nutritional support.

**References**


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Dual-energy X-ray absorptiometry (DEXA) can be used to evaluate total-body bone mineral content (BMC), bone mineral density (BMD), fat-free mass (FFM), and fat body mass (FBM), which are all frequently affected in patients (PD) on peritoneal dialysis. We used DEXA to evaluate body composition in children on PD and to establish whether relationships existed with nutrition status, dialytic parameters, and biochemical data.

We evaluated 20 PD patients (12 boys, 8 girls). The mean age of the patients was 5.84 years (range: 0.16 – 14.66 years). We carried out DEXA, anthropometry (weight/age, height/age, and body mass index), and measurements of dietary intake (protein, energy, calcium, and phosphorus), nitrogen balance (NB), dialysis dose (Kt/V), peritoneal equilibrium test (PET), and plasma calcium, phosphorus, and bicarbonate at months 1 and 6 of the study. Energy intake was prescribed according to the United States Recommended Dietary Allowances, and Kt/V and daily protein intake (DPI) according to the Dialysis Outcomes Quality Initiative (DOQI) guidelines.

In the patients, BMD increased to 0.769 ± 0.174 g/cm² from 0.747 ± 0.166 g/cm² (p < 0.05), and BMC increased to 680.3 ± 666.1 g from 632.6 ± 597.5 g (p < 0.01). The mean BMD Z score for patients older than 4 years (n = 11) was –0.69 at month 1, with a significant increase to –0.35 at month 6. The FBM and FFM increased, but without reaching statistical significance. At months 1 and 6, the DPI was 144.3% and 129.9% respectively (p = nonsignificant) and showed a negative correlation with BMD, BMC, and FFM (p < 0.05). Comparing DPI to plasma bicarbonate showed a negative correlation at month 1 (p < 0.05). Negative correlations were also found between NB and the parameters BMC, BMD, FBM, and FFM (p < 0.05).

All patients showed a positive NB. No correlation was found between DEXA and anthropometric measurements, energy intake, serum calcium, serum phosphorus, or Kt/V. Dialysate-to-plasma creatinine from the PET showed a negative correlation with BMD and FFM (p < 0.05).

In terms of positive NB and controlled Kt/V, we observed an increase in bone mineralization within the 6 months of follow-up. A high protein intake seems to negatively affect acid–base status, bone mineralization, and FFM.

Key words
Dual-energy X-ray absorptiometry, bone mineral content, bone mineral density, children

Introduction
In children with chronic renal failure (CRF) treated conservatively with dialysis, alterations of nutrition, metabolism, and fluid homeostasis may occur, critically affecting the acute and chronic well-being of the patients (1). In pediatric dialysis, malnutrition has been considered a major determinant of morbidity and mortality, and overcoming malnutrition remains one of the most important goals in the management of children on chronic peritoneal dialysis (PD) therapy (2,3).

Nutrition status can be monitored by dual-energy X-ray absorptiometry (DEXA), a noninvasive method of estimating bone mineral content and fat and lean body mass. Because of their varying density, bone, lean tissue, and fat attenuate the energy beams differentially. Therefore, by using dual-energy beams, it is possible to solve for three tissue compartments. Dual-energy X-ray absorptiometry is becoming increasingly available for clinical and research use. Radiation exposure in DEXA is extremely low (0.3 cGy), and whole-body estimates of body composition for infants, children, and adolescents can be obtained in less than 5 minutes (4).

Although the growing evidence about the critical meaning of nutrition in the long-term prognosis for
dialyzed children is well documented, management for optimal nutrition in children on PD requires strict dietary prescription (energy, proteins); dietary recall; monthly weight, length, head circumference (up to 2 years), mid-arm circumference, skin-fold thickness measurements; physical examination; and tests of biochemical and hematologic parameters and dialysis adequacy (5,6).

In the present prospective study, we used DEXA to evaluate the nutrition status of children on PD. We studied bone mineral content and fat and lean body mass; measured daily protein intake, daily energy intake, nitrogen balance, and dialytic parameters; and studied the correlations between those variables.

