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Practical issues of nutrition during continuous renal replacement therapy

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Abstract

Continuous renal replacement therapy (CRRT) in critically ill patients has significant impact on one's ability to provide efficient nutritional therapy. CRRT may help in the prevention of intestinal oedema and the maintenance of the proper function of the gastrointestinal tract by enabling strict control of the fluid balance. It facilitates early introduction of nutrition via the enteral route, as well as allowing for the composition of high-volume feeding mixtures. It is necessary to take into consideration that during CRRT, together with blood purification of toxic substances, nutritive elements are also eliminated to some extent (micro- and macronutrients). In this article, the authors discuss the impact of CRRT on nutritive elements loss, energetic balance and present the principles of adjusting feeding prescriptions to changes implied by CRRT.

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Nutritional therapy is one of the basic elements of the multifaceted treatment of patients in intensive care units (ICUs). The Nutrition Day ICU survey, based on a seven-year observation period of nutritional practices in 880 units from 46 countries, has demonstrated that the majority of ICU patients do not receive the recommended amounts of calories and proteins [1]. According to the findings of this survey, as well as of some other studies, an increasing energy-protein deficit is positively correlated with prolonged ICU stay, which in turn increases the risk of infections and death. On the other hand, it should be clearly emphasised that an excessive energy supply may also be associated with complications and increased mortality [1, 2]. Adequate tailoring of nutritional therapy is a great challenge; firstly, because the nutritional status of patients on admission to an ICU can differ markedly, ranging from cachexia to morbid obesity while secondly, the critical conditions presented by patients have extremely relevant metabolic implications. Unfortunately, the majority of studies that are the basis for guidelines of nutritional therapy are observational or involve small groups of patients and are therefore characterised by low precision and relatively high changeability over time.

Several randomised controlled studies have recently been published which have re-started the discussion on optimal nutritional practices in the ICU setting. One of the issues inadequately described and connected with nutritional therapy in ICU patients, concerns the effects of other elements of the multifaceted treatment of critically ill patients on the efficacy of nutritional interventions. It should be clearly stressed that continuous renal replacement therapy (CRRT) belongs to those interventions which most highly affect the outcomes of nutritional therapy in critically ill pa-

tients. Firstly, the use of CRRT facilitates optimal nutritional therapy by directly modifying the fluid balance of patients. This method enables the easy maintenance of a neutral and negative fluid balance. Thus, nutritional mixtures of a wide-ranging osmolarity, hence volume, can be prepared. Secondly, the introduction of CRRT can significantly reduce the formation of intestinal wall oedema, mainly associated with massive fluid resuscitation in the initial period of treatment of septic shock or during intensified systemic inflammatory response syndrome. The effects of CRRT on fluid balance described above can help in early initiation (up to 48 h) of enteral nutrition, which is recommended in the guidelines of many scientific societies (i.e. *European Society for Nutrition and Metabolism* [ESPEN], *American Society for Parenteral and Enteral Nutrition* [ASPEN], *International Symposium on Intensive Care and Emergency Medicine* [ISICEM]). The initiation of CRRT can also reduce the existing oedema, thus favourably affecting gastrointestinal motorics and the ability of absorbing nutrients administered enterally, which is the preferable route in ICU patients. On the other hand, since the majority of nutrients have the molecular weight smaller than the cut-off point of filters used in CRRT, substantial amounts of amino acids, vitamins, micro- and macroelements are lost during treatment. The studies carried out in the last decade demonstrate a positive correlation between the intensity of CRRT (clearance obtained during the procedure) and increased losses of nutrients; the differences among various types of renal replacement techniques were mostly statistically non-significant. Although much bigger differences were expected in clearances of electrolytes, a recent study by Bellomo *et al.* [acc. 3] has not shown significant differences between the techniques based on diffusion and convection. At present, there are no data concerning the effects of filters of higher adsorptive capacity or the high cut-off point on the loss of nutrients during CRRT procedures [3, 4].

The above findings clearly reveal that since the CRRT procedure significantly affects the supply of nutrients in critically ill patients, this kind of therapy should be considered in terms of energy-protein requirements.

