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An Assessment of aluminum contamination in neonatal parenteral nutrition solutions based on measured versus labeled content

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A B S T R A C T

Aluminum can potentially cause toxicity in pediatrics and neonates receiving parenteral nutrition. Some PN solutions and ingredients in Saudi Arabia do not comply with US FDA regulations regarding aluminum exposure. This study aims to determine the aluminum concentration in samples of PN solutions and ingredients used to feed infants in Saudi Arabia. The aluminum in the samples was determined using inductively coupled plasma mass spectrometry. The concentration of metal contaminants in each sample was determined in triplicate. The aluminum content of 38 samples was investigated, 15 of which originated from components included in the prepared PN solutions. Among the 15 samples, the least measurable aluminum content was detected in potassium chloride solutions (0.81 mcg/L). In contrast, the greatest amount of aluminum was detected in potassium phosphate and calcium gluconate (141,64 mcg/L and 462.7 mcg/L), respectively. The results showed that the final PN solution (PNS) product contained more aluminum levels than the content ingredients; in addition, the study found a statistically significant relationship among 18 pediatric patients at KFMC who had intestinal failure and needed long-term parenteral nutrition. Specifically, their high aluminum levels, exceeding the normal range of 0.6 ng/ml, indicate that the current use of PN solutions will likely cause toxicity due to aluminum contamination in additives. Hence, reducing aluminum in PN solutions is imperative to ensure patient safety.

1. Introduction

Parenteral nutrition (PN) is crucial for managing sick and growing preterm and term infants, as it can serve as the exclusive nutritional source for infants who are unable to be orally fed or as a complementary option to enteral feeding (Poole et al., 2012). Nonetheless, premature infants face an elevated risk of accumulating and experiencing aluminum toxicity since they frequently depend on days of parenteral nutrition (PN) support, and their underdeveloped kidneys are incapable of efficiently eliminating aluminum (Mirtallo et al., 2004; Harigaya et al., 2008). PN has been identified as a notable contributor to aluminum exposure because of the contamination found in its constituent ingredients. These include phosphate salts and calcium gluconate, which are frequently administered in significant quantities to premature infants to support bone mineralization (Mirtallo et al., 2004; Harigaya et al., 2008). Unfortunately, the raw materials of these component products contain aluminum contaminants, and there is additional exposure through byproducts resulting from the manufacturing process. This includes instances of leaching from glass vials during autoclaving and injection bags utilized in parenteral nutrition (Harigaya et al., 2008; Huston et al., 2017; Bohrer and do Nascimento PC, Binotto R, Pomblum SC. , 2001).

Glass containers are often the primary source of aluminum contamination in component products, as they are principally made up of silica (59–80 %) with variable degrees of sodium oxide (12–17 %), calcium oxide (5–12 %) and aluminum oxide (0.5–3.0 %) and are classified into four types based on their degree of chemical/hydrolytic resistance to water attack (Dildorakhan, 2022; Europian pharmacopoeia, 2019; The United States pharmacopeia, 2013).

The toxicity of aluminum in PN solutions (PNSs) has been a problem for decades. Despite valid efforts, there are still difficulties in meeting US Food and Drug Administration (FDA) recommendations for measuring or calculating the aluminum content to prepare a PNS that meets the patient's nutritional needs and reduces aluminum toxicity. To reduce the risk of aluminum toxicity, the FDA required that manufacturers of compounds used in preparing parenteral nutrition must assess the aluminum content of their products and include this information on the label by July 2004 (3). Large-volume parenteral solutions, such as

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concentrated dextrose solutions, sterile water for injection and amino acid solutions, are subject to a maximum allowable limit of 25 mcg/L of aluminum. In contrast, small-volume parenteral solutions like pharmacy bulk packages containing parenteral multivitamins, electrolyte salts and trace element solutions must bear labels indicating the maximum aluminum content in the product at its expiry date. However, it is worth noting that the FDA has established 5 mcg/kg/day as the highest extent of aluminum that can be considered safe for consumption.