Patients and methods
We performed prospective DEXA measurements in 20 stable PD patients, all of them being treated as outpatients at the Nephrology and Nutrition divisions of Luis Calvo Mackenna Children’s Hospital. The group included 12 boys and 8 girls whose mean age was 5.84 years (range: 0.16 – 14.66 years) and whose mean duration on PD was 11 months (range: 2 – 46 months). Underlying renal disorders included renal dysplasia (n = 10), reflux nephropathy (n = 3), hemolytic uremic syndrome (n = 1), obstructive uropathy (n = 1), chronic glomerulonephritis (n = 4), and an unknown disorder (n = 1). At the start of the study, 11 patients were on continuous ambulatory PD, and 9 were on automated PD. Four patients had no residual renal function. Patients with fever, infections, nephrotic syndrome, gastrointestinal absorption disturbances, steroid treatments, endocrine diseases, genetic syndromes, and compliance or behavioral disturbances were excluded. The study protocol was evaluated and approved by the ethics committee of the hospital, and written informed consent was obtained from all parents before the study was initiated.

Each month, we evaluated anthropology, dietary intake, nitrogen balance, serum bicarbonate, and dialysis dose. Whole-body DEXA was performed every 6 months, and a peritoneal equilibration test (PET) was performed at the start of the study.

Whole-body DEXA
The DEXA examinations were performed using a Lunar DPX-L 7660 densitometer (Lunar Radiation Corporation, Madison, WI, U.S.A.). We obtained bone mineral content (BMC), lean body mass (LBM), and fat body mass (FBM) in kilograms from the DEXA by using pediatric software for children with a weight less than 30 kg. All measurements were performed and analyzed by the same investigator.

Anthropometry
With the patient in minimum clothing, weight was measured on a mechanical Seca scale (Seca Corporation, Hamburg, Germany) of 0.1 kg precision and 150 kg capacity. All children on PD were weighed with a known dialysate volume in the peritoneal cavity, and the weight of the solution was deducted from the observed weight. Height was measured with 1 mm precision. All measurements were performed by the same investigator.

Dietary intake
Once each month, 24-hour-recall and a food frequency questionnaire were used to estimate intake of energy, macronutrients, and micronutrients. Usual portions were obtained from earlier studies plus food weighing during the interview when necessary. A Chilean food database stored in an Excel spreadsheet (Microsoft Corporation, Redmond, WA, U.S.A.) was used for the calculation. A nutritionist obtained the information. Food intake adequacy was compared with Dialysis Outcomes Quality Initiative (DOQI) guidelines for energy and protein requirements (5). Calcium and phosphorus intakes were compared with U.S. Recommended Dietary Allowances [RDA (7)].

Nitrogen balance studies
Blood samples and 24-hour dialysate and urine were collected on an outpatient basis. To avoid generation of urea secondary to bacterial activity, thimerosal was added to urine and dialysate samples. All samples obtained under noncompliance conditions were discarded. Total protein and albumin (turbidimetric assay) were measured in plasma, urine, and dialysate.

Dialysis dose
We calculated weekly Kt/V urea, both peritoneal and residual using the equation

\[
Kt/V \text{ urea} = \frac{[24 \text{-h dialysate volume (L)} \times D/P \text{ urea} \times 7]}{[0.60 \times \text{weight (kg)}]}
\]

Dialysis dose was prescribed to meet a minimum weekly Kt/V of 2 as specified in the DOQI guidelines.
(8), but no attempt was made to define a maximum Kt/V value in our patients.

**Peritoneal equilibration test**

The PET was performed according to a previously published protocol (9,10). Briefly, a standardized volume (1100 mL/m² body surface area) of Dianeal 2.5% solution (Baxter Healthcare SA, Castlebar, Ireland) was instilled into the peritoneal cavity, and dialysate samples were taken from the overnight exchange bag at 0, 120, and 240 minutes. A serum sample was taken at 120 minutes. Results were analyzed for the dialysate-to-plasma (D/P) creatinine and final-to-initial dialysate (D/D₀) glucose equilibration ratios at 4 hours, and each patient was categorized as a high, high-average, low-average, or low transporter according to pediatric values published by Warady et al. (9).