ENERGY REQUIREMENTS IN PATIENTS UNDERGOING CRRT

Both an insufficient and excessive supply of calories in the population of ICU patients can lead to an increased incidence of complications and higher mortality rates. The energy requirements of critically ill patients depend on their nutritional status, the intensity of their disease and metabolic stress, complications emerging during intensive treatment and the intensity of renal replacement therapy. It should be remembered that catabolism markedly exceeds anabolism during the initial stage of a severe disease, which results from the neurohormonal response of the body to trauma and leads to enhanced tension of the sympathetic system. In the catabolic phase, hormones such as adrenaline, glucogen and cortisol are also secreted while the effects of anabolic hormones are altered into catabolic effects, as in the case of growth hormone. Additionally, the catabolic phase of a severe disease is characterised by insulin resistance and increased gluconeogenesis, which results from the necessary provision of an adequate glucose supply, mainly to the CNS neurons. Glucose deficiency in the acute stage of shock, which increases gluconeogenesis, results predominantly from rapid depletion of the reserves of this substrate stored as glycogen in the liver and muscles. In such cases, amino acids become an alternative substrate for production of glucose; they are liberated due to decomposition of proteins of the skeletal muscles which results in a loss of muscle mass by about 1% per day. It should be emphasised that the nutritional intervention implemented in the catabolic state of a severe disease can slow down the loss of muscle mass having no effect on an increase in catabolism. Moreover, the excessive supply of energy substrates should be absolutely avoided in the catabolic state, as this kind of management has no beneficial effects on increased metabolic stress and can generate adverse effects, such as hyperglycaemia, hypertriglyceridaemia, hypercapnia with a resultant increase in respiratory work, metabolic acidosis, hepatic steatosis or overhydration. Considering the above, the interruption of the catabolic phase is not feasible via the increased transport of energy while the only measure to limit its adverse consequences is optimal intensive therapy and treatment of the underlying disease. Of note is that when the convalescence stage begins, the requirements for energy and nutrients significantly increase, often exceeding the pre-disease values. This is extremely significant as insufficient nutrition during the anabolic phase can markedly delay an improvement in the patient`s general condition, both during ICU treatment and rehabilitation.

In critically ill patients undergoing CRRT, energy requirements are estimated according to generally accepted rules which have been elaborated for a broad population of patients. The majority of guidelines recommend indirect calorimetry, considered to be the gold standard. Indeed, the TICACOS study has confirmed that indirect calorimetry is superior to formula-based calculations [5]. The authors have demonstrated that in the group of patients whose energy requirements were calculated using formulae, the incidence of complications was higher and the duration of substitutive ventilation, as well as ICU treatment was longer. Unfortunately, despite the unquestionable benefits of indirect calorimetry, its use is problematic in the population of critically ill patients. Firstly, indirect calorimetry calculations of energy requirements are poorly disseminated in ICUs, which predominantly results from the difficulties in interpre-

tation of results, especially in cases of strong metabolic stress in the acute phase of a severe disease. Secondly, as during extracorporeal therapies, patients should be protected against overcooling, fluids or/and blood have to be warmed. During the warming of fluids containing bicarbonates, CO_2 is released both in the system of extracorporeal circulation drains and in the blood of patients. This means that during CRRT the expiratory concentration of CO_2 increases, which does not result from increased metabolism. Thus, the phenomenon described above can falsify the results of measurements. Therefore, some clinicians suggest to carry out measurements during intervals in CRRT procedures, which, for obvious reasons, is likely to adversely affect the efficacy of treatment by reducing its intensity [6].

The Nutrition Day ICU survey has revealed that the most common method to estimate the energy requirements in critically ill patients is to calculate them based on the ideal body weight (IBW) [1]. The target amount of kilocalories calculated for IBW should be 25–35 kcal kg^{-1} day^{-1}, while the energy supply in the initial stage of increased catabolism should be about 30% of the value obtained (10 kcal kg^{-1} day^{-1}); the target values should be achieved only after transition to the anabolic phase during which the energy supply should be similar to the maximum value (35 kcal kg^{-1} day^{-1}), which should favour intensive rehabilitation. It should be remembered that the energy supply calculated based on the Harris and Benedict equation should be corrected with an appropriate coefficient, whose value depends, among other things, on the use of CRRT. The correction coefficient for a patient during CRRT ranges from 1.1 to 1.2, which reflects increased energy requirements. The above recommendation results from the fact that the majority of dialysis or substitutive fluids widely used in Poland contain glucose in a concentration of 5.5 mmol L^{-1}, which translates into hypoglycemising action and adversely affects the patient's energy balance. Additionally, the patient's energy balance can be impaired by unintended hypothermia during CRRT, which is most commonly associated with insufficient warming of the substitute or dialysate. When fluids are not warmed during the procedure, the energy requirements can increase by even 1000 kcal day^{-1}, which results directly from the initiation of thermogenesis and increased oxygen needs. Therefore, when the warmers incorporated into the CRRT system are found to be ineffective, the external warming of patients should be started to maintain a core body temperature of above 37°C.

