The In Vitro Effect of the Addition of Ion Exchange Resins on the Bioavailability of Electrolytes in Artificial Enteral Feeding Formulas

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Abstract

Objective: To determine in vitro free ion concentration in 3 standard artificial enteral feeding formulas following the addition of ion exchange resins.

Method: Three standard types of AEF were chosen: Osmolite HN®, Nutrison Standard®, and Isosource Standard®. The ion exchange resins used were: sodium polystyrene sulfonate and calcium polystyrene sulfonate. In a beaker were mixed 100 mL of AEF with 1.5 g or 3 g of ion exchange resins for 48 hours at 37ºC. Subsequently, the samples were precipitated and the supernatant obtained was used for determining the concentrations of calcium, magnesium, sodium, and potassium ions.

Results: The addition of sodium polystyrene sulfonate to different types of enteral feeding formulas reduced the concentrations of potassium, calcium, and magnesium ions by 70%, 78.2%, and 77.6% in the case of Osmolite HN®; by 72.3%, 69.2%, and 63.5% in the case of Nutrison Standard®; and by 78.3%, 80.5%, and 74.5% in the case of Isosource Standard®. In contrast, the addition of calcium polystyrene sulfonate reduced the concentration of potassium and magnesium by 50.5% and 55.5% in the case of Osmolite HN®; by 49.8% and 43% in the case of Nutrison Standard®; and by 42.6% and 37.7% in the case of Isosource Standard®.

Conclusion: The addition of ion exchange resins to different types of enteral feeding formulas, allows the in vitro free ion content of these to be reduced.

Key words: Sodium polystyrene sulfonate. Calcium polystyrene sulfonate. Enteral feeding. Hyperkalemia. Electrolytes.

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Efecto *in vitro* de la adición de resinas de intercambio iónico sobre la biodisponibilidad de electrolitos en fórmulas de nutrición enteral artificial

Objetivo: Conocer la concentración iónica libre *in vitro* en tres fórmulas de nutrición enteral artificial estándar, tras la adición de resinas de intercambio iónico.

Método: Se seleccionaron tres tipos de NEA estándar: Osmolite HN®, Nutrison Standard® e Issosource Standard®. Las resinas de intercambio iónico empleadas fueron: poliestireno sulfonato sódico y poliestireno sulfonato cálcico. En un vaso de precipitados se mezclaron 100 ml de la NEA con 1,5 g o 3 g de las resinas de intercambio iónico durante 48 h a 37 ºC. Posteriormente se precipitaron las muestras y el sobrenadante obtenido se utilizó para determinar las concentraciones de los iones calcio, magnesio, sodio y potasio.

Resultados: La adición de poliestireno sulfonato sódico a las diferentes nutriciones enterales redujo las concentraciones de los iones potasio, calcio y magnesio en un 70,9, 78,2, y 77,6% en el caso de Osmolite HN®, en un 72,3, 69,2 y 63,5% en el caso de Nutrison Standard®, y en un 78,3, 80,5 y 74,5% en el caso de Issosource Standard®. Por el contrario la adición de poliestireno sulfonato cálcico redujo las concentraciones de potasio y magnesio en un 50,5 y un 55,5% en el caso de Osmolite HN®, un 49,8 y un 43% en el caso de Nutrison Standard® y en un 42,6 y un 37,7% en el caso de Issosource Standard®.

Conclusiones: La adición de resinas de intercambio iónico a distintas nutriciones enterales permite reducir el contenido iónico libre *in vitro* de éstas.

Palabras clave: Poliestireno sulfonato sódico. Poliestireno sulfonato cálcico. Nutrición enteral. Hiperpotasemia. Electrolitos.

