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VETERINARIA

Assisted feeding through an oesophagostomy tube in patients with chronic kidney disease and uraemic syndrome: impact on body condition score, renal function and survival

Introduction – A renal diet is a fundamental part of the medical management of patients with acute and chronic kidney disease. Unfortunately, most patients are not able to eat a sufficient amount of a renal diet to achieve an adequate calorie intake. The aim of this study was to evaluate the Body Condition Score (BCS), renal function and survival rate in a group of uraemic patients managed with a feeding tube and compare the findings with those in a comparable group managed without a feeding tube.
Materials and Methods – Fourteen dogs with acute-on-chronic kidney disease formed the study population. Seven dogs were managed with the use of a feeding tube (FT group) and seven were managed without a feeding tube (control group). BCS, serum creatinine, urea and phosphate concentrations and survival rate were evaluated in both groups at time 0 (T0), after 1 month (T1) and after 2 months (T2). Data were analysed statistically.
Results – There were significant differences in BCS (p=0.04), creatinine (p=0.001), urea (p=0,005) phosphate (p=0.04) at the different time points in the control group. The FT group also had significant difference in BCS (p=0.03), creatinine (p=0.006), urea (p=0.0001) and phosphate (p=0.02) at the different time points. The survival rate was higher in the FT group than in the control group (p=0.01).
Discussion – The results of the present study show significant improvements in BCS, renal function and survival in patients managed with a feeding tube, compared to those in which a feeding tube was not used. A feeding tube seems to be a very useful therapeutic instrument for the management of patients with uraemic syndrome.

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INTRODUCTION

A proper diet is an integral part of the treatment of patients with acute kidney injury (AKI) and chronic kidney disease (CKD) and is the first therapeutic strategy to be taken to slow the progression of the disease and reduce the incidence of uraemic crises[1]. A fundamental goal of the diet is to maximise the duration and qual-

ity of life of patients, limiting the extent of the typical symptoms of uraemia and prolonging survival[2]. However, in clinical practice we are often faced with patients that are unable to assume a renal diet autonomously or to eat amounts adequate for their needs. In such patients, assisted feeding is not only the sole way of providing nutritional support, but is also a simple and practical way of maintaining the state of hydration and administering drugs. The objectives of dietary therapy in patients with uraemia are: to ensure an adequate calorie intake, based mainly on non-protein calorie sources; to maintain a correct nitrogen balance through the intake of proteins of high biological value; to minimise the state of azotaemia and associated clinical signs; to restrict the intake of phosphorus with the diet; to normalise the blood pH and control the symptoms of metabolic acidosis; to provide an appropriate supply of electrolytes; to ensure an adequate supply of free water and control the clinical signs of dehydration[3].
The primary purpose of this study was to compare clinical variables and laboratory parameters in patients during acute exacerbation or decompensation of CKD treated or not treated with assisted feeding through an oesophagostomy tube. In addition, the survival times of the patients in the two groups were evaluated for prognostic purposes.

Dietary therapy is an essential therapeutic aid in the course of acute kidney injury and chronic kidney disease.

MATERIALS AND METHODS

Fourteen dogs with acute worsening of CKD, referred for a specialist nephrology consultation between January 2011 and December 2013, took part in this retrospective study. All subjects, regardless of the cause of the uraemic crisis, were classified as having an acute exacerbation or decompensation of CKD, and indicated as subjects with AKI/CKD. Dogs with AKI which did not have a past medical history, signs, ultrasound or blood-biochemistry evidence of existing CKD were excluded. All subjects had an adequate urinary output. CKD was diagnosed as the presence of polyuria/polydipsia, azotaemia (serum creatinine >1.8 mg/dL) and renal ultrasound abnormalities attributable to chronic damage. A uraemic crisis was defined as progressive and persistent azotaemia (significant increase in serum creatinine compared to the value reported by the referring veterinarian in the previous 2-3 days) accompanied by one or more of the following clinical signs: altered appetite, nausea, vomiting, loss of weight, uraemic halitosis, uraemic stomatitis, hypothermia, sensorial depression, muscle tremors and sarcopenia. In order to minimise variability related to different instruments used for the analysis of creatinine, increases in creatinine were considered significant if they were twice (>1 mg/dL/day) the suggested value (0.5 mg/dL/day)[4]. Blood-biochemistry profiling, physical and chemical examination of urine and sediment, and abdominal ultrasonography were performed.
An oesophagostomy feeding tube was proposed to all subjects for the administration of the renal diet. All the owners were informed about the potential management and therapeutic benefits resulting from the presence of the feeding tube, the need to perform the procedure under sedation, the possible risks and possible complications[5]. The application of the feeding tube was recommended to all patients, since the potential benefits were considered significantly greater than the risks. Seven owners opted for the application of the feeding tube; the remaining seven preferred a traditional management. The patients were thus divided into two groups, depending on the choice made on whether to use the feeding tube or not.