Clinical studies have shown that premature newborns who received PN for longer than three weeks had ten times the concentrations of aluminum in their bones compared to infants who utilized enteral feeding, resulting in a 15 % decrease in bone mineral content and bone density, and an increased likelihood of osteomalacia (Appleman et al., 2013; Sedman et al., 1985). In the long term, aluminum may cause structural changes in liver cells, which may reduce hepatocyte secretion and block bile flow (Hall et al., 2018). Arnold et al. showed that after an average of 18 days of PN treatment, 25 % of neonates with intestinal disease and 40–60 % of long-term PN infants had cholestasis, which causes hepatic injury, severe illness, and death in some instances (Arnold et al., 2003; Viswanathan et al., 2014).

This study aims to ascertain the aluminum concentration in theoretically constructed samples of PNS as well as the aluminum contents of parenteral solutions used to feed newborn infants in Saudi Arabia. To compare the measured and expected values, we assessed the aluminum content of PNS utilized in the neonatal intensive care unit (NICU) at King Fahad Medical City (KFMC) and each component added to the solutions. The least polluted PNS that complied with the FDA's "safe limit" of less than 5 g/kg/day of aluminum was identified after we took note of the contamination degree of the items whose aluminum level was not indicated on the label. This study also intends to identify the least polluted goods available on the market and to highlight the efforts required to control the aluminum contamination of small- and large-volume parenteral medication products.

2. Material and methods

2.1. Samples collection

Samples (available from the companies and manufacturers in Saudi Arabia) were taken from 15 products used as ingredients in PNS for newborn infants at almost every hospital in Saudi Arabia. These products included sodium chloride, potassium acetate, potassium phosphate, sodium acetate, potassium chloride, sodium glycerophosphate, magnesium sulfate, 10 % amino acid solution, multivitamin solution, trace element, 20 % Smoflipid emulsion, 70 % dextrose, and water for injection (Table 1). In addition, samples were obtained from three PNSs prepared for patients with estimated body weights 670 g, 540 g, and 610 g. PNSs as per ASPEN neonatal dosing guidelines were formulated within the specified volume range: glucose perfusion rate 6–14 mg/kg/min; protein 3–4 g/kg/day; lipid 0.5–3 g/kg/ day; sodium 2–5 mEq/kg/day, potassium 2–4 mEq/ kg/day; phosphorus 1–2 mmol/kg/day; calcium 2–4 mEq/kg/day; magnesium 0.3–0.5 mmol/kg; trace element solution "Fresenius Kabi" (iron, chromium, zinc, magnesium, copper, selenium, molybdenum, iodine, fluorine) 1 ml/kg/day; water soluble vitamins solution " Sandoz" (riboflavin sodium phosphate, thiamine nitrate, pyridoxine hydrochloride, nicotinamide, pantothenic acid, biotin, sodium ascorbate, cyanocobalamin, folic acid) and fat soluble vitamins solution " Sandoz" (vitamin A, vitamin E, vitamin D2, vitamin K1) 2 ml/ kg/day, and the overall volume of the prepared solution was 130–160 ml/ kg/day (Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Pediatric Critically Ill Patient JPEN, 2017).

Table 1
Parenteral drug samples products used in PNS.

No.	drug	company	Container
1	Amino Acid 10 %	Primine Baxter	Glass
2	Lipid 20 %"SMOFlipid"	Fresenius Kabi	Glass
3	Dextrose70%	Baxter	polyethylene
4	Water for Injection B.P	PSI*	polyethylene
5	Sodium Chloride	PSI*	polyethylene
6	Sodium Acetate	Hospira	polyethylene
7	Sodium Glycophosphate	Fresenius Kabi	polyethylene
8	Heparin	Wockhardt	Glass
9	Potassium Chloride	PSI*	polyethylene
10	Potassium Acetate	Hospira	polyethylene
11	Potassium Phosphate	Sterop	Glass
12	Calcium Gluconate	PSI*	polyethylene
13	Magnesium Sulphate	PSI*	polyethylene
14	Trace elements	Fresenius Kabi	polyethylene
15	MultiVitamin	Sandoz	Glass

* PSI: Pharmaceutical Solutions Industry.

