

## **Case study**

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### **Safety and efficacy profile of CSE-1034 as a prolonged de-escalation therapy in prosthetic joint infection: A case report**

#### **Abstract**

##### **Background**

Although rare, infection is considered to be most dreadful of the prosthetic related complications resulting in repeated surgical intervention, extended hospitalization or sometimes in loss of implant or permanent disability if not treated promptly. Poor treatment outcome associated with prosthetic joint infections (PJIs) could be partly attributed to rise in anti-microbial resistance among the causative agents.

##### **Case presentation**

This is a first reported case of ceftriaxone + sulbactam + ethylenediaminetetraacetic acid (CSE 1034) being used as an de-escalation therapy for more than 24 days with good safety and efficacy outcome in a 78 year male patient with PJI associated with hip replacement surgery, treated initially with meropenem and colistin followed by prolonged de-escalation therapy (24 days).

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- Comment [VS2]: s
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- Comment [VS4]: prosthetic joint infection (PJI)

##### **Conclusions**

In clinically complicated cases of deep infections where prolonged use of last resort antibiotics is used, CSE-1034 can be considered as a safe, efficacious and economical de-escalating antibiotic to complete the treatment course and prevent recurrence of infection, especially in PJI.

29 **Introduction**

30 The number of hip replacement surgeries has rapidly increased in recent years. The joint  
31 prosthesis is recognized as one of the most successful surgical interventions in medicine and  
32 provides significant reduction in pain, improves joint function and minimizes disability [1]. The  
33 worldwide literature survey has shown infection rates for primary total hip revision to be 1-2%  
34 and higher in cases undergoing revised total hip surgeries [2][3]. Although rare, infections  
35 following joint replacement surgery are the most devastating prosthetic-related complications  
36 and challenging to treat [3].

37 Prevention of prosthetic joint infections is of utmost importance, and success in treating  
38 these infections depends on extensive debridement, removal of dead and extraneous tissue and  
39 most importantly effective antibiotic therapy [4]. Antibiotics form an important part of current  
40 medical care and effective antibiotic prophylaxis constitutes an important part in the treatment of  
41 bacterial infections. Although infections following joint prosthetic surgeries are rare, however  
42 with emerging bacterial resistance, its occurrence can be increasingly difficult to eradicate [5][6]  
43 PJIs with drug resistant pathogens may require prolonged medical management resulting in  
44 extended and expensive hospital stays, repeated surgical intervention and sometimes can end up  
45 in definitive loss of implant [5]. The failure of first choice of antibiotic used in empirical therapy  
46 requires the treatment with second or third choice drugs that could be more expensive, less  
47 effective and indeed more toxic. Here, **we** present a case of post-surgical infection treated  
48 initially with a combination of meropenem and colistin followed by de-escalation therapy of  
49 CSE-1034.

**Comment [VS5]:** Researchers

50 **Case presentation**

51 A 78 year old male was admitted to **our** department with chief complain of oozing at  
52 operation site. He also complained of pain in left hip joint with instability while walking.

**Comment [VS6]:** Name of the department should be mentioned.

53 The patient's medical history showed that he was operated for total left hip replacement  
54 (THR) **recently**. He also had a history of diabetes, hypertension and ischemic heart disease.  
55 Moreover, the patient had also undergone coronary artery bypass grafting (CABG) about 8 years  
56 ago. After recently performed hip replacement surgery, the patient complained of occasional  
57 pain. PBH X-ray had shown femur splinting in proximal medial aspect and the patient was re-