When the patient`s energy supply is estimated, we should consider the effects of regional trisodium citrate anticoagulation on energy balance (5 millimoles of metabolised citrate supplies, about three kilocalories), as well as the additional sources of energy present in the dialysis fluids. When dialysis fluids containing only trisodium citrate are used, the additional energy supply does not exceed 200 kcal day^{-1} — hence, its effect on the patient's energy balance is slight. Additionally, the amount of energy supplied with citrates balances the negative effects of CRRT on the supply of energy substances, associated with the loss of amino acids and glucose. Unlike the majority of dialysis fluids, the ACD-A contains not only citrate but also glucose and lactates; therefore, its use is associated with the risk of an increased supply of calories as the basic energy load can reach the values exceeding 1,500 kcal during 24 hours of treatment.

Despite the issues concerning optimal energy supply during CRRT described above, it seems that the biggest problem still is not the inability to supply energy in the amounts recommended by nutritional societies but the lack of nutritional interventions. As mentioned earlier, the most common method of estimating energy requirements in critically ill patients is to calculate them based on the ideal body weight. According to many authors, the target amount of calories which should be supplied is 25–35 kcal kg IBW^{-1} day^{-1}. Moreover, the recommended proportions of energy substrates are 60 % of carbohydrates and 40% of triglycerides. Although an energy supply lower than 10 kcal kg IBW^{-1} day^{-1} is obviously associated with increased mortality, recent studies have demonstrated that a supply of calories lower than the one recommended, i.e. 15–20 kcal kg IBW^{-1} day^{-1}, is not connected with adverse consequences, such as prolonged time of mechanical ventilation, prolonged ICU stay or increased 28-day mortality. Additionally, a reduced supply of energy was demonstrated to decrease the insulin requirements and to facilitate stabilisation of blood glucose levels [7]. It should be stressed that hypocaloric nutrition can be beneficial only when the supply of proteins is adequate to their requirements (at least 1.5 g kg IBW^{-1} day^{-1}).

AMINO ACID REQUIREMENTS IN PATIENTS DURING CRRT

Critically ill patients are characterised by an extremely high intensification of metabolic stress and catabolism, which leads to muscle mass losses. Increased decomposition of proteins of the skeletal muscles results from rapid depletion of energy reserves, stored as glycogen in the liver and muscles, thus from the necessity to supply glucose, mainly to the central nervous system. During the acute phase of a severe disease, amino acids become the source of glucose in the process of gluconeogenesis, thus becoming an energy substrate. According to estimates, the loss of amino acids associated with decomposition of proteins of the skeletal muscles during the catabolic phase can be 1.3 to 1.8 g kg IBW^{-1} day^{-1} and mainly depends of the intensity of catabolism. Of note is the fact that it is not possible to reduce the intensity of protein decomposition by increasing the supply of amino acids during nutritional interventions. It

should be remembered that apart from the adverse effects on nitrogen balance, the acute phase of a severe disease also affects the synthesis and metabolism of amino acids; therefore, non-essential amino acids (tyrosine, arginine, glutamine, cysteine, serine, ornithine, citrulline) can become conditionally essential.