Feeding tube group

The oesophagostomy feeding tube (FT) was positioned within a maximum of 24-48 hours after the dogs' presentation at our centre. This variability in time depended on whether or not the animals needed to be admitted for correction of dehydration before they could be sedated. The patients (n=7) were sedated and the left side of the neck shaven. An 18 Fr x 41 cm rubber oesophagostomy tube (Kendal ™, Fridley, USA) was used for all subjects. After having prepared the surgical field, curved-end forceps were introduced into the oesophagus through the oral cavity, until their tip reached the middle third of the cervical oesophagus. A blade was used to incise the skin and the tip of the forceps was exteriorised. The end portion of the feeding tube was grasped by the forceps and pulled out from the mouth. This portion was then redirected into the oesophagus in a caudal direction. A new set of sterile gloves was worn and the FT was secured to the skin using Roman sandal sutures (ETHILON® nylon 2 0). The position of the FT was checked by X-ray (lateral-lateral and ventral-dorsal views). The daily calorie requirements were calculated using the formula RER = BW x 30 + 70, where RER is the resting energy requirement and BW is the body weight of the animal in kilograms[6]. The assisted feeding was started 6 hours after the surgical procedure, by administering one-third of the daily requirements. The daily food ration was divided into a minimum of two and a maximum of four daily meals. Each patient was given a renal diet (Purina N/F, wet), blended in a 2:1 ratio with water and administered according to the following scheme: day 1, one-third of the RER; day 2, two-thirds of the RER; and day 3, total RER. At the end of each meal a bolus of approximately 30 mL of water was administered to remove any residual food. All the subjects were discharged from hospital the day after the procedure. The patients were re-evaluated clinically at our centre 1 and 2 months after placement of the FT. Values of the Body Condition Score (BCS), using the nine-point scale, and serum concentrations of creatinine, urea and phosphate were recorded for each patient at the time of the first assessment and at the subsequent controls. The survival time of patients was calculated from the first assessment at our centre (T0) until the moment of death.

Control group

The daily calorie requirements were calculated using the formula RER = BW (kg) x 30 + 70 [6]. Patients could take one of the following diets, depending on individual preference: Purina N/F, Royal Canin Renal, Hill's K/D (dry/wet). It was advised that a minimum of two to a maximum of four meals be given each day, according to the scheme: day 1, one-third of the RER; day 2, two-thirds of the RER; and day 3, total RER. The patients were re-evaluated clinically at our centre 1 and 2 months after the first assessment. BCS values (on a nine-point scale), serum creatinine, urea and phosphate concentrations were recorded for each patient at the time of the first assessment and at the subsequent controls. The survival time of patients was calculated from the first assessment at our centre, until the moment of death.

Medical therapy

The patients in both groups were given anti-emetic therapy (maropitant 2 mg/kg sid), an antacid (ranitidine 2 mg/kg every 12 hours orally), a cytoprotective agent (sucralfate 500-1000 mg/dog every 8 hours orally) and a phosphate chelator (aluminium hydroxide 30-50 mg/kg every 12 hours orally with a meal). For patients in the FT group, dehydration was prevented by integration of an appropriate proportion of free water through the tube. These patients were also treated with an antibiotic (amoxicillin-clavulanic acid 12.5 mg/kg every 12 hours orally) for 1 week, as post-operative prophylaxis. Since it was not possible to increase the voluntary enteral intake of water in the dogs in the control group, fluid (Ringer's lactate) was administered subcutaneously in volumes that varied depending on the degree of dehydration.

