



# CEFTRIAXONE DOSING AND INFUSION TIME: EXPERIENCE IN FORTH VALLEY OPAT

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# AGENDA



Background

Methods

Results

Implications

# BACKGROUND

- European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoint for Methicillin Susceptible Staphylococcus Aureus (MSSA) recommend high (4g day<sup>-1</sup>) dosing in place of the standard (2g day<sup>-1</sup>) (1).
- The Scottish Antimicrobial Prescribing Group SAPG released guidance in February 2023 advising that 4g of ceftriaxone should be administered over 1 hour. This is based on manufacturer advice (2).
- The OPAT department at Forth Valley Royal Hospital (FVRH) use both the 2g and the 4 g doses for different indications. Currently we administer both doses of ceftriaxone over 30 minutes; as such, we do not follow SAPG guidelines
- Administering 4g of ceftriaxone over 1 hour would reduce the number of patients we could treat in the OPAT service
- We wanted to know if the higher dose of ceftriaxone are associated with a higher incidence of adverse effects, using our data set to investigate

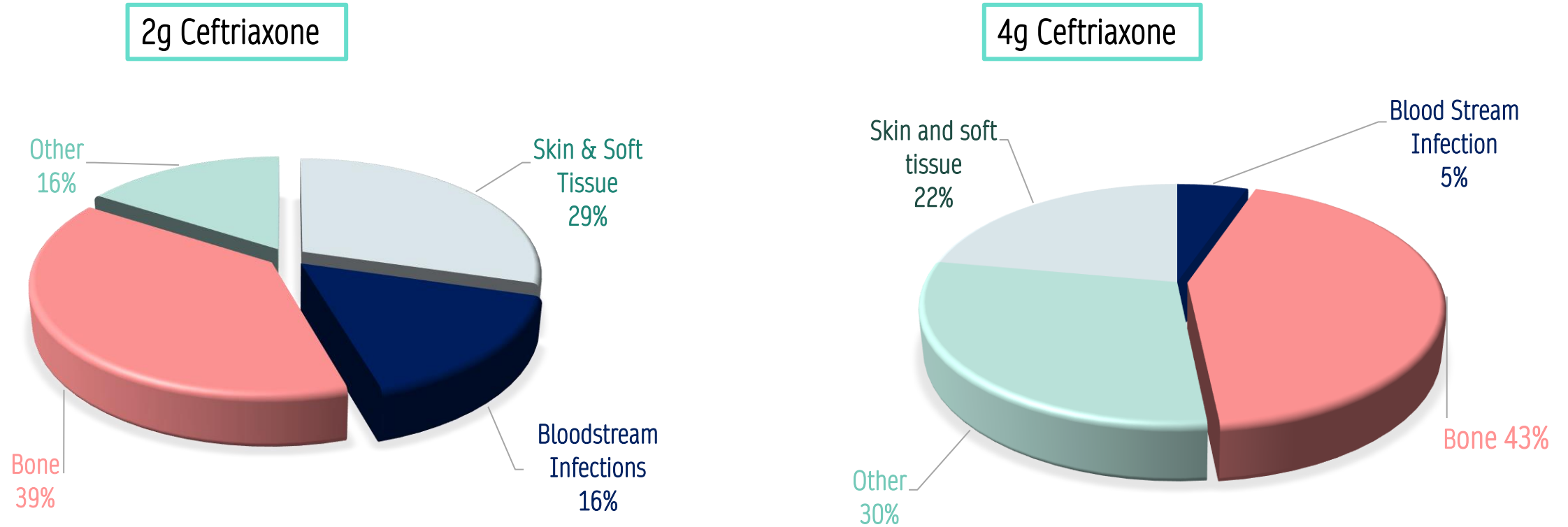
# METHODS

- Records of adult outpatients using the OPAT service between August 2018 and January 2023 were used
- We retrospectively collated data on ceftriaxone dose, patient demographics, type of infection, side effects, non-resolution of infection and need to switch to alternative antimicrobials
- We attempted to match the 2 groups (2g vs.4g), each of 88 patients, primarily in terms of source of infection, then age and then sex
- Side effects investigated were any new occurrence of:
  - Neutropenia  $<2.0 \times 10^9$ /litre
  - Thrombocytopenia  $<50.0 \times 10^9$ /litre
  - Rise in LFT X3 upper limit of normal
  - Rash
  - Diarrhoea