Amino acids are the molecules of a relative low molecular weight, ranging from 89 Da for alanine to 214 Da for tryptophan. Therefore, the loss of amino acids during CRRT procedures is substantial. A study by Scheinkestel *et al.* (8), which included 50 patients receiving parenteral nutrition, has shown that during continuous veno-venous haemodialysis (CVVHD) (blood flow rate: 100–175 mL min^{-1}, dialysate flow rate — 2 L h^{-1}), 17% of amino acids administered intravenously are lost on average (range 13–24%). Tyrosine was proved to be the amino acid particularly susceptible to migration into the ultrafiltrate and its loss during the procedure was estimated at 87% of the administered dose. It is worth emphasising that the study mentioned above has demonstrated a positive correlation between the total dose and the extent of amino acid loss during CRRT. Moreover, according to the study findings, the mean mass of amino acids migrating into the ultrafiltrate was 0.2 g L^{-1}. In critically ill patients undergoing CRRT procedures, an increase in protein supply should be considered during nutritional interventions; firstly, due to increased loss with the ultrafiltrate; secondly, because an increase in protein supply to values exceeding 1.5 g kg IBW^{-1} day^{-1}, can have beneficial effects on prognosis. The current ESPEN guidelines recommend protein supply in a dose of 1.5 g kg IBW^{-1} day^{-1} in critically ill patients during intensified metabolism; when CRRT is introduced, this dose should be increased by 0.2 g kg IBW^{-1} day^{-1} [3]. The 2016 ASPEN guidelines recommend the daily supply of proteins in critically ill patients in the amount of 2 g kg^{-1} bw^{-2}. Interestingly, although the neutral nitrogen balance in this population was obtainable after the use of very high doses of amino acids (up to 2.5 g kg IBW^{-1} day^{-1}), it has not be determined yet whether the prognosis can be beneficially affected in this way. It is definitely not recommended to reduce the dietary protein intake in order to avoid or delay the introduction of renal replacement therapy. It should be stressed that increased supply of proteins in critically ill patients is not identical to increased supply of energy [9]. This means that the Q coefficient, defined as a ratio of supply of extra-protein calories (kcal) to nitrogen (g), should be maintained at a relatively low level (even below 100) in order to prevent complications associated with excessive energy supply (see above). A study by Rugeles *et al.* [7] has demonstrated that a reduction of energy supply from 25 to 15 kcal kg IBW^{-1} day^{-1}, at a protein dose of 1.7 g kg IBW^{-1} day^{-1}, facilitated strict control of glycaemia without adversely affecting prognosis.

The optimal qualitative composition of proteins which should be administered to critically ill patients is the subject of extensive ongoing studies. Many of these studies concern glutamine, as its low concentration in blood positively correlates with increased mortality rates in critically ill patients. As glutamine is an amino acid synthesised mainly in the skeletal muscles, the loss of muscle mass during hypercatabolism reduces its synthesis, which can impair the function of immune cells, enterocytes and hepatocytes. A meta-analysis carried out by Novak *et al.* [10], which involved 485 patients, has demonstrated that supplementation of glutamine can reduce the incidence of infections, shorten hospital stays and decrease mortality rates. Considering the above, the authors of the 2009 ESPEN guidelines recommended the supplementation of alanyl-glutamine dipeptide during parenteral nutrition in a dose of 0.3–0.6 g kg IBW^{-1} day^{-1}, especially when renal replacement therapy is administered. Unfortunately, the results of the studies published after the publication of ESPEN guidelines have not confirmed the benefits resulting from the supplementation of glutamine. Although the SIGNET study, involving 500 patients receiving parenteral nutrition, set out to evaluate the effects of glutamine supplementation on treatment outcomes, the authors failed to show the beneficial effects of glutamine, which was used in the doses of 0.1 to 0.2 g kg IBW^{-1} day^{-1} [11]. Moreover, the REDOX study assessed the efficacy of high enteral glutamine doses (0.6 to 0.8 g kg IBW^{-1} day^{-1}) as supplementation of parenteral nutrition. Increased symptoms of multiple organ failure and higher mortality rates were found in the group of patients receiving glutamine [12]. The above-mentioned reports resulted in a limitation of indications for glutamine supplementation in patients in shock and with multiple organ failure [13]. It appears that when the decision to supplement glutamine has to be taken, the best solution would be to determine its concentrations in the blood; however, there are no studies confirming the efficacy of this management.