INTRODUCTION

Hyperkalemia is a serious metabolic disorder that occurs as a consequence of renal failure to excrete potassium and because of deficiencies in the incorporation of potassium from circulating blood to the intracellular space. The different measures encompassing the management of hyperkalemia include those designed to reach and maintain normal serum levels of potassium (3.5–5.5 mEq/L), reducing the amount of potassium in the diet, supporting renal excretion with diuretics and/or gastrointestinal excretion of potassium using ion exchange resins.[1] There are currently 2 types of ion exchange resins on the market in Spain with approved indications for the treatment and prophylaxis of hyperkalemia: sodium polystyrene sulfonate (SPS), which is capable of exchanging 2.81 and 3.45 mmol of potassium for each gram of resin, and calcium polystyrene sulfonate (CPS), which is able to exchange between 1.3 and 2 mmol of potassium for each gram of resin.[2] Many of the patients suffering from hyperkalemia in the hospital setting receive artificial enteral feeding (AEF) by catheter in its different forms, which implies providing an amount of potassium which varies according to the AEF chosen and the amount administered, since all of the current formulations of AEF include potassium among their ingredients. Different authors have suggested the usefulness of adding ion exchange resins to the different AEF formulas with the aim of reducing the amount of potassium to the greatest degree possible in patients with hyperkalemia.[3-6] However, published information is scarce, and varies depending on the AEF formula used. In this study, the in vitro sequestering action of SPS and CPS on potassium, calcium, magnesium, and sodium cations has been assessed in 3 standard types of AEF with the purpose of determining the free ion concentration of these ions available in vitro, for better management of both hyperkalemia and the different electrolyte imbalances that usually accompany it.

MATERIAL AND METHODS

In this work, we study the movement of the potassium, calcium, sodium, and magnesium electrolytes in vitro in 3 types of standard, widely-used types of AEF: Osmolite HN® (Abbott Laboratories), Nutrison Standard® (Nutricia Laboratories), and Isosource Standard® (Novartis Laboratories). The ion exchange resins used were: sodium polystyrene sulfonate (Resinsodio®, Rubio Laboratories) and calcium polystyrene sulfonate (Resincalcio®, Rubio Laboratories) at doses of 15 g/L and 30 g/L.

The analytical technique used to determine sodium and potassium was indirect potentiometry, performed by using the Olympus AU400 analyser. Calcium concentrations were measured using the absorption spectrophotometry technique with the Olympus AU2700 analyser. Magnesium concentrations were measured using the absorption spectrophotometry technique with the Olympus AU5400 analyser.

The sensitivity of the analytical methods were 0.344 mg/dL, 0.19 mg/dL, 0.5 mg/dL, and 0.46 mg/dL for Na^{2+}, K^{+}, Ca^{2+}, and Mg^{2+} respectively. The precision of the analytical methods used was 0.78%, 1.29%, 0.9%, and 0.5% for Na^{2+}, K^{+}, Ca^{2+}, and Mg^{2+} respectively, calculated as the coefficient of variation for the same sample analysed 10 times over 10 days.

The main study variable was a significant reduction in potassium ion content of the different AEF when SPS or CPS were added, as well as the superiority of one or another ion exchange resin in potassium ion reduction.

The secondary variables considered were the significant changes in calcium, magnesium, and sodium ions.

Reductions in potassium content of AEF over 50% were considered to be significant.

In a beaker, 100 mL of each of the 3 AEF were mixed with 15g/L or 30g/L of ion exchange resins. Twelve groups were made corresponding to the 3 AEF and the 2 doses of the 2 ion exchange resins. At the same time, electrolyte determinations were performed in a total of 5 samples per group and in duplicate. The mixture was initially stirred for 15 minutes for homogenisation, increasing the contact time between the corresponding resin and the AEF for 48 hours at 37ºC.[4,6] Subsequently, a total of 5 mL of trichloroacetic acid were added (20% at 4ºC) to each of the samples, precipitating these by centrifuging at 5000 rpm for 10 minutes to separate the aqueous phase where the electrolytes are found from the lipoprotein phase that interferes with their determination.[7] The aqueous phase obtained was used to determine the concentrations of calcium, magnesium, sodium, and potassium ions. The outcomes were expressed as mean (standard deviation) (mEq/L or mg/L), and as a percentage of the initial content of each of the ions studied. A statistical analysis was carried out of the data by comparing the ion percentages between the basal situation and the situation analysed using the Bonferroni Student *t* test. A *P* value less than .05 was considered significant. The statistical analysis was performed using the SPSS 8.0 software.

RESULTS

The sequestering effect of the SPS and CPS ion exchange resins on potassium, sodium, calcium, and magnesium cations contained in the AEP Osmolite HN®, Nutrison Standard®, and Isosource Standard® is detailed below in Figures 1 and 2.

DISCUSSION

In this work, there were chosen 3 AEF that are widely-used in clinical practice, not only by hospital nutrition departments but also in the great majority of hospital services, what justifies its use in this study.