The daily aluminum intake was determined by summing the aluminum content contributed by each component, following the routinely prescribed volumes for neonates (Table 2). The PNSs were prepared in a sterile environment in the Children's Hospital Cleanroom Sterile Compounding Facility. The facility was designed to reduce the potential for airborne contamination by employing a unidirectional airflow system with high-efficiency particulate air (HEPA) filtration within the ISO Class 5 area. Pharmaceutical Compounding Sterile Preparations USP ⟨797⟩ was applied (Bulletin, 2020), and an Automated Compounding Device was employed to produce parenteral nutrition. This device streamlines the process of transferring dextrose, amino acids, sterile water, and small volume injectables, such as minerals and electrolytes, into the ultimate parenteral nutrition container. The device's operation is controlled by BAXA® computer software. Samples were also taken from two sterile water for injection bags. The first bag was prepared by passing sterile water before starting compounding using the automated compounding device, and the second bag was prepared by passing sterile water at the end of the day after preparing all PN formulations (Table 3). Finally, samples were taken randomly from 18 pediatric patients with intestinal failure at KFMC (Table 4).

2.2. Samples and standards preparation

Standard calibration solutions were prepared by blending and diluting a 1 $g{\cdot}L^{-1}$ single element in ultrapure water acidified with HNO3 1 %. This involved a sequential dilution process, resulting in five distinct concentration levels: 0, 1, 3, 5, and 10 mcg·L–1 for external calibration quantification using ICP-AES. For both samples and parenteral drug products, dilutions were carried out to 1/100 and 1/200 with ultrapure water acidified with 1 % HNO3, except for one sample that required further dilution to 1/1000. A blank solution was prepared using a 1 % (v/v) HNO3 aqueous solution. The quantification of aluminum contents in sample products was measured in mcg/L.

2.3. Reagents

All solutions were made using purified water obtained from the Milli-Q Synthesis water purification system (Millipore, Tokyo, Japan). The standard aluminum solution employed was a commercially available aluminum (Al) solution (Merck, Darmstadt, Germany) with a content of 1,000 mg of aluminum. For optimization purposes, ultra-pure nitric acid HNO3 (Merck KGaA, Darmstadt, Germany) was utilized.

2.4. Instrumentation

The aluminum contents in the samples were determined utilizing Inductively Coupled Plasma Mass Spectrometry (ICP-MS) with Elan DRC II Axial Field Technology from PERKIN ELMER Inc., USA. This study utilized an ELAN DRC II ICP-MS instrument (PerkinElmer, Concord, Ontario, Canada) equipped with Dynamic Reaction Cell (DRC). The instrument was supplied with a platinum cone, a quartz injector (2.0 mm

Table 2
Components of neonates PN admixture and estimated aluminum content.