REQUIREMENTS FOR LIPID EMULSIONS IN PATIENTS DURING CRRT

In the course of acute kidney injury (AKI), the activity of hepatic lipase and lipolysis are impaired, which leads to increased contents of triglycerides in lipoproteins and reduced HDL cholesterol fraction. Additionally, impaired metabolism of triglycerides leads to their accumulation in the body, which at a reduced clearance of fatty substances can result in hypertriglyceridaemia, particularly in patients fed parenterally. The use of CRRT does not significantly affect lipid disorders in AKI as the high molecular weight of lipids prevents their effective permeation through the dialyser membrane, irrespective of whether the techniques applied are based on convection or diffusion. It should be

remembered that in the ICU setting, lipid emulsions are administered not only as an integral part of the nutritional intervention but also as suspensions of drugs, such as propofol and etomidate, among others. In cases of continuous infusion of propofol, the lipid emulsion contained within can cover even a third of daily lipid requirements. Unlike fatty substances, L-carnitine, an amino acid indispensible for the utilisation of fatty acids in the mitochondria, is increasingly lost during CRRT, which can additionally increase the accumulation of lipids in critically ill patients. At present, there are studies demonstrating beneficial effects of L-carnitine substitution on lipid metabolism during CRRT. Although it appears that L-carnitine deficiencies could be balanced by the supply of medium chain triglycerides as their metabolism does not require the presence of this amino acid, there are no studies confirming this hypothesis. Therefore, the blood concentrations of triglycerides should be monitored in AKI patients undergoing CRRT, mainly to prevent hypertriglyceridaemia. It is worth emphasising that lipids may be responsible for accelerated blockage of haemofilter capillaries (high molecular weight), which can lead to accelerated clotting in the filter, particularly in cases of anticoagulation with unfractionated heparin. This adverse impact of lipids on the dialyser survival time is less pronounced when local citrate-based anticoagulation is applied [14].

The effects of unsaturated fatty acids on functioning of the immune system depend on the location of a double bond of their molecules. Omega-3 acids are associated with anti-inflammatory effects, omega-6 acids with pro-inflammatory impact while omega-9 acids are described as the most immunologically neutral. Since patients with symptoms of acute respiratory distress syndrome are found to have lower blood concentrations of omega-3 acids, attempts have been made to use the nutritional mixtures with increased contents of these acids in this population. The findings of initial studies have confirmed reduced mortality rates and shortened ICU stays when modified diets are used. Unfortunately, the most recent study based on the largest number of patients (OMEGA) has not confirmed the benefits described above. Additionally, the authors have demonstrated that the use of a diet containing large amounts of omega-3 acids is associated with prolonged mechanical ventilation and prolonged ICU treatment duration. Likewise, the benefits connected with increased supply of omega-9 acids have not been proven. There are still no high-quality data that can be used to formulate guidelines recommending the increased supply of any fatty substances [15].

ELECTROLYTES

The incidence of hypokalaemia in patients undergoing renal replacement therapy is 5-25% [3]. The condition is most commonly caused by the use of fluids low in potassium for correction of hyperkalaemia. In cases of blood potassium levels < 3 mEq L^{-1}, the risk of ventricular fibrillation substantially increases while rapid correction of the deficiency also increases the mortality [16]. Therefore, fluids with normal amounts of potassium are preferable during CRRT while fluids without potassium or those low in potassium should be used only for life-threatening hyperkalaemia.

The content of sodium ions in the substitutive/dialysis fluid is 140 mEq L^{-1} (in fluids for citrate anticoagulation — 133 mEq L^{-1}, yet this deficiency is supplemented via the supply of sodium citrate also containing up to about 140 mEq L^{-1}). Therefore, CRRT has stabilising effects on blood concentrations of sodium in patients with normonatraemia. In patients with hyper- and hyponatraemia, CRRT normalises the concentration of sodium with the rate dependent on the procedure intensity. For patients with chronic or sub-acute dysnatraemia, a too-rapid correction of the sodium concentration can lead to lethal consequences (brain oedema in hypernatraemia, acute pontine demyelination or subarachnoid haemorrhage in cases of hyponatraemia). The rate of changes in plasma sodium concentrations should not exceed 0.5 mmol L^{-1} h^{-1} , 2 mmol L^{-1} 6 h^{-1} and 8 mmol L^{-1} day^{-1}. Therefore, the procedure intensity should be adjusted to the dynamics of changes; when this is not possible, the concentration of sodium in the substitutive fluid/dialysate should be increased for correction of hypernatraemia or additional intravenous supply of low-sodium fluid should be started in cases of hyponatraemia.