**Biochemical measurements**

We obtained plasma measurements of bicarbonate (mEq/L, by bromcresol blue), phosphate (mg/dL, by phosphomolybdate complex colorimetry at 340 nm), calcium (by the cresolphthalein complexone method), alkaline phosphatase (by 4-nitrophenyl phosphate), and hemoglobin (by cyanmethemoglobin).

**Statistical analysis**

Means, standard deviations, correlation coefficients, and t-tests were performed using Excel 5.0 (Microsoft Corporation) and Statistica for Windows, version 4.5 (StatSoft, Tulsa, OK, U.S.A.). Values of p < 0.05 were accepted as statistically significant.

**Results**

**Body composition**

Between the start of the protocol and month 6, the 20 patients evaluated by DEXA showed an increase in BMD to 0.769 ± 0.174 g/cm² from 0.747 ± 0.166 g/cm², p < 0.05. The BMC in the group also increased to 680.3 ± 666.1 g from 632.6 ± 597.5 g, p < 0.01.

The mean BMD Z score at the beginning of the study in patients older than 4 years (n = 11) was –0.69 (range: 0.3 to –2.2). The mean BMD Z score for those 11 patients showed a significant increase to –0.35 at month 6. The FBM and FFM also increased, but without reaching statistical significance.

The patients’ DPI showed a negative correlation with BMD, BMC, and FFM (p < 0.05; Table I).

**Anthropometry**

The mean Z score for height/age was –2.17 (range: –4.75 to –0.3) at the start of the study, and –2.14 (range: –3.98 to –0.2) at month 6 [p = nonsignificant (NS)]. The Z score for weight/age was –1.6 (range: –3.15 to –0.39) and –1.94 (range: –2.25 to 0.39) at the same time periods (also p = NS).

**Dietary intake**

Most of the patients showed a caloric intake above the RDA recommendations (mean values: 115.11% ± 37.21% at month 1 and 108.16% ± 35.84% at month 6). In addition, the patients’ DPI exceeded the DOQI (5) recommendations (mean values: 144.77% ± 48.74% at month 1 and 140.85% ± 52.13% at month 6, p = NS). Table II shows other dietary intake values.

The patients’ mean DPI was 3.32 ± 1.6 g/kg/day at the beginning of the study and 3.3 ± 1.3 g/kg/day at month 6 (p = NS). A comparison of DPI versus bicarbonate showed a negative correlation at the beginning of the study (r = –0.46, p < 0.05), but only a tendency toward a negative correlation at month 6.

**Nitrogen balance studies**

All patients showed a positive NB initially and at month 6 of follow-up. Initially, mean DPI was 3.32 ± 1.05 g/kg/day, and mean daily protein losses were 1.19 ± 0.47 g/kg/day, for a mean net protein balance of +2.1 g/kg/day. At month 6 of the study, mean DPI was 3.30 ± 1.7 g/kg/day, and mean daily protein losses were 1.7 ± 0.47 g/kg/day, for a net protein balance of +1.6 g/kg/day. We observed no difference in the protein balance between month 1 and month 6 of the study. We found a negative correlation between BN and the parameters BMD, FBM, and FFM (r = –0.8, r = –0.55, and r = –0.7 respectively; p < 0.05).

**Dialysis dose**

The mean weekly total Kt/V urea was 3.31 ± 1.1 at the beginning of the study and 2.57 ± 1.53 at month 6. The mean weekly peritoneal and residual Kt/V urea values were, respectively, 1.7 ± 0.81 and 1.5 ± 1.24 at the beginning of the study, and 1.6 ± 0.58 and 1.5 ± 1.18 at month 6.

**Peritoneal equilibration test**

The mean 4-hour D/P creatinine was 0.78 ± 0.02 initially and 0.74 ± 0.13 at month 6 (p = NS). The mean
**Discussion**

Body composition has been measured by whole-body DEXA in a number of wasting diseases (including HIV, cystic fibrosis, pulmonary disease, CRF, and renal transplantation), but experiences in children on PD are scarce (11–14). Historically, the pediatric dialysis population has been characterized by progressive growth retardation. That trend is reflected in the 2001 Annual Report of the North American Pediatric Renal Transplant Cooperative Study (16), in which the mean height standard deviation score (SDS) of the PD patients was −1.69 at baseline and −1.92 at 24 months after initiation of PD.

