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Review Article

Water, electrolytes, vitamins and trace elements – Guidelines on Parenteral Nutrition, Chapter 7

Wasser, Elektrolyte, Vitamine und Spurenelemente – Leitlinie Parenterale Ernährung, Kapitel 7

Abstract

A close cooperation between medical teams is necessary when calculating the fluid intake of parenterally fed patients. Fluids supplied parenterally, orally and enterally, other infusions, and additional fluid losses (e.g. diarrhea) must be considered. Targeted diagnostic monitoring (volume status) is required in patients with disturbed water or electrolyte balance. Fluid requirements of adults with normal hydration status is approximately 30–40 ml/kg body weight/d, but fluid needs usually increase during fever. Serum electrolyte concentrations should be determined prior to PN, and patients with normal fluid and electrolyte balance should receive intakes follwing standard recommendations with PN. Additional requirements should usually be administered via separate infusion pumps. Concentrated potassium (1 mval/ml) or 20% NaCl solutions should be infused via a central venous catheter. Electrolyte intake should be adjusted according to the results of regular laboratory analyses. Individual determination of electrolyte intake is required when electrolyte balance is initially altered (e.g. due to chronic diarrhea, recurring vomiting, renal insufficiency etc.). Vitamins and trace elements should be generally substituted in PN, unless there are contraindications. The supplementation of vitamins and trace elements is obligatory after a PN of >1 week. A standard dosage of vitamins and trace elements based on current dietary reference intakes for oral feeding is generally recommended unless certain clinical situations require other intakes.

Keywords: fluid intake, trace elements, zinc, selenium, vitamins

Zusammenfassung

Für die Berechnung der Flüssigkeitszufuhr bei parenteral ernährten Patienten ist eine enge Absprache zwischen den betreuenden ärztlichen Teams notwendig. Neben der PE muss auch die oral und enteral zugeführte Flüssigkeit sowie ggf. eine weitere Infusionstherapie und außergewöhnliche Flüssigkeitsverluste (z.B. Diarrhöe) berücksichtigt werden. Für Patienten mit gestörtem Wasser- oder Elektrolythaushalt ist eine gezielte Diagnostik (Volumenstatus) zur Ermittlung des individuellen Flüssigkeitsbedarfs erforderlich. Während der Flüssigkeitsbedarf für Erwachsene mit normalem Volumenstatus bei ca. 30–40 ml/kg KG/d liegt, ist der Flüssigkeitsbedarf bei Fieber üblicherweise erhöht. Bei normalem Flüssigkeits- und Elektrolythaushalt erfolgt die Zufuhr von Elektrolyten initial standardisiert nach allgemeinen Empfehlungen. Die Serumelektrolytkonzentrationen sollten vor Beginn einer PE bestimmt werden. Eine Elektrolytzufuhr im Bereich des normalen Bedarfs wird mit der appliziert. Bei deutlich gesteigertem Bedarf sind zusätzliche Zufuhrwege (z.B. über separate Infusionspumpen) sinnvoll. Die isolierte Zufuhr von hochdosierten Kalium- (1mval/ml) bzw. NaCl 20%-Lösungen sollte über einen zentralen Venenkatheter erfolgen. Die Elektrolytzufuhr muss im Verlauf der PE nach regelmäßig durchgeführten Laborkontrollen angepasst werden. Bei initial verändertem Elektrolythaushalt (z.B. be-

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dingt durch chronische Diarrhöe, rezidivierendes Erbrechen, Niereninsuffizienz etc.) ist eine individuelle angepasste Elektrolytzufuhr erforderlich. Vitamine und Spurenelemente sollten bei PE grundsätzlich substituiert werden, sofern keine Kontraindikationen bestehen. Ab einer PE-Dauer >1 Woche ist die Supplementation von Vitaminen und Spurenelementen obligat. Die Zufuhr von Vitaminen und Spurenelementen in Anlehnung an Dosisempfehlungen für die orale Ernährung wird generell empfohlen falls nicht spezielle Krankheitssituationen andere Zufuhren erfordern.

Schlüsselwörter: Flüssigkeitsaufnahme, Spurenelemente, Zink, Selen, Vitamine

Preliminary remarks

Fluid and electrolyte requirements, of patients receiving PN are administered by means of parenteral infusions, oral and/or enteral intake. A close cooperation is, therefore, necessary between medical teams, involved in the overall care of the patient and the team prescribing the PN intakes of the patient, especially if the teams are mutually exclusive.

Many of the practices involved in providing fluid and electrolyte requirements of the patients, particularly the substitution of vitamins and trace elements, are clinically established practices that are not based on randomized studies. Some recent clinical studies evaluating high-dosage vitamins or trace elements are mostly prospective, controlled and randomised studies. Although these studies have the highest level of evidence (A), general recommendations cannot not always derived from these studies, because they usually included small patient numbers only.