# RESULTS: BASELINE CHARACTERISTICS

PARAMETER	2G CEFTRIAXONE	4G CEFTRIAXONE	P VALUE <0.05
Number of patients	88	88	-
Mean Age (SD)	57.75 (15.0)	55.5 (15.4)	0.3
Number of females (%)	34 (38.2%)	33 (37.1%)	1.0
Median duration of ceftriaxone therapy in days (IQR)	13 (6-30.25)	21 (11-35.3)	<b><u>0.02</u></b>

# SOURCE OF INFECTION BY DOSE



**Fig. 1** Pie charts demonstrating the source of infection in the 2g ceftriaxone group (left) and 4 g ceftriaxone group (right)

# INFECTING ORGANISMS

Organism	2g Ceftriaxone		4g Ceftriaxone	
	Frequency	%	Frequency	%
<b>Staph. Aureus</b>	24	27.3	37	42.0
<b>No pathogen isolated</b>	43	48.9	32	36.4
<b>Beta-haemolytic streptococcus</b>	4	4.5	5	5.7
<b>Streptococcus viridans</b>	6	6.8	3	3.4
<b>Other</b>	11	12.5	11	12.5
<b>TOTAL</b>	<b>88</b>	<b>100.0</b>	<b>88</b>	<b>100.0</b>

# SIDE EFFECTS: NEUTROPENIA

PARAMETER	2G CEFTRIAZONE	4G CEFTRIAZONE	ODDS RATIO (95%CI)	P VALUE <0.05
Neutropenia <2.0 (%)	8 (9.0%)	9 (10.2%)	1.1 (0.4-3.1)	0.8
Clinically Significant Neutropenia <1.0 (%)	1 (1.1%)	3 (3.0%)	3.0 (0.3-30.1)	0.3
Mean number of treatment days neutropenia occurred	<b><u>14.6</u></b>		-	-
Severe sequelae (e.g. opportunistic infection)	0	0	-	-



# OTHER SIDE EFFECTS

PARAMETER	2G CEFTRIAZONE	4G CEFTRIAZONE	ODDS RADIO (95%CI)	P VALUE <0.05
Rise in ALT/ALP>3x ULN	0	2 (2.3%)	5.1 (0.24-108.1)	0.3
Thrombocytopenia <150 (%)	5 (5.7%)	10 (11.3%)	0.47 (0.2-1.4)	0.2
Clinically significant Thrombocytopenia <50	0	0	-	-

# OTHER SIDE EFFECTS

FVRH OPAT

PARAMETER	2G CEFTRIAZONE	4G CEFTRIAZONE	ODDS RADIO (95%CI)	P VALUE <0.05
Diarrhoea	2 (2.3%)	2 (2.3%)	1.0 (0.1-7.3)	1.0
Clostridioides difficile with diarrhoea	1 (1.1%)	0	0.3(0.01-8.2)	0.5
Rash (%)	0	1 (1.1%)	3.0 (0.1-75.5)	0.5

# OUTCOMES

PARAMETER	2G CEFTRIAZONE	4G CEFTRIAZONE	ODDS RATIO (95%CI)	P VALUE <0.05
Cessation due to all ceftriazone adverse effects (%)	0	5 (5.7%)	11.7 (0.6-214.1)	0.1
OR Adjusted by length of treatment (cut-off 13 days)	-	-	5.18 (0.61, 44.29)	0.1
Reason for early cessation of ceftriazone	-	3 x neutropenias (1x 0.5 and 2x 0.9  1 X new ALT/ALP rise (ALT 510)  1 x New Rash	-	-
Non-resolution of infection	4 (4.5%)	4 (4.5%)	1.0 (0.3-3.6)	1.0
Treatment failure any cause: S/E+ non- resolution of infection (%)	5 (5.7%)	9 (10.2%)	1.9 (0.6-5.9)	0.3

# STAPHYLOCOCCUS AUREUS SUBGROUP: BASELINE CHARACTERISTICS

PARAMETER	2G CEFTRIAXONE	4G CEFTRIAXONE	P VALUE <0.05
Number of patients	24	37	-
Mean Age in Years (STD)	56.7 (14.7)	52.9 (15.6)	0.3
Number Female (%)	8 (33.3%)	18 (48.6%)	0.3
Median duration of ceftriaxone therapy in days (IQR)	10.5 (6-13.5)	15 (11-34)	<b><u>0.01</u></b>