Statistical analysis

The BCS values and serum creatinine, urea and phosphate concentrations at T0 and at subsequent intervals (1 and 2 months) were normally distributed (D'Agostino and Pearson's test; alpha = 0.05). The BCS values and creatinine, urea and phosphate concentrations of the animals in the FT and control groups at their first assessment in our centre (T0) and after 1 month (T1) and 2 months (T2) were compared using one-way ANOVA ($p<0.05$).
All patients completed the follow-up until the time of death. The survival times of each subject were calculated and survival rates of the two groups compared using Kaplan-Meier analysis ($p<0.05$).
The data were analysed statistically using GraphPad Prism® (GraphPad Software, La Jolla, CA, USA).

The BCS, creatinine, urea and phosphate concentrations and survival were evaluated at the start of the study and 1 and 2 months later in patients managed with and without assisted feeding.

RESULTS

Fourteen dogs were included in the study (4 spayed females and 10 intact males). The animals ranged in age between 4 and 12 years (mean 9.5 ± SD 3.2 years) and weighed between 10 kg and 36 kg (mean 22.2 ± SD 5.1 kg). As far as concerns breed, five of the 14 subjects were mongrels, and there were two English setters, two Boxers, one Italian hound, one Siberian Husky, one Bull Mastiff, one Australian shepherd dog and one Italian wolfdog.
At the initial assessment the 14 subjects had a mean BCS of 3.5/9 ± SD 1.34 (minimum 2/9, maximum 7/9), mean serum creatinine of 6.21 ± SD 2.52 mg/dL

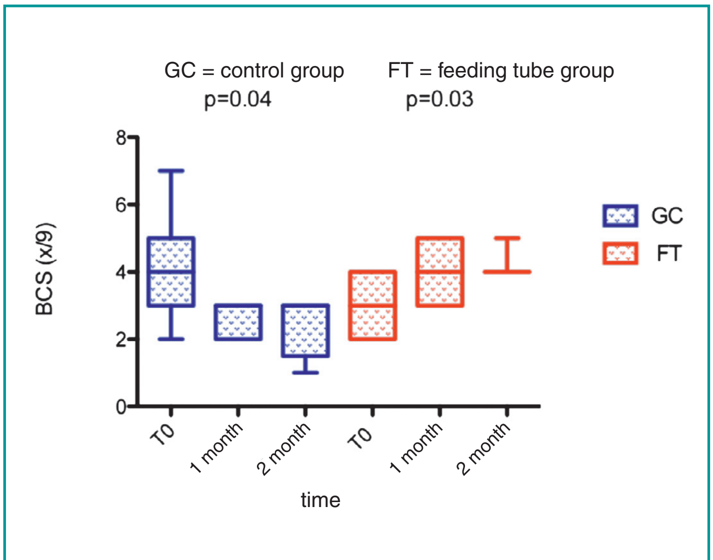

Figure 1 - One-way ANOVA between the BCS values at T0, T1 (1 month) and T2 (2 months) of the subjects in the control group and the FT group.

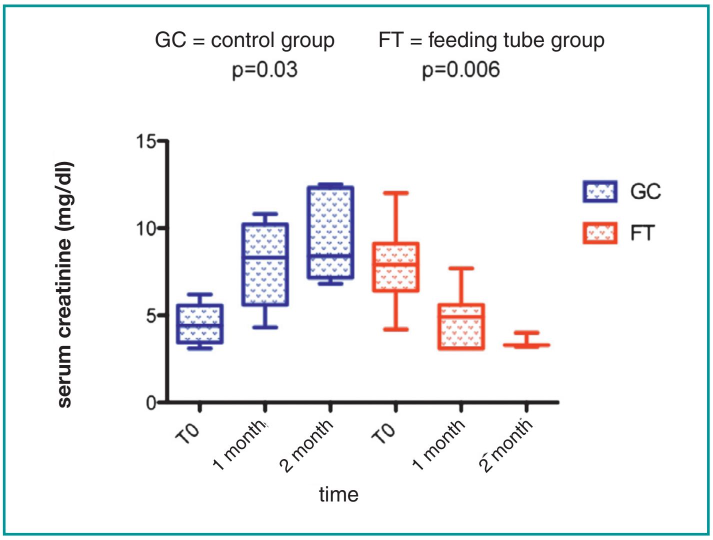

Figure 2 - One-way ANOVA between the serum creatinine concentrations at T0, T1 (1 month) and T2 (2 months) of the subjects in the control group and the FT group.

