# Quantifying the Incidence of Adverse Reactions to Rapid Iron Infusions

**Kerryn Griffett, Poppy Savage, Daniel O'Brien, Paul Toner**

Pharmacy Department, The Royal Melbourne Hospital

## Introduction

Ferric Carboxymaltose (FCM) was listed on the medication formulary for rapid iron infusion at our major tertiary/quaternary referral hospital.

As part of our medication strategy and formulary review a tender process was undertaken to review the preferred agent. A multidisciplinary team reviewed all responses and based on evidence and value agreed to switch this to ferric derisomaltose (FDI).

Changing from FCM to FDI required a multifactorial approach and included updates to our electronic medical record (EMR), medication guidelines, infusion device libraries and staff education.

Following the implementation, an unexpected increase in the incidence of adverse reactions was anecdotally reported. These were primarily reported in day-centre patients rather than multiday stay patients.

## Aim

To review the incidence of infusion reactions associated with FDI and FCM, and identify any factors associated with the occurrence of reactions.

## Methods

A single centre retrospective cohort study was conducted at a tertiary/quaternary referral hospital. The EMR was used to identify all patients (day admission and multiday stay) who had been administered a rapid iron infusion (FCM or FDI) over a ten month period in 2021.

Low-dose iron as part of dialysis therapy was excluded, and remaining patients were randomised (using a random number generator in Microsoft Excel®) for inclusion in the sample.

The EMR was audited to retrieve the following data points:

- Patient demographics
- Patient characteristics associated with reactions to iron infusions
  - COVID-19 vaccination was hypothesised as a potential cause of increased reactions, due to the timeline of vaccine roll-out
  - Other patient characteristics were included based on literature review
- Iron infusion details
- Location of administration (day-centre vs inpatient ward)
- Documented adverse reaction to the iron infusion

Data were entered into an electronic database (RedCAP®) and statistical analysis undertaken using Mircosoft Excel® and R (version 4.2.2). Multivariable logistic regression analysis was undertaken to determine the effect of pre-determined variables on the odds of the outcome (reaction to rapid iron infusion).

## Results

A total of 1,817 iron infusions met the inclusion criteria. Of these, 450 were randomly selected for auditing:

- 276 (61.3%) FCM
- 174 (38.7%) FDI

Summary of infusion characteristics in table 1 below:

| | FCM | FDI |
|---|---|---|
| **Dose (mg)** | 1,000 (IQR=0) | 1,500 (IQR=500) |
| **Volume (mL)** | 250 (IQR=0) | 100 (IQR=0) |
| **Prescribed duration (minutes)** | 16 (IQR=0) | 30 (IQR=0) |

*Table 1: Summary of Iron Infusion Characteristics (continuous variables reported as median and interquartile range)*

Summary of patient demographics in table 2 below:

| | **FCM** (n=276) | **FDI** (n=174) |
|---|---|---|
| **Age (years)** | 58.5 (23.7) | 61.3 (22.5) |
| **Sex (male)** | 91 (33.0%) | 66 (37.9%) |
| **Weight (kg)** | 71.7 (20.0) | 78.7 (25.5) |
| **Location** | | |
| Day-centre | 140 (50.7%) | 69 (39.7%) |
| Inpatient ward | 136 (49.3%) | 105 (60.3%) |
| **Medication allergy/ADR** | | |
| NKDA | 184 (66.7%) | 105 (60.3%) |
| ≥ 1 allergy/ADR | 92 (33.3%) | 69 (39.7%) |
| **Co-morbidities** | | |
| Asthma | 13 (4.7%) | 13 (7.5%) |
| Eczema/atopic allergies | 10 (3.6%) | 6 (3.4%) |
| Inflammatory condition* | 34 (12.3%) | 34 (19.5%) |
| Anxiety | 13 (4.7%) | 9 (5.2%) |
| **COVID-19 vaccination status** | | |
| Fully vaccinated | 4 (1.4%) | 13 (7.5%) |
| Partially vaccinated | 4 (1.4%) | 39 (22.4%) |
| Not vaccinated/unknown | 268 (97.1%) | 122 (70.1%) |

*Table 2: Summary of Patient Demographics (continuous variables reported as mean and standard deviation, categorical variables reported as number and percent)*
**including, but not limited to: rheumatoid arthritis, systemic lupus erythematous*

### Adverse Reactions

The incidence of documented adverse reactions to rapid iron infusions is detailed in figure 1 below:

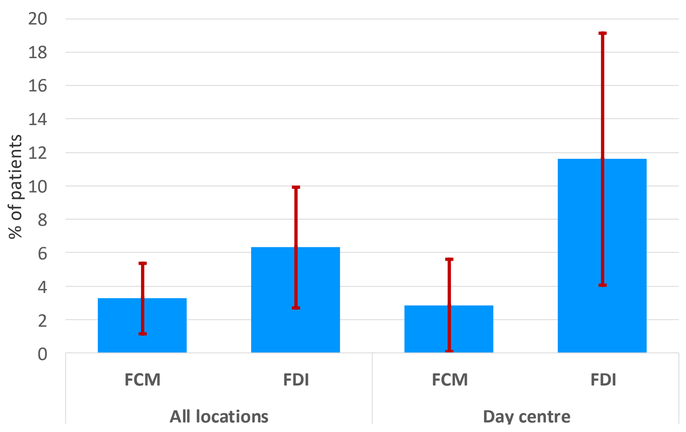


*Figure 1: Incidence of iron infusion reactions (percentage and 95% confidence interval (CI))*

Multivariable logistic regression analysis results are reported in table 3 below:

| | Odds Ratio | 95% CI | p value |
|---|---|---|---|
| **Location** | | | |
| Inpatient ward | ref | - | - |
| Day centre | 1.68 | 0.63 - 4.51 | 0.30 |
| **Anxiety** | 4.16 | 1.07 - 16.13 | 0.04 |
| **Multiple medication allergies*** | 3.04 | 0.73 - 12.66 | 0.12 |
| **Previous reaction to iron infusion** | 6.66 | 1.40 - 31.60 | 0.02 |
| **Iron formulation** | | | |
| Ferric derisomaltose | ref | - | - |
| Ferric carboxymaltose | 0.50 | 0.20 - 1.29 | 0.15 |

*Table 3: Multivariable logistic regression*

*ref=reference category*
** Defined as 3 or more allergies or ADRs*

A range of adverse reactions were reported. Refer to figure 2 below:

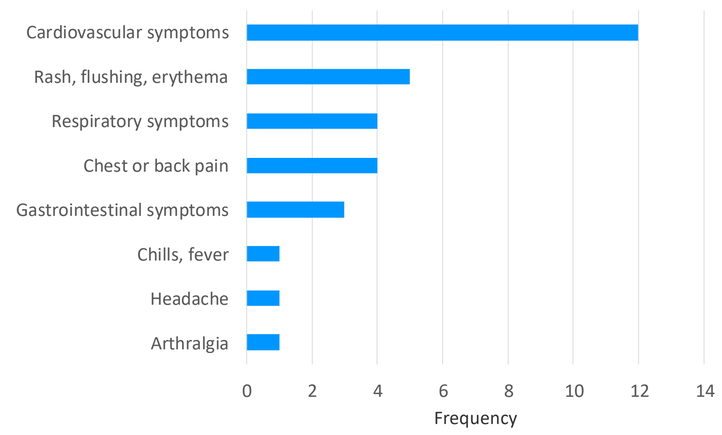


*Figure 2: Frequency of adverse reaction types reported (some patients experienced >1 adverse reaction type)*

## Discussion

A higher incidence of infusion reactions was observed in patients who received FDI, compared with FCM, especially in those who received iron infusions in the day centre. However, 95% CIs were wide (and overlapped) due small numbers of patients experiencing a reaction. The incidence of adverse reactions was similar to the ranges reported in the product information for both FCM and FDI.

Multivariable logistic regression analysis demonstrated previous reaction to an iron infusion and history of anxiety as factors associated with a higher odds ratio of having a reaction.

Despite anecdotal reports of more FDI reactions, formulation was not shown to be a variable that affected the odds of a reaction, once other factors were controlled for.

### Limitations

- Retrospective study:
  - Available data limited to what had been documented in the EMR. Lack of documented information was particularly evident for patients having iron administered in the day-centre.
  - Incomplete COVID-19 vaccination data (therefore not included in the model)
  - Limited information regarding delayed reactions, which can occur can occur up to two days following iron infusion. The majority of iron infusions administered to inpatients on the day of discharge, and nearly half of iron infusions were administered in the day-centre.
- Relatively small study, with low numbers of adverse reactions identified.
  - Larger study would increase precision of estimates and may be able to identify patient factors that increase the risk of iron infusion reactions with more certainty.

## Acknowledgements

- 2021/2022 SHPA summer placement students for assistance with data collection
- Study data were collected and managed using REDCap electronic data capture tools hosted by the Royal Melbourne Hospital Business Intelligence Unit

*For further information please contact Kerryn.Griffett@mh.org.au*