SPS resin, at a 15 g/L concentration, exercises a sequestering power of approximately 65%, while the 30 g/L concentration provided a sequestering capacity of approximately 75%. This capacity was similar on all 3 AEF formulas. The study by Hampton

Table 1. Changes in the Electrolyte Concentration of: OsmoliteHN®, Nutrison Standard®, and Isosource Standard® After the Addition of SPS[a]

Simple (n=5)	Basal Concentration, mEq/L	Final Concentration, mEq/L	Percentage of Basal Concentration, %	Basal Concentration, mEq/L	Final Concentration, mEq/L	Percentage of Basal Concentration, %
	Sodium Content				**Potassium Content (*P<.05)**	
Osmolite HN®	38.3 (0.4)		100	37.8 (0.1)		100
Osmolite HN® + SPS 15g/L		48.6 (5.03)	126.9		11.0 (1.73)	29.1*
Osmolite HN® + SPS 30 g/L		68 (6)	177.5		9.8 (1.05)	25.9*
Nutrison Std®	43.48 (0.06)		100	38.36 (0.02)		100
Nutrison Std® + SPS 15 g/L		70.88 (6.1)	162.6		16.78 (1.67)	43.8*
Nutrison Std® + SPS 30 g/L		78.21 (4.16)	179.9		10.56 (0.3)	27.5*
Isosource Std®	30.4 (0.29)		100	34.5 (0.04)		100
Isosource Std® + SPS 15 g/L		46.0 (9.13)	151.3		11.5 (2.66)	33.3*
Isosource Std® + SPS 30 g/L		65.3 (8.26)	214.8		7.5 (1.47)	21.7*
	Calcium Content (*P<.05)				**Magnesium Content (*P<.05)**	
Osmolite HN®	68.2 (0.03)		100	29 (0.03)		100
Osmolite HN® + SPS 15g/L		14.9 (0.95)	21.9*		5.51 (0.5)	27.6*
Osmolite HN® + SPS 30 g/L		14.82 (1.81)	21.8*		4.48 (1.44)	22.4*
Nutrison Std®	80 (0.7)		100	23 (0.4)		100
Nutrison Std® + SPS 15 g/L		44.8 (4.62)	55.6*		11.15 (0.57)	48.5*
Nutrison Std® L + SPS 30 g/		24.64 (2.4)	30.8*		8.39 (0.42)	36.5*
Isosource Std®	55 (0.05)		100	22 (0.3)		100
Isosource Std® + SPS 15 g/L		12.0 (1.9)	21.8*		6.1 (0.41)	27.7*
Isosource Std® + SPS 30 g/L		10.7 (2.02)	19.5*		5.6 (0.75)	25.5*

[a]SPS indicates sodium polystyrene sulfonate.

et al[4] describes the sequestering effect of 15 g/L and 30 g/L of SPS on the potassium ion concentration contained in 2 formulas of AEF (Deliver® 2.0 and Nutren® 1.0, Lab Clintec nutrition), this being situated at around 35%-45%, with a similar effect on both formulas. In the communication by Hoyos et al,[6] the addition of 15g/L and 30 g/L of SPS gave effects found to be between 30% and 37% reduction in the potassium concentration. The power was similar with the 2 AEF formulas designed for renal failure (Nepro® and Suplena®, Abbot Lab.). Furthermore, Andrew et al[3] found a reduction of 25% and 36% in the potassium ion concentration on adding 15 g/L and 30 g/L of SPS in the AEF formula Impact® 1.5 (Novartis Lab.). It is interesting to note that in this study, as well as in the works referred to above, when the SPS dose is doubled, only a moderate increase in the effect is obtained in comparison to the lower dose of 15g/L. This would be the basis for preferring the lower dose of SPS, in order to

Table 2. Changes in the Electrolyte Concentration of: OsmoliteHN®, Nutrison Standard®, and Isosource Standard® After the Addition of CPS[a]