# SIDE EFFECTS

PARAMETER	2G CEFTRIAZONE	4G CEFTRIAZONE	ODDS RATIO (95%CI)	P VALUE < 0.05
Neutropenia <2.0 (%)	1 (4.1%)	3 (8.1%)	3.1 (0.3-30.1)	0.3
>ALT/ALP x3 (%)	0	2 (5.4%)	3.5 (0.2-75.1)	0.4
Thrombocytopenia <150 (%)	2 (8.3%)	4 (10.8%)	1.3 (0.2-7.9)	0.8
Diarrhoea	0	1 (2.7%)	2.0 (0.1-51.4)	0.7
Rash	0	1 (2.7%)	2.0 (0.1-51.4)	0.7

# STAPHYLOCOCCUS AUREUS OUTCOMES

FVRH OPAT

PARAMETER	2G CEFTRIAZONE	4G CEFTRIAZONE	ODDS RADIO (95%CI)	P VALUE <0.05
Cessation due to all ceftriazone adverse effects (%)	0	3(8.1%)	4.8 (0.2-97.8)	0.3
Reason for early cessation of ceftriazone	-	1X Neutropenia = 0.9 1 X ALT = 510 1X Rash	-	-
Non-resolution of infection	0	1(2.7%)	2.0(0.1-51.4)	0.7
Treatment failure any cause (%)	0	4(10.8%)	6.6(0.3-128.0)	0.2

# IMPLICATIONS OF FINDINGS

## SIDE EFFECTS MONITORING

- THERE IS SOME EVIDENCE OF INCREASED FREQUENCY OF SIDE EFFECTS WITH 4G OF CEFTRIAXONE GIVEN OVER 30 MINUTES VS. 2G GIVEN OVER 30 MINUTES, ALTHOUGH IT DID NOT REACH STATISTICAL SIGNIFICANCE (OR 11.7, 0.6-214.1 P=0.1)
- HOWEVER, SEVERE SIDE EFFECTS ARE ONLY SEEN IN 5-8% OF PATIENTS ON THE HIGHER DOSE AND RESOLVE QUICKLY AFTER CESSATION WITHOUT SIGNIFICANT SEQUELAE
- THIS EMPHASISES THE IMPORTANCE OF CLOSE MONITORING FOR SIDE EFFECTS

## POSSIBLE CONFOUNDERS

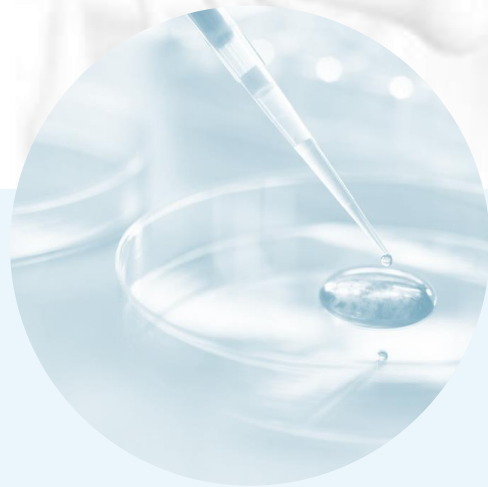
- WE ACKNOWLEDGE THAT WE WERE NOT COMPARING LIKE-FOR-LIKE: PATIENTS ON 4G WERE MORE LIKELY TO RECEIVE A LONGER COURSE AND BE MORE UNWELL AT BASELINE AS A RESULT OF HAVING A MORE DEEP-SEATED INFECTION
- THIS CONFOUNDED RESULTS
- WE WOULD LIKE TO OBTAIN A DATA SET WHERE 4G HAS BEEN ADMINISTERED OVER 1 HOUR IN PATIENTS WITH DEEP SEATED INFECTIONS
- PLEASE GET IN CONTACT IF YOU WOULD BE INTERESTED IN WORKING ON THIS WITH US!

# REFERENCE LIST

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- 1) European Committee on Antimicrobial Susceptibility Testing. Guidance Document on Cefotaxime and Ceftriaxone for Staphylococcus aureus infection. 2023. [eucast](#): The use of cefotaxime and ceftriaxone in S. aureus infections - guidance document. [Internet] Accessed 31/06/23. Available from: [Cefotaxime and Ceftriaxone for Staphylococcus aureus Infections - January 2023.pdf \(eucast.org\)](#)
- 2) Scottish Antimicrobial Prescribing Group (SAPG). Ceftriaxone: Adult outpatient parenteral antimicrobial therapy (OPAT) good practice prescribing guide [Internet]. Scottish Antimicrobial Prescribing Group; 2023. Accessed 31/06/23. Available from: [sapg-opat-gppg-ceftriaxone-feb-2023-final.pdf](#)





# THANK YOU



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