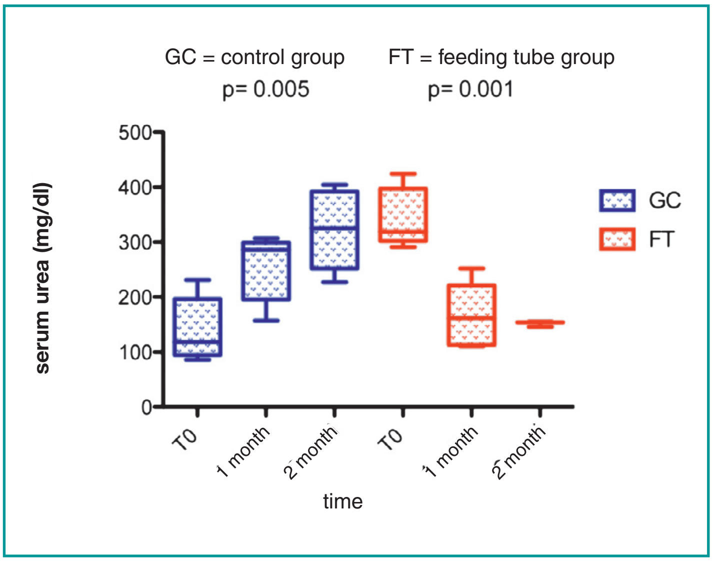

Figure 3 - One-way ANOVA between the serum urea concentrations at T0, T1 (1 month) and T2 (2 months) of the subjects in the control group and the FT group.

(minimum 3.10 mg/dL; maximum 12.00 mg/dL), mean serum urea of 271.40 ± SD 114.20 mg/dL (minimum 86.00 mg/dL; maximum 424.00 mg/dL), mean serum phosphate of 8.43 ± SD 3.69 mg/dL (minimum 4.50 mg/dL; maximum 15.40 mg/dL).

Patients in both groups had statistically significant changes in BCS values (Figure 1), and serum creatinine (Figure 2), urea (Figure 3) and phosphate (Figure 4) between T0, at 1 month (T1) and at 2 months (T2).

At the assessments after T0, some of the patients in the FT group had a variable degree of dehydration (from a minimum of 5% to a maximum of 8%). These patients were rehydrated by increasing the proportion of water given via the FT. In contrast, in patients in the control group, clinical signs of dehydration (from a minimum of 8% to a maximum of 12%) made it necessary to give the animals cycles of crystalloid-based, subcutaneous fluid therapy or, in more serious cases, to resort to intravenous rehydration following hospitalisation. None of the dogs in the FT group were given fluid therapy.

The mean survival of the subjects in the control group was 55.71 ± 20.70 days, compared with 154.30 ± 149.40 days for the animals in the FT group. At 90 days after the diagnosis of the uraemic crisis, 100% of the patients in the control group had died. The maximum survival of patients in the FT group was 480 days (Table 2). Patients in the FT group had a significantly higher survival rate than those in the control group (p=0.01) (Figure 5).

Patients given assisted feeding had significant improvements of BCS, renal function parameters and survival compared to patients in the group managed traditionally.

Table 1 - Mean values ± SD of the BCS and serum creatinine, urea and phosphate concentrations of the subjects in the control group (n=7) and the feeding tube (FT) group (n=7) at different time points (T0, T1 and T2). p values refer to the ANOVA comparing BCS values and serum creatinine, urea and phosphate concentrations of the subjects in the control group (n=7) and the FT group (n=7) at different time points (T0, T1 and T2). *Indicates statistically significant difference (p<0.05)