Neonate PNS	Components	Dose	Volume (ml)	Labeled Al (mcg)	Estimated aluminum content from REF. (mcg)	Concentration mcg/L	Estimated aluminum content FROM MEASURED (mcg)
admixture 1	primene 10 %	2.35 g	23.5	25	587.5	50.4	1184.4
(neonate weight = 670 g)	dextrose 70 %	10 %	14.4	25	360	27.5	396
Overfill to 131 ml	sodium chloride	4.02 mmol	1.6	200	320	13.9	22.24
	sodium glycerophosphate	1.34 mmol	1.34	263.7	353.358	280	375.2
	potassium chloride	2.01 mmol	1	1000	1000	0.81	0.81
	potassium phosphate	0.67 mmol	0.22	32,800	7216	14,164	3116.08
	calcium gluconate	0.201 mmol	0.86	31	26.66	462.7	397.922
	magnesium sulphate	0.134 mmol	0.07	300	21	68.8	4.816
	multiple vitamin	1.34 ml	1.34	30	40.2	74.8	100.232
	trace elements	0.67	0.67	5000	3350	29.5	19.765
	heparin	50 units	0.1	49	4.9	452.2	45.22
	water		85.9	25	2147.5	1.7	146.03
					15427.118		5662.685
Admixture 2							
	primene 10 %	2.4 g	24	25	600	50.4	1209.6
(Neonate weight = 540 g)	dextrose 70 %	8 %	12.5	25	312.5	27.5	343.75
overfill to 139 ml	sodium chloride	0.54 mmol	0.27	200	54	13.9	3.753
	sodium glycerophosphate	0.81 mmol	1.02	263.7	268.974	280	285.6
	potassium phosphate	0.54 mmol	0.23	32,800	7544	14,164	3257.72
	calcium gluconate	0.162 mmol	0.88	31	27.28	462.7	407.176
	magnesium sulphate	0.081	0.05	300	15	68.8	3.44
	multiple vitamin	1.08 ml	1.36	30	40.8	74.8	101.728
	trace elements	0.54	0.68	5000	3400	29.5	20.06
	heparin	55 units	0.11	49	5.39	452.2	49.742
	water		97.9	25	2447.5	1.7	166.43
					14715.444		5682.569
Admixture 3							
	primene 10 %	1.95 g	19.5	25	487.5	50.4	982.8
(neonate weight = 610 g)	dextrose 70 %	10 %	12.1	25	302.5	27.5	332.75
overfill 115 to ml	potassium acetate	1.22 mmol	0.65	200	130	105.3	68.445
	potassium phosphate	0.305 mmol	0.11	32,800	3608	14,164	1558.04
	calcium gluconate	0.183 mmol	0.84	31	26.04	462.7	388.668
	multiple vitamin	1.3 ml	1.3	30	39	74.8	97.24
	trace elements	0.65	0.65	5000	3250	29.5	19.175
	heparin	45 units	0.09	49	4.41	452.2	40.698
	water		79.76	25	1994	1.7	135.592
					9841.45		
							3623.408

Table 3
Water inlet test results.

No.	Sterile Water preparation	Al concentration mcg/L
1st bag	before starting compounding	0
2nd bag	after preparing all PNSs	0

orifice), a PC3 spray chamber, and a PFA nebulizer. The ICP-MS system was operated under the following conditions: argon gas flow rate-17 L/min, nebulizer gas flow rate- 0.92 L/min, argon auxiliary gas flow rate-1.2 L/min, integration time- 0.3 s, sample uptake rate- 1.0 ml/min and RF power-1200 W, Cell gas (NH_3) flow rate-0.5 ml/min, and the sample introduction gas (O_2) flow rate- 30 ml/min.

The apparatus was calibrated using the standard solution (Perkin Elmer, Concord, Ontario, Canada) supplied by the manufacturer. The concentration of metal contaminants in each sample was determined in triplicate.

2.5. Statistical analysis

The statistical significance, determined by the Z test, was expressed through the calculated p-value, with values less than 0.05 considered as statistically significant.

3. Results

In this study, the aluminum levels were examined in 38 samples, with 15 of them originating from the ingredients incorporated into the prepared PNS. (Table 1); 3 samples were from the ready-made PNS prepared for three newborns in different weights in the NICUs (Table 2).

Table 4
Aluminum level and calculated p- values for eighteen pediatric patients with intestinal failure necessitating long-term parenteral nutrition at KFMC.

Patient NO.	Aluminum Level	Normal Range	P-value
1	10 mcg/L	0–6 mcg/L	<0.001
2	6.2 mcg/L	0–6 mcg/L	0.841
3	8 mcg/L	0–6 mcg/L	0.046
4	8 mcg/L	0–6 mcg/L	0.046
5	8 mcg/L	0–6 mcg/L	0.046
6	9 mcg/L	0–6 mcg/L	0.003
7	7.4 mcg/l	0–6 mcg/L	0.162
8	7 mcg/L	0–6 mcg/L	0.317
9	20.5 mcg/L	0–6 mcg/L	<0.001
10	7.7 mcg/L	0–6 mcg/L	0.089
11	9 mcg/L	0–6 mcg/L	0.003
12	7 mcg/L	0–6 mcg/L	0.317
13	16.8 mcg/L	0–6 mcg/L	<0.001
14	7.3 mcg/L	0–6 mcg/L	0.194
15	9 mcg/L	0–6 mcg/L	0.003
16	9 mcg/L	0–6 mcg/L	0.003
17	11 mcg/L	0–6 mcg/L	<0.001
18	7 mcg/L	0–6 mcg/L	0.317

