AKADEMISKA BARNSJUKHUSET

SAFETY OF INTRAVENOUS FERRIC CARBOXYMALTOSE IN TREATMENT OF IRON DEFICIENCY IN CHILDREN UNDER TWO YEARS WITH INTESTINAL FAILURE

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Introduction

Children with intestinal failure (IF) who are treated with iron-free parenteral nutrition (PN) are at risk for developing iron deficiency (ID). Oral or enteral iron supplementation (IS) is generally avoided in children with IF because of the reduced absorptive capacity and increased risk for gastrointestinal side effects.

Intravenous IS with ferric carboxymaltose (FCM) is a safe and effective treatment of ID in older children and adults [1], however there is lack of knowledge on the efficacy and safety of intravenous FCM treatment in younger children [2].

Table 1. Parenteral iron products licensed in Sweden according to www.mpa.se/lmf (excluding parenteral trace element solutions).

Product	Manufacturer	Paediatric indication in SPC?
Cosmofer (iron dextran) Solution for infusion and injection 50 mg/ml	Pharmacosmos	>14 years
Diafer (iron (III) isomaltoside 1000) Solution for injection 50 mg/ml	Pharmacosmos	>18 years
Ferinject (ferric carboxymaltose) [3,4] Solution for injection/infusion 50 mg iron/ml	Vifor Pharma	>14 years *
Iron Sucrose Rechon (iron sucrose) Solution for infusion and injection 20 mg/ml	Sobi	Not recommended for use in children.
MonoFer (iron (III) isomaltoside) Solution for injection/infusion 100 mg/ml	Pharmacosmos	>18 years
Venofer (iron sucrose) Solution for injection or concentrate for solution for infusion 20 mg/ml	Vifor Pharma	Not recommended for use in children.*

* Documented in ePed [5]

Objectives

The purpose of this study was to evaluate the safety of IV IS with FCM for patients with IF under the age of two years.

Methods

Part I study: The Swedish Medical Products Agency (MPA) was contacted to get adverse drug reaction report data for the period 2007 - 2016.

Part II study: A retrospective study of the records of 14 children with IF and ID who had been treated with IV FCM before 2 years of age at our tertiary center for pediatric IF, were performed. Ganzoni's equation was used for calculating the FCM dose, Serum levels of Hemoglobin, Mean Corpuscular Volume and ferritin were measured before and 1-3 months after FCM treatment. Statistical analysis of collected data.

Patient Characteristics	
Total, n	11
Sex, n (%) male female	 6 (54,5%) 5 (45,5%)
Age, months mean (SD) median (min, max)	 12.55 (5.35) 12 (5, 20)
Medical history, n NEC Small bowel atresia Diaphragmatic hernia Aganglionosis Gastroschisis CIPO Volvulus	 4 2 1 1 1 1 1

Details of the Preparation and Administration:

- Intravenous infusion
- Ferinject 50 mg/mL diluted in sodium chloride 9 mg/mL solution for infusion to minimum 2 mg/mL Ferinject.
- *Example 150 mg = 3 mL in 20 mL NaCl*
- The infusion is given during 1h.
- Recommendation to split the dose on two administration days, with a 10-14 day interval.

Results

Reported reactions MedDRA PT, <18 yrs	2009	2010	2011	2012	2013	2014	2015	2016
Hot flush							1	
Hypertension							1	
Hypotension	1		1					
Venous thrombosis limb			1					
Total Reports	**1**		**2**				**2**	

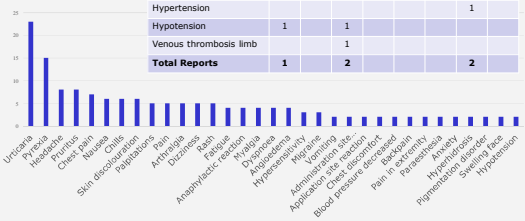
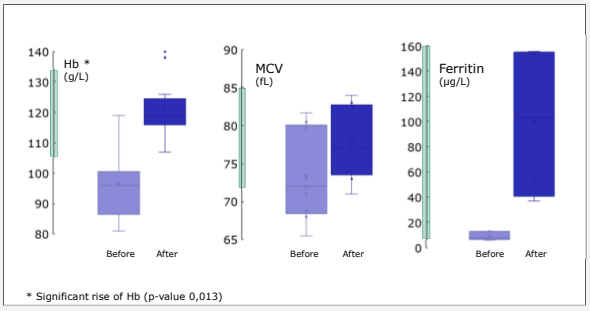


Fig 1. Bar chart: Adverse drug reactions reported for Ferinject (Vifor Pharma) to the Swedish Medical Products Agency (20070101-20161231). Number of cases. **Table**: Reported reactions in patient population under 18 years.



* Significant rise of Hb (p-value 0,013)

Fig 2. Serum levels of Hemoglobin (Hb), Mean Corpuscular Volume (MCV) and ferritin measured *before* and *after* FCM treatment. Green bars show reference values.

Part I: During the 10-year period MPA only received five Adverse Drug Reaction Reports (ADR): Hot flush, hypertension, hypotension and venous thrombosis limb were reported. The ADR data is likely based on treatments for patients >14 years.

Part II: All children received one or two doses of FCM administered as intravenous infusion. All children responded to FCM treatment with complete or partial normalization of biochemical markers for ID. No major or minor adverse events were reported.

Conclusions

The treatment of iron deficiency with intravenous ferric carboxymaltose in children under two years of age with intestinal failure was found effective in the retrospective study of the limited number of patients from our clinic. We did not find any evidence of adverse events.

References

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4. Geisser P., The pharmacology and safety profile of ferric carboxymaltose (Ferinject®): structure/reactivity relationships of iron preparations Port J Nephrol Hypert 2009; 23(1): 11-16
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