**Biochemical measurements**

Table III lists values for serum concentrations of creatinine, calcium, phosphorus, and intact parathyroid hormone, and for alkaline phosphatase activity. No correlations were found between BMD, BMC, LBM, or FBM and weight/age, height/age, body mass index, energy intake, or serum concentrations of calcium or phosphorus.
In renal failure, growth is acknowledged to be influenced by a variety of endocrine, nutritional, and metabolic factors. The impact of dialysis dose on growth remains undetermined (15,16). Thus, to obtain a more detailed nutrition assessment and follow-up in CRF patients, it could well be imagined that DEXA could be used as a complementary method of assessing body composition, as suggested by the ad hoc European committee on the assessment of growth and nutrition status in children on chronic PD (6).

The reproducibility of DEXA measurements is excellent: 1.2% for total fat-free and fat mass, and 0.5% for bone mineral content. The precision is 1.0% and 2.0% for FFM and fat mass respectively. The fat mass derived from DEXA measurements correlates well with the fat mass determined by hydrodensitometry and total-body \(^{40}\text{K}\). A limitation of DEXA is that it does not measure total body water (TBW); instead, an assumption is made that TBW is 73.2% of FFM. However, that assumption could result in an underestimation of protein mass in underhydrated individuals and an overestimation of protein mass in overhydrated individuals (4,11).

A limitation of the present study is a lack of local reference values. As a result, we had to compare our results with the NHANES (National Health and Nutrition Examination Survey) curves with SDS for BMD for whole-body DEXA for children under 4 years of age (17). The same is true for FFM and FBM. That bias must be taken in account when the data presented here are discussed.

In terms of controlled dialysis and nutrition, we observed a significant increase in bone mineralization: at 6 months of follow-up, BMD had risen to 0.769 ± 0.174 g/cm\(^2\) from 0.747 ± 0.166 g/cm\(^2\), and BMC had risen to 680.3 ± 666.1 g from 632.6 ± 597.5 g. The BMD Z score is available from 4 years of age, and, in our patients older than 4 years \((n = 11)\), we found a significant increase to –0.35 from –0.69 (range: 0.3 to –2.2) during the observation period. An increase in FBM and FFM that did not reach statistical significance was also observed.

Most of the patients showed a daily caloric intake higher than the RDA (mean of 115.11% ± 37.21% for energy and 108.16% ± 35.84% for protein). Values for DPI were higher than the DOQI recommendations (144.77% ± 8.74% at month 1 and 140.85% ± 52.13% at month 6, \(p = \text{NS}\)). But despite the high dietary intake, we did not see catch-up growth in all patients.

Recent reports have identified certain factors that could interfere with control of protein turnover in CRF patients and therefore interfere with growth. Those factors include acidosis, inflammation, and resistance to anabolic hormones (18).

Schaefer et al., (19) observed a significant negative correlation between delta height SDS and the creatinine equilibration rate in the initial study PET \((r = –0.31, p < 0.05)\). Multiple regression analysis confirmed a negative effect of the high transport state \((\text{partial } r^2 = 0.07)\) on delta height SDS. In the present study, it is interesting that we found a negative correlation between the mean 4-hour D/P creatinine and both the BMD and FFM parameters \((p < 0.05)\), suggesting for the first time that a high transport state is an adverse risk factor for nutrition status in children on PD.

Conclusions
In terms of positive NB and controlled Kt/V, we observed an increase in bone mineralization within a 6-month period of follow-up. A high protein intake seems to negatively affect acid–base status, bone mineralization, and FFM. We also observed that a high transport state, as measured by 4-hour D/P creatinine, may adversely affect the fat and mineral content of the body.

Acknowledgment
This study was supported by research grant FONDECYT 1010632.

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