6.2 20.50 ng/ml.
The p-value, indicating statistical significance, was calculated using the Z test, and a value below 0.05 was considered significant.

Table 2 shows the Al content of the additives were derived from the manufactures, pharmacopeias and published studies (Bohrer et al., 2001; Food and Drug Administration, 2000; Food and Drug Administration, 2002; Migaki et al., 2012; Poole et al., 2011; Huston et al., 2012; Fortenberry et al., 2017 Nov 16; Europian pharmacopeia, 2008; The United States pharmacopeia, 2015; de Oliveira et al., 2010; European pharmacopoeia, 2008; Medicines and Healthcare Products Regulatory Agency, 2010). Two samples were taken from two sterile water for injection bags, one passing through an automated compounding device before starting compounding parenteral drugs. The second sample was taken at the end of the day after preparing all PN formulations to ensure that the inlet tubing used for compounding PN formulations does not preserve any aluminum contamination (Table 3). Then 18 samples were taken randomly from 18 pediatric patients in KFMC with intestinal failure characterized by malabsorption resulting from the loss of absorptive surface or intestinal dysfunction, requiring prolonged parenteral nutrition (Table 4).

The name of the Small Volume Parenteral (SVP) drug products used as the ingredients of the PNS, the aluminum amount (mcg/L) measured, and the respective manufacturer of the samples taken from the SVP drug products are summarized in Table 5. Aluminum contents in SVP drug products obtained by ICP-MS were in the range of 0.81 – 14,164 mcg/L. The aluminum levels in the samples varied depending on the type and composition of the raw materials utilized in the SVP drug products. Among the fifteen samples, heparin, potassium phosphate, and calcium gluconate gave higher aluminum contents compared with other SVP drug products. This can be attributed to the diverse range and composition of raw materials employed in these products. Therefore, the least measurable aluminum content was detected in potassium chloride solutions (0.81 mcg/L). The potassium phosphate and calcium gluconate showed the highest aluminum content, 14,164 mcg/L, and 462.7 mcg/L, respectively. Inorganic phosphates are recognized for their elevated aluminum content, and potassium phosphate typically contributes more aluminum to parenteral nutrition solutions than sodium phosphate. Opting for a sodium phosphate solution instead of a potassium salt would markedly decrease aluminum exposure in parenteral nutrition. Table 6 presents the outcomes for three PNS Admixtures formulated for neonate patients with estimated weights of 670 g, 540 g, and 610 g. For the infant weighing 670 g, the total aluminum content in the ingredients of the PNS (Admixture-1) was 5,662.7 mcg, whereas the aluminum amount in the final product from the KFMC parenteral unit was measured at 8,948.6 mcg. Consequently, the daily aluminum intake through PN was calculated as 13,356.1 mcg/kg/day. Similarly, for the infant weighing 540 g, the total aluminum content in the ingredients of the PNS (Admixture-2) was 6,582.6 mcg, and the aluminum content in the final product from the KFMC parenteral unit was measured at 9,104.5 mcg (Table 2). This led to a calculated daily aluminum intake through PN of 16,926.9 mcg/kg/day. Additionally, for the infant weighing 610 g, the total aluminum content in the ingredients of the PNS (Admixture-3) was 3,623.4 mcg, and the aluminum content in the final product from the KFMC parenteral unit was measured at 5,727 mcg (Table 2). Consequently, the daily aluminum intake through PN was calculated as 9,388.5 mcg/kg/day.