The incidence of hypophosphataemia during CRRT is high and ranges from 10.9 to 65% [3]. Once the fluids containing physiological concentrations of phosphates have been introduced, its incidence substantially decreases. Phosphates are involved in many vital functions, such as enzymatic processes, oxygen transport, intracellular energy turnover, while their deficiency can have relevant clinical implications. Therefore, determinations of blood phosphate concentrations should be suitably frequent (a minimum of once a day), especially when phosphate-free fluids are used. In such cases, additional substitution of phosphates is necessary, either by commercially available preparations (Addiphos®, Glycophos®) for enteral feeding or their doubled supply for parenteral feeding. Special attention should be paid to patients at risk of re-feeding syndrome; in this group phosphate concentrations in plasma should be determined even 3 times a day until the risk of this syndrome has subsided.

Hyperphosphataemia is rare during CRRT and requires an increased intensity of the procedure or phosphate-free fluids. Phosphates are predominantly located intracellularly

in the human body. Therefore, persistently increased concentrations of phosphorus despite CRRT may be a marker of massive cell necrosis (e.g. intestinal ischaemia) [3].

Hypomagnesaemia is relatively rarely observed during CRRT (< 3%). It occurs more commonly during regional anticoagulation with citrates, which bind not only calcium ions but also magnesium ions [17]. The citrate-magnesium complexes are eliminated on the haemofilter, increasing the pool of lost magnesium. This phenomenon can be compensated by an increase in magnesium concentration in dialysis/substitutive fluids or by an additional intravenous supply of 2–4 g day^{-1} of magnesium sulphate. Commercially available fluids for citrate anticoagulation (without calcium) contain higher concentrations of magnesium (0.75 mmol L^{-1}), as compared with the fluids containing calcium, thus the loss of magnesium with citrates is almost fully compensated. In the fluids containing calcium, the concentration of magnesium ions is slightly lower that which is physiological (0.5 mmol L^{-1}).

Hypocalcaemia is relatively common during CRRT with, in some series of cases, up to 50% of patients being affected [3]. According to a 2016 meta-analysis, hypocalcaemia was more common in cases of citrate-based anticoagulation [18]. Due to immobilisation, the bones of critically ill patients undergo demyelination while the additional pool of calcium ions is liberated to blood. This pool can mask the insufficient supply of calcium, both in diets and during substitution in regional anticoagulation. The above-mentioned phenomenon is particularly dangerous in patients bedridden for a long time as it can lead to pathological fractures. Therefore, blood concentrations of ionised calcium should be frequently monitored in order to prevent its decrease below 1 mmol L^{-1}. It seems that strict adherence to protocols during regional anticoagulation and taking care of the reliability of laboratory determinations of ionised calcium concentrations should allow one to reduce the incidence of hypocalcaemia.

TRACE ELEMENTS

In the majority of critically ill patients, the concentration of trace elements in plasma is reduced, which results from numerous causes, including the following: redistribution between the plasma and tissues; reduced concentration of albumins; loss of body fluids; haemodilution; an already reduced initial concentration; insufficient dietary intake; impaired absorption; and loss during renal replacement techniques. The optimal dose of multi-ingredient preparations of trace elements has not been determined yet. It is assumed that in order to equalise the CRRT-associated loss, the daily dose should be doubled or even tripled (according to some authors) using intravenous preparations, also in patients fed enterally [3].

Considering the antioxidative effects of selenium and zinc, the impact of their additional supplementation on the survival of critically ill patients and the duration of ICU treatment has been studied. However the study findings are inconsistent. While some studies demonstrate evident benefits, other have found no effects while there are also study findings demonstrating negative effects of additional supplementation. This may result from differences in populations, different routes of administration, as well as different times and doses of additional supplementation. It has not been explicitly determined when the additional supply of antioxidative microelements can be beneficial for patients [19].

