Open Journal of
Clinical & Medical
Case Reports

Volume 9 (2023)
Issue 29

Case Report ISSN: 2379-1039

Therapeutic drug monitoring of suppressive treatment with dalbavancin: Case report and review of the literature

Benjamin Valentin*; Sophie Putman; Benjamin Hennart; Odou Pascal; Caroline Loiez; Henri Migaud; Bertrand Decaudin; François Jehl; Eric Senneville

***Corresponding Author: Benjamin Valentin**
Clinical Pharmacist, CHU Lille, France.
Email: benjamin.valentin@chu-lille.fr

Abstract

The use of dalbavancin as a suppressive treatment is describe but not with therapeutic drug monitoring during a suppressive treatment. Our patient benefit of 20 month treatment of suppressive therapy with dalbavancin (1500 mg at each administration). Drug concentration was evaluated before re-administration. Interval of administration was discuted according to blood concentration of dalbavancin. The best interval of re-administration was each 6 week with an administration of 1500 mg for a patient without renal failure or hypoalbuminemia.

Keywords: Dalbavancin; Therapeutic drug monitoring; Prosthetic joint infection; Suppressive antibiotic treatment.

Introduction

Periprosthetic Joint Infections (PJIs) are difficult to treat and require medico-surgical management according to multidisciplinary setting. Suppressive Antibiotic Treatment (SAT) can be used when the infected implants cannot be exchanged or removed and when the conditions for optimal debridement with antibiotics and implant retention are not fulfilled. Dalbavancin (DAL) is a bactericidal lipoglycopeptide with a long half-life approved for skin and soft-tissue infections but is frequently used in off-label indications such as PJIs and SAT [1-3].

Case Presentation

A 47-year-old man, with a BMI of 25.7 kg/m^2, albuminemia of 47 g/L and normal serum creatinine was diagnosed with a polymicrobial infection of a total knee prosthesis due to methicillin-susceptible *Staphylococcus aureus*, *Enterococcus faecalis*, *Bacillus cereus* with minimal inhibitory concentrations for DAL

of 0.015 mg/L, 0.03 mg/L and 0.06 mg/L, respectively (broth microdilution). A treatment was initiated on February 2020 consisting in a 2 h intravenous administration of DAL 1,500 mg at D1 and D14 followed by repeated reinjections every 3 to 6 weeks depending on residual blood concentrations values. Table 1 describes the evolution of DAL residual concentrations before each re-administration. An analytical procedure based on liquid chromatography coupled with diode array detector has been developed to determinate blood concentration of DAL. The mean +/- SD trough concentrations of DAL were 22.1 ± 2.4 mg/L, 18.2 ± 4.1 mg/L and 9.3 ± 0.2 mg/L with a dosing interval of respectively, 21 days (n=8), 28 days (n=4) and 42 days (n=3). After 20 month of treatment, patient didn't present any infection due to gram positive. During the 20-month period of SAT, patient's tolerance to DAL was good with no adverse events identified.

Table 1: Dalbavancin trough blood concentration (mg/L) and delay since previous administration (days)).

Date of administration	Delay since previous administration (days)	Dalbavancin trough blood concentration (mg/L)
17.02.2020	14	26
04.03.2020	16	39.4
01.04.2020	28	27.5
04.05.2020	33	15.8
25.05.2020	21	16.6
15.06.2020	21	23.6
06.07.2020	21	22.4
27.07.2020	21	18.2
17.08.2020	21	21.8
07.09.2020	21	22.3
28.09.2020	21	25.1
19.10.2020	21	26.7
16.11.2020	28	26.4
14.12.2020	28	15.1
11.01.2021	28	17.8
08.02.2021	28	13.4
22.03.2021	42	9.3
03.05.2021	42	9
14.06.2021	42	9.7
16.07.2021	32	13.4
30.07.2021	14	32.1
09.09.2021	41	12.5
18.10.2021	39	11.3

Discussion

We present herein the first case of SAT with DAL to treat a polymicrobial PJI and for which therapeutic drug monitorinig was performed. In the literature, a total of 9 patients treated with DAL as SAT for various infections (cardiac/vascular [1,4,5] and orthopedic [6-8] devices in 6 and 3 cases, respectively. The results of plasma concentrations of DAL were reported in only one case. Infections were monomicrobial,

due to Gram-positive cocci (*Staphylococcus* spp., *Streptococcus* spp., and *Enterococcus* spp.). DAL dosages were highly variable, ranging from 350 - 1000 mg per week [1] to 1500 mg every 4 weeks [8]. The authors did not report any dosing adaptation of DAL based on trough plasma concentration values except in the study from Spaziente et al. [5] in which the serum bacterial activity was measured to determine the most appropriate time for the next reinjection.

The main interest of our report was to describe a therapeutic drug monitoring of DAL before each re-administration for a long period of time (i.e., 20 months). Andes and coll [9] defined the *area* under the concentrations curve/MIC (AUC/MIC) as the pharmacodynamic (PK/PD) parameter of interest for DAL against *S. aureus* with target values established at 50 and 100 for 1-log and 2-log bacterial counts reductions respectively in a neutropenic mice model. The DAL breakpoint of 0,125 mg/l defining susceptible *S. aureus* strain is likely to easily allow to reach this target with a probability >90% (PTA>90%). This was confirmed by Cojutti et al. [10] who proposed that a total DAL concentration ≥ 8.04 mg/L was likely to ensure ≥90% probability of pharmacodynamic target attainment against *S. aureus* with an MIC = 0.125 mg/L. A targeted trough concentration of DAL ≥ 20 mg/L could takes into account some potential interindividual variations due to multiple parameters affecting the total clearance of DAL such as creatinine clearance, body weight, and albumin, uncertainty of MIC evaluation and the reduction of DAL activity in the context of chronic infections involving biofilms [11]. Indeed, the aim of SAT is to maintain a remission status during which the bacterial load and metabolic activity are likely to be limited in comparison to an active infection.