Also, we analyzed the aluminum content of two samples of sterile water for injection bags using an automated compounding device. The first sample was taken at the beginning of the day before starting to compound PNSs for patients. In contrast, the second sample was taken at the end of the day after completing all preparations and no aluminum was detected (Table 3).

Table 4 shows the results obtained for 18 children experiencing intestinal failure necessitating prolonged parenteral nutrition at KFMC. The Aluminum contents in patient serum obtained by ICP-MS were in the range of 6.2 – 20.5 mcg/L with p value from less than 0.001 to 0.841.

4. Discussion

Aluminum constitutes roughly 8 % of the Earth's crust. Despite the abundance of this element in our environment and no reported diseases stemming from its deficiency, aluminum toxicity remains a significant

Table 5
Aluminum concentration of parenteral nutrition individual components.

PN ingredients	Manufacturer	Concentration mcg/L	Range by manufacturer	P-value
Amino Acid 10 %	Primine Baxter	50.4	25 mcg/L	<0.001
Lipid 20 % "SMOFlipid"	Fresenius Kabi	116.6	25 mcg/L	<0.001
Dextrose70%	Baxter	27.5	25 mcg/L	<0.001
Water for Injection B.P	PSI *	1.7	25 mcg/L	<0.001
Sodium Chloride	PSI *	13.9	200 mcg/L	<0.001
Sodium Acetate	Hospira	4	200 mcg/L	<0.001
Sodium Glycophosphate	Fresenius Kabi	280	263.7 mcg/L	<0.001
Heparin	WOCKHARDT	452.2	49	<0.001
Potassium Chloride	PSI *	0.81	1000 mcg/L	<0.001
Potassium Acetate	Hospira	105.3	200 mcg/L	<0.001
Potassium Phosphate	Sterop	14,164	32,800 mcg/L	<0.001
Calcium Gluconate	PSI *	462.7	31 mcg/L	<0.001
Magnesium Sulphate	PSI *	68.8	300 mcg/L	<0.001
Trace elements	Fresenius Kabi	29.5	5000 mcg/L	<0.001
MultiVitamin	Sandoz	74.8	30 mcg/L	<0.001

The p-value, indicating statistical significance, was calculated using the Z test, and a value below 0.05 was considered significant.
* PSI: Pharmaceutical Solutions industry.

Table 6
Daily aluminum intake for three neonates based on the total aluminum amounts detected in individual parenteral nutrition components.

Neonate PN admixture	Volume, ml	Estimated aluminum content (mcg) from reference	Estimated aluminum content (mcg) from measured	Measured aluminum content, mcg	Aluminum intake, mcg/kg/day	P-value
Admixture 1 (neonate weight = 670 g)	131	**15427.1**	**5662.7**	8948.6	13356.1	<0.001
Admixture 2 (neonate weight = 540 g)	139	**14715.4**	**5682.6**	9104.5	16926.9	<0.001
Admixture 3 (neonate weight = 610 g)	115	**9841.45**	**3623.4**	5727	9388.5	<0.001

The p-value, indicating statistical significance, was calculated using the Z test, and a value below 0.05 was considered significant.

concern. The adverse consequences of aluminum toxicity in premature infants have been acknowledged for nearly three decades (Aşut et al., 2018). In 1989, Bishop et al. (Bishop et al., 1989) was the first to shed light on this issue, presenting a case of aluminum intoxication in a premature baby who tragically passed away. After this landmark report, efforts have been undertaken to mitigate aluminum toxicity.

Building on their initial study, Bishop et al. (Bishop et al., 1997) investigated a total of 277 premature infants who received either a standard PNS or a low-aluminum-content PNS. Newborn infants who were administered PNSs containing increased aluminum levels demonstrated reduced scores on the Bayley Mental Developmental Index at the 18th month. This led Bishop et al. (Bishop et al., 1997) to propose that infants receiving high-aluminum-content PN might experience a daily decrement of 1 point on the Bayley Mental Developmental Index. In the subsequent year, Stockhausen et al. (von Stockhausen et al., 1990) highlighted that conditions such as bronchopulmonary dysplasia, necrotizing enterocolitis, osteopenia and cholestasis were more prevalent among premature infants exposed to high aluminum content.