Fluid intake in parenteral nutrition

- The fluid requirement in adults with normal hydration status is approximately 30–40 ml/kg body weight/d. Depending on their age, children have a much higher fluid intake per kg body weight (cf. chapter "Neonatology/Paediatrics"; http://www.egms.de/en/gms/2009-7/000074.shtml) (C).
- In the event of fever, fluid needs usually increase by approximately 10 ml/kg body weight/d per 1°C rise in temperature above 37°C (C).
- Targeted diagnostic monitoring is required in patients with disturbed water or electrolyte balance (e.g. shock, sepsis, renal insufficiency) to determine individual fluid needs (C).
- When calculating the fluid intake of parenterally fed patients, fluids supplied parenterally, orally and enterally, other infusions, and additional fluid losses (e.g. diarrhea) must be considered (C).

Commentary

The recommended daily fluid supplies are not based on systematic studies, but on clinical experience and recommendations by experts and medical societies [1]. [2], [3], [4], [5]. There is no conclusive literature on fluid requirements in patients with fever, or in patients with disturbed water or electrolyte balances. The recommendations made here are, therefore, based on expert opinion (C).

The determination of the hydration of a patient is a prerequisite for calculating parenteral fluid requirements, especially when a disturbance in fluid balance is clinically suspected. In such patients, transitions between hypovolaemia, euvolaemia and hypervolaemia are frequent. The current fluid volume status may be evaluated by clinical symptoms (change of body weight, skin turgor, central venous pressure (CVP), sonographic evidence of vena cava filling) and laboratory parameters (haematocrit, serum sodium, serum and urine osmolarity). Hypovolaemia is characterised by weight loss, reduced skin turgor, dry mucous membranes, reduced arterial and central venous pressure (collapsed jugular vein, CVP <4 cm H_2O, collapsed vena cava in sonography), tachycardia, and where applicable increased serum sodium and increased serum osmolarity as well as increased urine osmolarity (>450 mosmol/kg). Symptoms of hypervolaemia are typically the formation of edema, in the legs or on the coccyx in bedridden patients, pulmonary edema, ascites, a tendency towards arterial hypertension, and increased filling pressure in the large veins. Laboratory tests may also show reduced plasma osmolarity and hematocrit levels [6]. These criteria usually allow for estimates of the current fluid volume status, both at the beginning of and during PN. Treatment of the underlying illness causing a fluid imbalance should also be initiated. Fluid imbalance can be symptomatically treated by means of individually adapted PN, for example, in critically ill patients and patients with acute or chronic renal, liver, heart or lung insufficiency. Strict monitoring of and appropriate changes in fluid and electrolyte intake are necessary in patients at-risk for disturbances in fluid and electrolyte balance, especially in critically ill patients and in patients with renal failure or chronic renal insufficiency (cf. chapter "Parenteral nutrition in patients with renal failure"; http://www.egms.de/en/gms/2009-7/000070.shtml).

Electrolyte intake in parenteral nutrition

- Electrolyte intake in patients with normal fluid and electrolyte balance should follow general recommendations (Table 1). Serum electrolyte concentrations (Na, K, Ca, Mg, phosphate) should generally be determined prior to commencing PN (C).

Table 1: Standard daily doses of parenterally administered electrolytes in PN in adult patients (adapted from [5])

Sodium	60–150 mmol
Potassium	40–100 mmol
Magnesium	4–12 mmol
Calcium	2.5–7.5 mmol
Phosphate	10–30 mmol

- Electrolyte supplies in the normal range may be administered with the glucose-amino acid solution (C). Additional requirements should be administered by other methods (i.e. via separate infusion pumps), to avoid compatibility problems (C). Isolated potassium (1 mval/ml) or 20% NaCl should be infused via a central venous catheter (C).
- Electrolyte intake should be adjusted according to the results of regular laboratory analyses performed during PN. Individual determination of electrolyte intake is required when electrolyte balance is initially altered (e.g. due to chronic diarrhea, recurring vomiting, renal insufficiency etc.) (A).

Commentary

Electrolyte supply with PN is closely linked to fluid intake. The values for standard electrolyte intake (Table 1) have been adapted from the guidelines of the American Gastroenterological Association (AGA) [5], which are based on the "FDA Requirements for Marketing" published in 2000 [7]. These values should be seen as general guidelines and may be used in patients with normal renal and liver functions as well as normal electrolyte concentrations in the blood. Restrictions may be necessary in disorders where limited intake is recommended, e.g. of sodium in hypertension and cardiac insufficiency. Currently available recommendations for standard electrolyte intake are based on oral intake and have been extrapolated for the parenteral situation. The requirement of laboratory checks at the beginning of PN is an expert opinion. When determining the electrolyte intake in PN, it should be taken into consideration that many commercially available multi-chamber bags and amino acid solutions contain electrolytes in various doses, which do not always meet patients' requirements in the long run. These quantities need to be taken into account when calculation additional needs that may need to be added to the PN bag.