	Control group				FT group			
	BCS* x/9	Creatinine* (mg/dl)	Urea* (mg/dl)	Phosphate* (mg/dl)	BCS* x/9	Creatinine* (mg/dl)	Urea* (mg/dl)	Phosphate* (mg/dl)
T0	4/9 ± 1.63	4.51 ± 1.15	200.80 ± 117.9	7.33 ± 3.70	3/9 ± 0.81	7.91 ± 2.39	342.0 ± 52.23	9.54 ± 3.62
T1 (1 month)	2.5/9 ± 0.53	7.69 ± 2.16	317.0 ± 135.8	15.33 ± 8.47	4/9 ± 0.81	4.87 ± 1.61	172.0 ± 57.38	5.80 ± 1.02
T2 (2 months)	2.4/9 ± 0.89	9.46 ± 2.65	322.6 ± 32.5	14.82 ± 2.90	4.3/9 ± 0.57	3.50 ± 0.43	151.7 ± 4.93	5.13 ± 1.05
P value	0.04	0.001	ns	0.04	0.03	0.006	0.0001	0.02

DISCUSSION

At T0 all patients in the study had serum concentrations of creatinine and urea well above the normal reference ranges. These patients presented with clinical and pathological changes and symptoms typical of uraemic syndrome, such as severe azotaemia, hyperphosphataemia, vomiting, dejection and uraemic halitosis.

At the follow-up assessments after T0, the serum creatinine, urea and phosphate concentrations increased significantly in patients in the control group, while their BCS decreased. In contrast, in patients in the FT group, the creatinine, urea and phosphate levels, although remaining above the reference range, decreased significantly after T0, while the BCS increased significantly over time. These differences could be explained by the higher prevalence of hypercatabolism and malnutrition[7] among patients in the control group. Indeed, the increases in the mean concentrations of urea and creatinine in the control group were accompanied by a significant decrease in the BCS, which could have been secondary to the inability of these patients to assume an adequate amount of the renal diet. In fact, a significant association was previously demonstrated, in dogs with different International Renal Interest Society (IRIS) stages of CKD, between a reduction of BCS and shortened survival[8]. Although a renal diet was recommended for the subjects in both groups, none of the patients in the control group was able to meet its energy needs completely and the owners were often forced to administer other types of non-renal food and/or human food to encourage assumption of the renal diet. In addition, as the weeks passed, most of the subjects in the control group became unable to eat any kind of food voluntarily and the owners were compelled to blend the renal diet with water and to administer it forcibly by mouth using a syringe. Even when this was done, none of the subjects was able to assume the amount of the diet necessary to meet its needs.

As the weeks passed, the animals in the control group had decreasing capacity to eat amounts of the renal diet sufficient to cover their needs.

In contrast, the patients in the FT group had a significant increase of BCS over time. In these patients the BCS increased compared to the initial value already by 1 month and tended to remain stable over time. This reflects a greater ability of the subjects in the FT group to maintain an adequate nutritional status, limiting the negative effects of hypercatabolism and malnutrition on residual renal function.

In the control group the creatinine concentration increased significantly with time, reaching double the T0

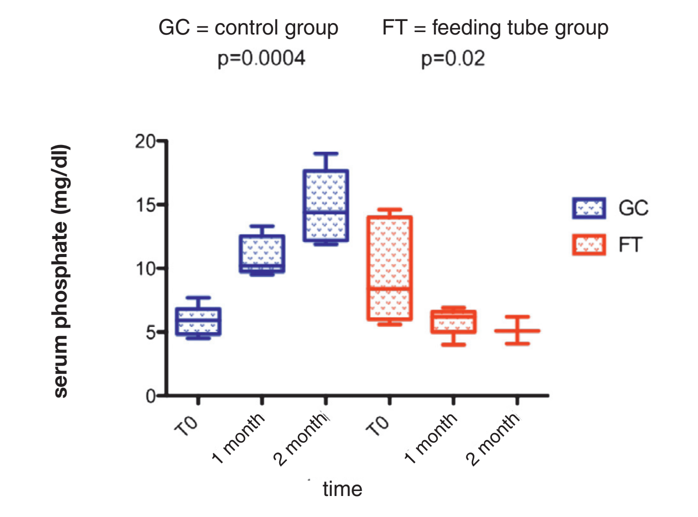

Figure 4 - One-way ANOVA between the serum phosphate concentrations at T0, T1 (1 month) and T2 (2 months) of the subjects in the control group and the FT group.

Table 2 - Percentage survival of patients in the control group and the feeding tube (FT) group at different time points.