VITAMINS

Water-soluble vitamins are extensively lost during CRRT. Their supplementation suggested by ESPEN is as follows: 100 mg of vitamin B_1 (thiamines); 2 mg of B_2; 20 mg of B_3; 10 mg of B_5; 100 mg of B_6; 200 µg of biotin (vitamin B_7); 1 mg of folic acid (B_9); 4 µg of B_{12}; and 250 mg of vitamin C. As the content of some vitamins (thiamine, folic acid, vitamin C) in the available multi-vitamin preparations is markedly lower than that recommended, they should be additionally supplemented during CRRT. On the other hand, the long-term administration of vitamin C in the doses exceeding the recommended level in patients with kidney injury can lead to nephrotoxic secondary oxalosis. Despite poor elimination via renal replacement techniques, fat-soluble vitamins should also be additionally supplemented (except for vitamin A). The daily supply of vitamin E during CRRT should be 10 IU day^{-1} and of vitamin K — 4 mg $week^{-1}$. Due to reduced breakdown of retinol in patients with acute kidney injury, additional supplementation of vitamin A is required. It is extremely difficult to observe the above-mentioned recommendations based on complex preparations of vitamins. A safe solution may be to double the daily vitamin dose during CRRT. However, it should be remembered that there are no data proving the beneficial effects of an increased supply of vitamins during CRRT on the survival of critically ill patients [3] (Table 1).

SUMMARY

As CRRT is increasingly used in ICU patients, clinicians must pay attention not only to positive aspects of this form of extracorporeal therapy, but also to its potential adverse effects. The impact of CRRT on the possibility to administer adequate nutritional intervention to critically ill patients is significant due to increased losses of amino acids, L-carnitine and some vitamins, as well as microelements during the procedure. On the other hand, CRRT can increase the supply of extra-protein energy. In order to improve treatment

Table 1. Recommended supply of nutrients during continuous renal replacement therapy (CRRT)

Component	Recommended daily supply during CRRT	Comment
Energy	20–25 kcal kg IBW^{-1} day^{-1}. in the catabolic phase 25–35 kcal kg IBW^{-1} day^{-1} in the anabolic phase	Coefficient for CRRT when resting energy expenditure calculations are based on the H-B formula is 1.1–1.2
Glucose	4 g kg IBW^{-1}.	CRRT does not necessitate the correction of dietary carbohydrate supply
Fats	0.7–1.5 g kg IBW^{-1}	Although CRRT does not necessitate the correction of dietary supply of lipids, it does not prevent their accumulation
Protein/amino acids	1.7–2.0 g kg IBW^{-1}	An increase in requirements by 0.2 g kg IBW^{-1}, compared to patients without CRRT The nitrogen-calorie ratio lower than 100
Sodium	1.1–1.4 mmol kg IBW^{-1}	Too-rapid changes in sodium levels should be prevented by increasing the sodium concentration in fluids or the intravenous supply of low-sodium fluids
Potassium	0.9–2.1 mmol kg IBW^{-1}	The concentration should be higher than 4 mmol L^{-1} Normokalaemic fluids should preferably be used, potassium-free and low-potassium fluids - only in life-threatening hyperkalaemia
Phosphates	0.2–0.4 mmol kg IBW^{-1} (PN) 0.3–0.6 mmol kg IBW^{-1} (EN)	Additional substitution required (Glycophos®, Addiphos®) when phosphate-free fluids are used
Magnesium	0.1–0.2 mmol kg IBW^{-1} (PN) 0.15–0.25 mmol kg IBW^{-1} (EN)	In hypomagnesaemia caused by CRRT (rare) — 2–4 g $MgSO_4$ *i.v.*
Calcium	0.4–0/8 mmol kg IBW^{-1} (PN) 4–8 mmol kg IBW^{-1} (EN)	Possible hypocalcaemia requiring additional intravenous substitution of $CaCl_2$
Microelements	A doubled dose of commercial preparations for PN, additional intravenous substitution for EN	
Water-soluble vitamins	B_1 — 100 mg, B_2 — 2 mg, B_3 — 20 mg, B_5 — 10 mg, B_6 — 100 mg, biotin (B_7) — 200 µg, folic acid (B_9) 1 mg, B_{12} — 4 µg C — 250 mg	A doubled dose of commercial preparations for PN, additional intravenous substitution for EN
Fat-soluble vitamins	E — 10 IU K — 4mg week^{-1} Without supplementation of vit. A	In practice, unfeasible in Poland, the dose of commercial multi-vitamin preparations may be doubled

IBW — ideal body weight; PN —parenteral nutrition; EN — enteral nutrition

outcomes in critically ill patients, all aspects of CRRT discussed in this paper should be considered while planning nutritional interventions.

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