In case of a standard electrolyte intake, this should be administered via the PN bag (C). Higher doses may be required in the event of large fluid losses (e.g. vomiting, diarrhea, large wounds, high-output fistulae, renal illnesses). Such additional electrolytes should generally be given as a separate infusion, e.g. via infusion pumps, if requirements exceed the upper end of the ranges shown in Table 1. Compatibility problems are thus prevented, and short-term adjustments in electrolyte levels are possible.

There are no studies evaluating the adequate frequency of laboratory monitoring of serum electrolytes during PN. A check every 24 hours was found beneficial in intensive care patients at the beginning of PN (week 1–2), whilst twice weekly testing for ward patients was considered adequate as long as there were no special risk factors (8). The time intervals between tests might be extended with longer duration of PN, provided the electrolyte values were stable; checks every 1–2 weeks in the first three months, and then every month in the following three months generally are sufficient in stable patients on at-home parenteral nutrition [8]. This recommendation is in agreement with the Mayo scheme, which is presented in more detail in the chapter on "Complications and monitoring"; http://www.egms.de/en/gms/2009-7/000076.shtml.

Supply of vitamins and trace elements during parenteral nutrition under standard conditions

- Parenteral vitamins and trace element supplies should be provided to patients receiving total PN (C).
- Vitamins and trace elements should be generally substituted in PN, unless there are contraindications. The supplementation of vitamins and trace elements is obligatory after a PN duration of >1 week.
- A standard dosage of vitamins and trace elements is generally recommended because individual requirements cannot be easily determined. Preferably, all vitamins and trace elements supplied with a normal diet should also be substituted with PN as available (C). The quantities of daily parenteral vitamin and trace element supplies are based on current dietary reference intakes for oral feeding (A).

Commentary

Vitamins and trace elements must be administered as essential nutrients to parenterally fed patients to prevent deficiency syndromes [9], [10], [11]. There is a lack of studies clearly indicating when it is necessary to substitute vitamins and trace elements with PN. In patients who receive home PN, deficits have been shown to occur without substitution, and they can be completely or partially corrected with standard supplies [9], [10], [11]. The

Table 2: Estimated daily requirements of parenterally administered vitamins and trace elements in adult patients (adapted from [5, 7])

Vitamin B1 (thiamine)	6 mg
Vitamin B2 (riboflavin)	3.6 mg
Vitamin B6 (pyridoxine)	6 mg
Vitamin B12 (cobalamine)	5 µg
pantothenic acid	15 mg
niacine	40 mg
biotin	60 µg
folic acid	600 µg
Vitamin C (ascorbic acid)	200 mg
Vitamin A	3300 I.U. (= 1 mg)
Vitamin D	200 I.U.
Vitamin E	10 I.U. (= 9.1 mg)
Vitamin K	150 µg
chromium	10–20 µg (= 0.05–0.10 µmol)
copper	0.3–1.2 mg (= 4.7–18.8 µmol)
iodine	70–140 µg (= 0.54–1.08 µmol)
iron	1–1.5 mg (= 18–27 µmol)
manganese	0.2–0.8 mg (= 3.6–14.6 µmol)
selenium	20–80 µg (= 0.25–1.0 µmol)
zinc	2.5–4 mg (= 38–61 µmol)

NB: the values given here reflect recommendations of the American Gastroenterological Association [5]. The values for certain vitamins and trace elements deviate considerably from the dietary reference values by the German-speaking nutrition societies (D-A-CH) [3].

supply of vitamin E reduces the formation of lipid peroxides during PN [12].

The recommended standard supplies of vitamins and trace elements in adults (Table 2) have been adapted from the guidelines for electrolytes by the American Gastroenterological Association (AGA) and should be regarded as estimated requirements [5], which are based on the "FDA Requirements for Marketing" from 2000 [7]. They do not completely correspond to the reference intake values for healthy, orally fed subjects [3]. Recommendations for parenteral trace element supply in children are provided (Table 3) [13], [14]. While standardised vitamin supplementation does not result in desirable blood or tissue concentrations for all vitamins [15], [16], it is not possible to determine individual requirements of vitamin and trace elements with clinical routine care.

Vitamins and trace elements should be added to the parenteral solutions. Vitamins should be added just before using the nutrition bag. Loss of activity can be minimized by dissolving the vitamins in a lipid solution or by using a light protection covering [17] (cf. chapter "Practical Handling of AIO Admixtures"; http://www.egms.de/en/gms/2009-7/000077).