Day	% survival control group	% survival FT group
30	71.49 %	100 %
60	14.28 %	57.14 %
90	-	57.14 %
120	-	42.85 %
150	-	14.28 %
480	-	-

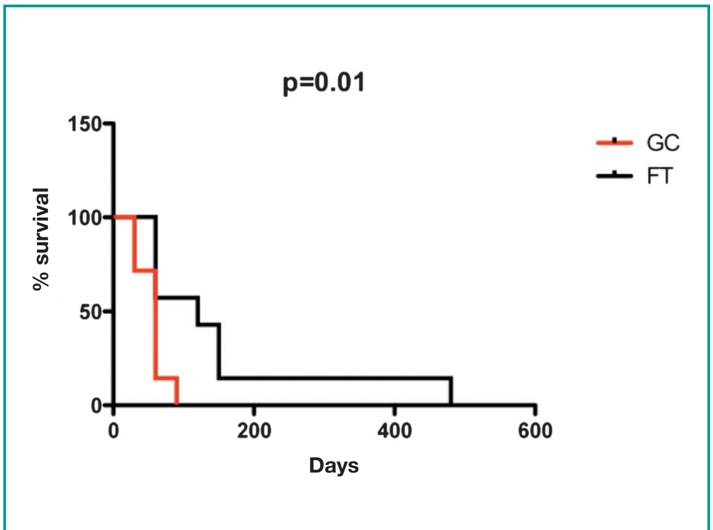

Figure 5 - Kaplan-Meier survival curves of patients in the control and FT groups. The FT patients had a significantly higher survival rate than that of animals in the control group (p=0.01).

value by 2 months. In the FT group, on the contrary, the creatinine level decreased significantly. This difference could have a multifactorial origin. One of the causes of the increased creatinine in the control group could have been the higher prevalence of dehydration in these patients. The animals in the FT group had a better state of hydration than those in the control group since the FT was used not only for the administration of food, but also for integration of free water. In the control group, however, it was not possible to increase the proportion of water supplied enterally. These patients had to be administered crystalloid solutions subcutaneously. In the more severe cases, the animals were admitted to hospital and given intravenous rehydration. Patients with CKD primarily need rehydration of the intracellular compartment through free water. The use of crystalloids with a high sodium chloride content can contribute to aggravating a pre-existing state of hypertension and result in the formation of peripheral oedema[9].

The different trends of creatinine and urea concentrations in the two groups could be secondary to a different capacity to control factors that cause progression of CKD, such as hyperphosphataemia. In the control group the increase in creatinine was associated with a significant increase in phosphataemia. Contrariwise, in the FT group, the phosphate concentration decreased compared to that at T0, in agreement with reports in the literature, according to which the intake of an appropriate amount of a renal diet significantly reduces the uraemic syndrome and lowers the risk of death[1,5]

The decrease in blood phosphate levels in the FT group may also have been the consequence of a more effective delivery of the phosphate chelator. In the FT group aluminium hydroxide was mixed with the daily food ration, and administered with each meal. All drugs were delivered via the FT, so doses and dosing intervals were controlled precisely, unlike in the control group, in which the reluctance of the patients to take food spontaneously made accurate administration of the drugs more complex.

The subjects in the FT group also had a significantly higher survival rate than controls. The median survival of the FT group was 154.30 ± 149.40 days, compared to 55.71 ± 20.70 days for the control group. Although there was a large variability of survival within the group, as indicated by the standard deviation, the data show that at 90 days about 60% of subjects in the FT group were alive, whereas none of the patients in the control group was still alive at 90 days. It is also interesting to note that use of a FT during uraemic syndrome was positively associated with greater long-term survival. In fact, in the FT group the survival rates at 120 and 150 days were 42.85% and 14.28%, respectively.

None of the animals in which the FT was used showed post-insertion problems (infections at the suture site, displacement, poor initial placement). In our experience, the development of infections at the suture site is extremely rare if the device is introduced in a sterile manner and if antibiotic cover is provided for the first 7-10 days. In particular, unpublished experience has highlighted the importance of changing gloves, after having redirected the FT caudally in the oral cavity, in reducing the occurrence of infections at the suture site. In our opinion, displacement of a FT appears to be more common when using silicone tubes, rather than rubber ones. Poor positioning is a complication that can be identified and resolved easily by performing a chest X-ray after placing the FT. Post-placement radiography (latero-lateral and ventral-dorsal) is indispensable and should always be carried out to check the correct position of the tube.

