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DO WE KNOW THE CONTENT OF HARMFUL EXCIPIENTS IN MEDICINES THAT NEONATES RECEIVE?

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BACKGROUND

Excipients in drug formulations have been historically considered **harmless** to the patient. This may **NOT** be true in specific populations **PAEDIATRIC** or **NEONATAL** patients.

METABOLISM IMMATURITY IN NEONATES → CONTINUOUS EXPOSURE → EXCIPIENTS ACCUMULATION → exceeding the **acceptable daily intake (ADI)** → Possible **harmful effects**

PURPOSE

- Analyse the **content** of **harmful excipients (HE)** of the medications included in the hospital's neonatal intensive care unit (NICU) treatment guide.
- Elaborate **educational material** about different **toxicities** of HE, addressed to physicians and nurses of NICU.

MATERIAL AND METHODS

- Bibliographic revision of HE, potential toxicities and ADI in neonatology (if established).
- Revision of the summary of product characteristics (SmPC) of the pharmaceutical products (PP) and compounded preparations (CP) used in our NICU, to determine the qualitative and quantitative composition in HE. Total daily excipient exposures, for each drug, were established by calculating the average amount of HE administered secondary to the recommended maximum daily drug doses for newborns that appears in Neofax®.

RESULTS

9 HE and their toxicities were considered (Table 1). **227 medicines were analysed.** Quantitative analysis was not possible with the SmPC in 28 of them.

- 182 PP → 52 contained ≥ one HE (28.6%) → **13 (7%) > ADI defined**
- 45 CP → 17 contained ≥ one HE (40%) → **None exceeded ADI defined**

ADI	TOXICITY	COMMENTS
BENZOIC ACID, SODIUM BENZOATE and POTASSIUM BENZOATE		
5 mg/kg	Kernicterus, gastric and skin irritation.	Should avoid in prematures and neonates
BENZYL ALCOHOL		
0 mg/kg *(adults 5 mg/kg)*	Fatal toxic syndrome, metabolic acidosis, seizures	Not recommended in neonates
ASPARTAME		
Not available	Increase of phenylalanine levels	Not recommended in neonates
BENZALKONIUM chloride		
Not available	Ototoxicity (local), eye irritation, skin irritation, hypersensitivity, bronchospam in asthmatic patients.	As residue in food
ETHANOL		
1 mg/dL (blood level)	Lactic acidosis, hypoglycaemia, CNS effects (somnolence, depression, seizures), gastrointestinal discomfort.	CNS effects at 10 mg/dL
POLYSORBATE 80		
10 mg/kg	Metabolic acidosis, thrombocytopenia, renal dysfunction, hepatomegaly, cholestasis, ascites, hypotension.	
PROPYLENE GLYCOL		
2 mg/kg	CNS depression; cardiovascular, hepatic and respiratory adverse events; hyperosmolality; lactic acidosis; skin irritation.	
PARABEN (Propylparaben and Methylparaben)		
2 mg/kg	Oestrogenic effects, hyperbilirubinemia, hypersensitivity reactions.	
SORBITOL		
Not available *(adults 20 g/day)*	Osmotic diarrhoea, gastrointestinal discomfort, nutrient malabsorption, diabetic- like symptoms, retinopathy.	Suitable for diabetic patients

CNS: central nervous system
Table 1: Harmful excipients with their function and toxicities.

- **Training Session** for prescribers and nurses
- **Leaflets** with reviewed medications and toxicities

CONCLUSION

- HE are frequently present in medications available in the NICU. Raising the awareness of healthcare professionals is important in order to choose, if it is possible, safer alternatives.
- The quantitative composition in HE was lacking in some SmPC despite it being a requirement from the EMA. The development of paediatric medicines with appropriate excipients is necessary.

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