Sample (n=5)	Basal Concentration, mEq/L	Final Concentration, mEq/L	Percentage of Basal Concentration, %	Basal Concentration, mEq/L	Final Concentration, mEq/L	Percentage of Basal Concentration, %
	Sodium Content				**Potassium Content (*P<.05)**	
Osmolite HN®	38.3 (0.4)		100	37.8 (0.1)		100
Osmolite HN® + CPS 15g/L		41.3 (2.3)	107.8		24.3 (1.79)	64.3*
Osmolite HN® + CPS 30 g/L		45.3 (5.03)	118.3		18.7 (2.08)	49.5*
Nutrison Std®	43.48 (0.06)		100	38.6 (0.02)		100
Nutrison Std® + CPS 15 g/L		46.6 (4.16)	105.2		23.6 (0.61)	61.2*
Nutrison Std® + CPS 30 g/L		42 (3.46)	92.0		19.23 (1.3)	50.2*
Isosource Std®	30.4 (0.29)		100	34.5 (0.04)		100
Isosource Std® + CPS 15 g/L		32 (4)	105.3		24.5 (1.47)	71.0*
Isosource Std® + CPS 30 g/L		37.3 (3)	122.7		19.8 ± 0.53	57.4*
	Calcium Content (P<.05)				**Magnesium Content (*P<.05)**	
Osmolite HN®	68.2 (0.03)		100	29 (0.03)		100
Osmolite HN® + CPS 15g/L		103.2 (5.1)	143.3		9.86 (0.23)	49.3*
Osmolite HN® + CPS 30 g/L		112.8 (10.46)	156.7		8.89 (0.75)	44.5*
Nutrison Std®	80 (0.7)		100	23 (0.4)		100
Nutrison Std® + CPS 15 g/L		143.84 (2.89)	179.8		15.06 (0.5)	65.5*
Nutrison Std® + CPS 30 g/L		175.36 (15.5)	219.2		13.11 (0.4)	57.0*
Isosource Std®	55 (0.05)		100	22 (0.3)		100
Isosource Std® + CPS 15 g/L		102.9 (5.1)	187.1		14.3 (0.23)	65.0*
Isosource Std® + CPS 30 g/L		151.6 (2.88)	275.6		13.7 (0.23)	62.3*

[a]CPS indicates calcium polystyrene sulfonate.

reduce the risk of adverse effects associated with the administration of ion resins[8].

The SPS has also a sequestering effect on the magnesium and calcium contained in the AEF formulas which, in percentage terms, is similar to the figures mentioned for potassium. In this work the mixing method used by Hampton et al[4] has been modified, as an extraction with trichloroacetic acid was used to ensure that the ions determined were only those in the aqueous phase of the mixture, ie, only the 3 ions. Also, the mixing methods used by Hoyos et al[6] and Andrew et al[3] involved only 24 hours of contact between the AEF and the ion exchange resins. These facts, together with the different AEF analysed, can explain why in this work a greater percentage reduction of free ion concentration is achieved.

Another aspect that should not be forgotten is the amount of sodium associated with SPS administration. In our study, the sodium content includes values of between 150% and 215% of the amount contained in the AEF formula. This content has also been mentioned in the above studies[3,4,6] and must be taken into account, especially in situations where there are hepatic or renal conditions, where salt intake must be reduced.

In patients unable to tolerate a sodium overload, the resin of choice will be Calcium PS (CPS). The CPS has a lower sequestering effect on potassium than SPS, justified by the reduced sequestering capacity of the CPS molecule.[2] On the contrary and as one would expect, there is an increase in the calcium supply given the calcic nature of this resin, which must be taken into account in conditions such as alkaline milk syndrome and renal failure situations with hypercalcaemia. The addition of both resins to the 3 AEF formulas does not change the stability of the latter, nor their organoleptic properties, as happened in the aforementioned studies.[3,4,6] It is worth to mention that in patients fed by enteral feeding catheter, joint administration avoids the adherence of the resin to the walls of the catheter and reduces the risk of obstruction. Nevertheless, the study has some limitations intrinsic to in vitro studies, ie, it tells us the free ion concentration so we can discover the exact ion feeding content, but we do not know the effect on the reduction in plasma levels of potassium in patients with hyperkalemia receiving AEF. However, the work performed by Hampton et al[4] includes a clinical case in which hyperkalemia is normalised after adding 15g/L of SPS. So once the free ion concentrations were known for these 3 AEF following the addition of SPS and CPS, these formulas could be applied to patients with hyperkalemia who do not tolerate normal feeding. This project can be the subject to future studies.

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