Guidelines on the deviation from standard conditions in the substitution of vitamins and trace elements

- A deviation from the standard intake of vitamins and trace elements may be indicated under certain clinical situations (C).

Commentary

A standard supplementation of micronutrients may not be sufficient for certain medical situations, for instance, in bone marrow transplants [18] and in dialysis patients (cf. chapter "Parenteral nutrition in patients with renal failure"; http://www.egms.de/en/gms/2009-7/000070). There are studies where pharmacological doses of certain vitamins and trace elements were used. It was shown that low plasma concentrations of vitamin C could be normalised after administration of high doses of vitamin C in perioperative intensive care patients [19]. The use of pharmacological doses of specific micronutrients exceeds the requirements of PN and therefore, will not be discussed here (Table 4).

Table 3: Estimated daily requirements of parenterally administered vitamins and trace elements in infants and children (according to [13, 14])

Element	Infants (µg/kg body weight/d)		Children (µg/kg body weight/d or [maximum µg/d])	
	preterm	term		
Zinc	400	250 <3 Mo 100 >3 Mo	50	[5000]
Copper	20	20	20	[300]
Selenium**	2.0	2.0	2.0	[30]
Chromium**	0.2	0.2	0.2	[5.0]
Manganese**	1.0	1.0	1.0	[50]
Molybdenum**	0.25	0.25	0.25	[5.0]
Iodine	1.0	1.0	1.0	[1.0]

* not in cholestasis
** not in renal dysfunction

Table 4: Risk constellations for potentially increased requirements of vitamins and trace elements

Illness	**Postulated affected micro nutrients [ref. in brackets]**
Trauma	Vitamins C and E, zinc [20-22]
Sepsis	Selenium, Vitamins C and E? [20, 23-26]
Burns	Vitamin C, zinc, copper and selenium [27-30]
ARDS	Vitamin C? [21] n-Acetyl cysteine? [31]
Renal insufficiency	Water-soluble vitamins like Vitamin C? Cave at: Risk in oxalate formation [32]
Wernicke's encephalopathy	Thiamine (when there is a risk constellation of alcoholism, dialysis, malabsorption) [8, 33-35]
Liver disease	Cholestatic liver disease: in particular fat-soluble vitamins A, D, E, K Alcoholic liver disease: risk of general micronutrient deficiency caused by malnutrition
Advanced liver cirrhosis:	Electrolyte disturbances (Na+, K+, Ca, Mg) as well as a lack of zinc

An up-to-date overview of the vitamins and trace elements supplements presently available for parenteral use in Germany is provided (Table 5 and Table 6). These supplements can be used in daily clinical practice, even though the composition of these supplements does not correspond exactly to the estimated vitamin requirements (Table 2).

Notes

This article is part of the publication of the Guidelines on Parenteral Nutrition from the German Society for Nutritional Medicine (overview and corresponding address under http://www.egms.de/en/gms/2009-7/000086.shtml).
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Table 5: Vitamin supplements for parenteral administration available in Germany

A. Vitamin Supplements

Supplements	A [I.U.]	D [I.U.]	E [I.U.]	K [µg]	C [mg]	B1 [mg]	B2 [mg]	B6 [mg]	B12 [µg]	Folic acid [mg]	Pantothenic acid [mg]	Biotin [mg]	Niacine [mg]
Cernevit®*	3500	220	11.2	---	125	3.5	4.14	4.53	6	0.41	17.25	0.07	46
Frekavit® fat-soluble	3300	200	10	150	---	---	---	---	---	---	---	---	---
Frekavit®* water-soluble	---	---	---	---	100	3	3.6	4	5	0.40	15	0.06	40
Multibionta®N* for infusions	3000	---	5.5	---	100	10	7.3	15	---	---	25	---	40
Soluvit®*	---	---	---	---	100	2.5	3.6	4	5	0.4	15	0.06	40
Vitalipid®	3300	200	10	150	---	---	---	---	---	---	---	---	---

* Vitamin K is recommended during long-term PN use, i.e. 1 x per week

Table 6: Trace element supplements for parenteral application available in Germany

B. Trace Element Supplements

	Zn [µmol]	Mn [µmol]	Cu [µmol]	Fe [µmol]	Mo [µmol]	Se [µmol]	I [µmol]	F [µmol]	Cr [µmol]
Addel®N	100	5	20	20	0.2	0.4	1	50	0.2
Tracitrans®plus	100	5	20	20	0.2	0.4	1	50	0.2
Tracutil®	50	10	12	35	0.1	0.3	1	30	0.2

All specifications refer to a packaging unit (10 ml or 1 ampule). See reference [8] for comparison with the USA.

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