In response to these studies, the FDA released recommendations to limit aluminum intake to 5 mcg/kg/day and mandated that large-volume parenteral products bear labels indicating “Contains no more than 25 mcg/L of aluminum.” Small-volume parenteral products were also required to list their aluminum content on labels. (Food and Drug Administration, 2002) Nevertheless, Poole et al. (Poole et al., 2012) contested that this suggestion could apply only to individuals weighing over 50 kg.

Our current investigation observed that the aluminum levels in PNSs prepared using widely used products in our country significantly exceeded recommended thresholds. As per the American Society for Clinical Nutrition (AScN) and American Society for Parenteral and Enteral Nutrition (ASPEN), a daily aluminum intake of 60 mcg/kg is associated with toxicity. (Klein et al., 1991).

Existing literature identifies calcium and phosphate salts as principal sources of aluminum in PN solutions. Huston et al. (Huston et al., 2017) compared CaCl2 and Ca-gluconate preparations, revealing that Ca-gluconate should be avoided due to its high aluminum content. Furthermore, studies suggest that trace elements and vitamin solutions contain substantial aluminum. (Fanni et al., 2014) In alignment with these findings, selecting products labeled as having low aluminum content is imperative.

We also measured the cumulative aluminum content of products used in PNS preparation in this study. A comparison was drawn between the final products and total aluminum content of ingredients and. The results demonstrated a higher aluminum content in the final product. Likewise, our research indicated the aluminum concentration in the final PN solution was at least 50 % greater than the combined aluminum content of the ingredients. De Oliveira et al. (de Oliveira et al., 2010) discovered that the aluminum content of the products increased by approximately 40 % during the preparation and administration phases. They recognized this phenomenon in the materials used and concluded that around 60 % is essential in the commercial products, with the remaining portion accumulating during the preparation and administration process. Interestingly, this study revealed a statistically significant relationship when assessing aluminum levels in the 18 children experiencing intestinal failure requiring long-term parenteral nutrition at KFMC. Indeed, the results indicated that the high aluminum levels of these patients (higher than the normal range of 0.6 ng/ml) were more statistically significant (Table 4), implying the significance of reducing aluminum levels in PNS to ensure patient safety.

5. Conclusion

Mitigating aluminum contamination in Parenteral Nutrition Solutions (PNS) requires collaborative efforts between manufacturers and healthcare providers. While Large Volume Parenteral (LVP) must declare their aluminum content below 25 mg/L, the exact quantity often remains unspecified. Conversely, Small Volume Parenteral lacks established safety thresholds for aluminum content. Not all PNS ingredients or products in Saudi Arabia adhere to FDA regulations. Though aluminum estimation requires labeling, this isn’t mandated by the FDA. Pharmacists are left to compute the maximum aluminum in patient PNS, a task simplified with proper aluminum labeling. Given manufacturers’ inconsistent labeling, measuring aluminum content in all PNS becomes crucial.

Revamping PNS manufacturing is vital. Manufacturers must refine FDA-endorsed techniques, offering a range of low-aluminum PNS options to meet requirements. Unfortunately, limited low-aluminum products exist, and the industry hasn’t issue tackled the aluminum issue universally. A few manufacturers have shifted additives into plastic containers.

Healthcare providers must prioritize low-aluminum ingredients, ensuring safe macronutrient and micronutrient levels in PNS preparation. Pharmacists should identify manufacturers with minimal aluminum contamination, curbing exposure, and toxicity risks. Opting for alternative electrolyte salts is advisable to minimize aluminum exposure.

Further research is necessary to define optimal parenteral aluminum levels for adults and children. This entails creating commercially available low-aluminum solutions aligned with these requirements. Current PNS usage might lead to toxicity due to aluminum contamination in additives. Thus, reducing PNS aluminum is paramount for patient safety.

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Conflict of interest

The authors declare no conflict of interest.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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