The findings of this study seem to support the role of the FT as a significant therapeutic aid for patients with uraemic syndrome. The use of a FT appears to allow easier and more accurate management of drug therapy. Although the FT is primarily a therapeutic aid to ensure the intake of an adequate quantity of a renal diet of appropriate quality, it is also used as a route of administration for drugs and free water. In addition, certain medications (such as phosphate and potassium chelators) are not available for parenteral use and their forced oral administration may result in reduced bioavailability or complications, such as aspiration pneumonia. Patients with CKD and uraemic syndrome require multiple drugs, which can be very difficult to administer to animals with decreased appetite.

The use of a feeding tube in patients with uraemic syndrome seems to be associated with improvements of the BCS, renal function parameters and survival.

Main limitations of the study:

One of the main limitations of this study is the small number of subjects assessed. An expansion of the cohort would be desirable in order to obtain a more accurate evaluation of the magnitude of the differences between the two groups of subjects in terms of BCS, serum creatinine, urea and phosphate concentrations and survival. It would be also very interesting to evaluate changes in other parameters of malnutrition, such as albumin. Unfortunately, being a retrospective study involving owned dogs, it was not possible to get a full profile of examinations at each assessment. Further-

more, it should be pointed out that patients with CKD and uraemic syndrome constitute a pool of particularly unstable patients and they may progress rapidly towards renal failure and death. This may be the reason for the lack of follow-up after 90 days in the control group. The absence of subjects (because they had all died) in the assessments after 90 days in the control group did not permit the use of the initially selected statistical tests and is an objective limitation of this study.
Finally, it cannot be ruled out that the owners of the dogs in which a feeding tube was used were more motivated than the others and, therefore, that they also had a greater propensity to follow the medical recommendations.

KEY POINTS

- Dietary therapy is the first therapeutic strategy in patients with acute kidney injury and chronic kidney disease, but such patients are often unable to assume a sufficient quantity of the diet.
- BCS value, creatinine, urea and phosphate concentrations and survival rate were compared in a group of patients with uraemic syndrome given a renal diet via a feeding tube and in a comparable group of patients given a renal diet without the assistance of a feeding tube.
- The use of a feeding tube was associated with significant improvements of the BCS, renal function parameters and survival.
- A feeding tube seems to be a valuable aid in the dietary and therapeutic management of patients with chronic kidney disease.

Alimentazione tramite sonda esofagostomica nel paziente affetto da malattia renale cronica in crisi uremica: effetti su BCS, funzionalità renale e sopravvivenza

Introduzione e Scopo del Lavoro -. La dietoterapia rappresenta il primo strumento terapeutico nel paziente in danno renale acuto e malattia renale cronica. Tuttavia la maggior parte di tali pazienti non è in grado di assumere volontariamente il quantitativo adeguato ai propri fabbisogni. Obiettivo del presente studio è di valutare BCS, parametri di funzionalità renale e sopravvivenza in pazienti in crisi uremica sottoposti o meno ad alimentazione assistita.
Materiali e Metodi -. Quattordici cani con pregressa CKD e in fase di riacutizzazione o scompenso. Sette pazienti sono stati gestiti mediante impiego di feeding tube (FT), 7 mediante terapia medica tradizionale (GC). Per ciascuno dei due gruppi, BCS, creatinina, urea, e fosforo sierici e sopravvivenza, sono stati valutati a T0 e ad uno (T1) e due mesi (T2). I dati sono stati elaborati statisticamente.
Risultati -. Il GC presentava una differenza significativa di BCS (p=0.04), creatinina (p=0.001), urea (p=0,005) e fosforo (p=0.04) a diversi controlli. Il FT presentava una differenza significativa di BCS (p=0.03), valori sierici di creatinina (p=0.006), urea (p=0.0001) e fosforo (p=0.02) ai diversi controlli. Il FT mostrava una sopravvivenza alla crisi uremica maggiore (p=0.01) del GC.
Discussione - Le evidenze del presente studio riportano un significativo miglioramento di BCS, parametri di funzionalità renale e sopravvivenza nei pazienti gestiti con feeding rispetto agli altri. Il feeding tube sembra rappresentare un ausilio terapeutico estremamente utile nella gestione medica del paziente in crisi uremica.

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