Conclusions

SAT with DAL seems to be a potential option in patients with resistant Gram positive cocci PJIs where the other alternatives are not possible. The good tolerance of DAL and the absence of drug-drug interactions increase the probability to complete the scheduled duration of the treatment with injections of 1500 mg every 5 to 6 weeks.

Declarations

Acknowledgements: Thanks to the members of the CRIOAC Lille Tourcoing.

Fundings: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Transparency declarations: ES has received honoraria for speaker buro, advisory board, HM is Chief editor Orthopaedics & Traumatology: Surgery & Research (Elsevier), and received outside the scope of the current study consultancy fees from Zimmer-Biomet, Corin-Tornier and MSD. SP received outside the scope of the current study consultancy fees from Zimmer-Biomet, Corin-Tornier.

Co-authors participation: BV and ES wrote the manuscript, SP and HM participated in the surgical management of the patient, BH performed the DAL dosages, CL performed the antibiotic susceptibility profile of the bacterial strains, PO, BD and FJ reviewed the manuscript.

References

1. Hitzenbichler F, Mohr A, Camboni D, Simon M, Salzberger B, et al. Dalbavancin as long-term suppressive therapy for patients with Gram-positive bacteremia due to an intravascular source-a series of four cases. Infection. févr. 2021; 49: 181-6.

2. xydalba-epar-product-information_fr.pdf. Disponible sur: https://www.ema.europa.eu/en/documents/product-information/xydalba-epar-product-information_fr.pdf

3. Morata L, Cobo J, Fernández-Sampedro M, Guisado Vasco P, Ruano E, et al. Safety and Efficacy of Prolonged Use of Dalbavancin in Bone and Joint Infections. Antimicrob Agents Chemother. Mai 2019; 63: e02280-18.

4. Howard-Anderson J, Pouch SM, Sexton ME, Mehta AK, Smith AL, et al. Left Ventricular Assist Device Infections and the Potential Role for Dalbavancin: A Case Report. Open Forum Infect Dis. Sept 2019; 6: ofz235.

5. Spaziante M, Franchi C, Taliani G, D'Avolio A, Pietropaolo V, et al. Serum Bactericidal Activity Levels Monitor to Guide Intravenous Dalbavancin Chronic Suppressive Therapy of Inoperable Staphylococcal Prosthetic Valve Endocarditis: A Case Report. Open Forum Infect Dis. 2019; 6: ofz427.

6. Núñez-Núñez M, Casas-Hidalgo I, García-Fumero R, Vallejo-Rodríguez I, Anguita-Santos F, et al. Dalbavancin is a novel antimicrobial against Gram-positive pathogens: clinical experience beyond labelled indications. Eur J Hosp Pharm. 2020; 27: 310-2.

7. Matesanz M, Poza A, Iñurrieta A, Fernández-Diaz E, Arroyo M, et al. Dalbavancin was effective and safe after one year of treatment in a complicated osteoarticular infection caused by methicillin-resistant Staphylococcus aureus. Rev Esp Quimioter. 2021; 34: 396-9.

8. Barbero Allende JM, García Sánchez M, Culebras López AM, Agudo Alonso R. [Suppressive antibiotic treatment with dalbavancin. A case report]. Rev Esp Quimioter. avr. 2021; 34: 151-3.

9. Andes D, Craig WA. In vivo pharmacodynamic activity of the glycopeptide dalbavancin. Antimicrob Agents Chemother. mai. 2007; 51: 1633-42.

10. Cojutti PG, Rinaldi M, Zamparini E, Rossi N, Tedeschi S, et al. Population pharmacokinetics of dalbavancin and dosing consideration for optimal treatment of adult patients with staphylococcal osteoarticular infections. Antimicrob Agents Chemother. 2021; AAC: 02260-20.

11. Carrothers TJ, Chittenden JT, Critchley I. Dalbavancin Population Pharmacokinetic Modeling and Target Attainment Analysis. Clin Pharmacol Drug Dev. janv. 2020; 9: 21-31.

Manuscript Information: Received: July 11, 2023; August 22, 2023; Published: August 31, 2023

Authors Information: Benjamin Valentin[1]*; Sophie Putman[1]; Benjamin Hennart[1]; Odou Pascal[1]; Caroline Loiez[1]; Henri Migaud[1]; Bertrand Decaudin[1]; François Jehl[2]; Eric Senneville[3]

[1]Hospital University of Lille, F-59000 Lille, France.

[2]Hospital University of Strasbourg, Pharmacy, F-67000, France.

[3]Infectious Diseases Department, Gustave Dron Hospital, 59200 Tourcoing, France.

Citation: Benjamin V, Sophie P, Benjamin H, Odou P, Caroline L, Migaud H, Decaudin B, et al. Therapeutic drug monitoring of suppressive treatment with dalbavancin: Case report and review of the literature. Open J Clin Med Case Rep. 2023; 2100.