**Comment [VS7]:** Period should be mentioned.

58 operated for tension wiring of implant and started with meropenem. On the post operation third  
59 day patient had an episode of rigor, the patient was transferred from surgery ward to our  
60 department, for further treatment management. Physical examination revealed the patient to be  
61 afebrile with all his vitals normal, temperature: 98.4°F, blood pressure: 120/90, pulse: 78/min.  
62 Systemic examination of central nervous system showed the patient was conscious and oriented,  
63 cardiovascular examination revealed S1 and S2 within normal limits, per abdomen was soft and  
64 non-tender and respiratory system was clear. Hematology tests done revealed deranged TLC  
65 count (18500/cu-mm) with neutrophil count on higher side ( $6.58 \times 10^3$  cells/cu-mm), normal  
66 hemoglobin (11.8 g/dl); raised ESR (45 mm/hr.) and hs-CRP (10.4 mg/dL) levels. Venous  
67 Doppler of both lower limbs showed normal flow in both lower limbs veins with no deep vein  
68 thrombosis. Mild sub-cutaneous edema was observed in left leg on both sides and continuous  
69 discharge from the operation site was noticed. Because of continuous discharge from wound;  
70 surgical site wash, wound exploration and debridement of all deep infected tissues above fascia  
71 and below deep fascia were performed. In the process, pulse lavage of the wound was done with  
72 3-4 liters of normal saline. After wound cleansing, closure was done in layers followed by  
73 dressing. Wound discharge was forwarded to laboratory for culture and sensitivity testing. Based  
74 on Musculoskeletal Infection Society criteria, a provisional diagnosis of PJI was arrived at, and  
75 the patient was re-shifted to ICU and started immediately with intravenous (IV) dose of  
76 antibiotics (meropenem + colistin) and other supportive treatment. The antibiotic choice was  
77 based on the hospital antibiogram data and the patient's hematological parameters. Laboratory  
78 culture and sensitivity report didn't reveal any pathogenic growth. After 48hr of ongoing  
79 antibiotic treatment, the patient was observed to respond to treatment and the exudates from the  
80 surgical site started decreasing. The patient continued to receive same IV treatment with  
81 antibiotics for 7 days. Repeat hematological tests and other parameters confirmed patient's  
82 improvement. On 8<sup>th</sup> day of admission, the patient was shifted to de-escalation therapy of CSE-  
83 1034 (3gm/12hr), considering its broad-spectrum activity in targeting various resistant  
84 mechanisms of pathogens. The patients responded well to the de-escalation treatment and was  
85 thus continued with CSE-1034. After 10 days of treatment, the patient was hemodynamically  
86 stable and shifted to ward. He was discharged on 18<sup>th</sup> day of admission and advised to continue  
87 CSE-1034 1.5 gm /12hr via IV and other basic supportive medicine for 2 weeks. The patient was  
88 advised for follow-up and to report immediately in case of fever, pain at operation site,

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89 convulsions, headache, chest pain and breathlessness and loss of consciousness. On regular  
90 follow-ups and clinical examination, it was observed that the patient didn't show any sign and  
91 symptoms of recurrence or superinfection and was hemodynamically stable.

Comment [VS16]: super infection

## 92 Discussion

93 Despite the high success rate, joint prosthetic surgeries are not without complications. Of  
94 all prosthetic related complications, infection is probably the most threatening one. Although  
95 rare, prosthetic infections after total hip replacement surgeries require prolonged surgical and  
96 medical management. The costs of treating an infection after THR are reported to a minimum  
97 amount of 50,000 US dollars per patient. Moreover, the steep rise in the number of operations for  
98 implanting these prostheses in past few years, has been simultaneously accompanied by number  
99 of PJIs [7]. Although, the recent technical advances in the field of medicine accompanied by use  
100 of laminar air flow, exhaust systems, antibiotic-loaded acrylic bone cement and antibiotics have  
101 all contributed to reduced infection rate, however PJIs still occur in 1-3% of patients[7].

Comment [VS17]: total hip replacement (THR)

102 Frequently, the organisms implicated in infected prosthetic joints are usually relatively  
103 benign organisms or simple contaminants. These microorganisms may penetrate wound during  
104 surgical procedures from both endogenous and exogenous sources including patient's external  
105 microbiota, microbiota of surrounding surgical team, hospital environment, surgical instruments  
106 and even contaminated implants. PJIs that develop during first year after prosthetic implant are  
107 considered to be SSIs and are usually treated using broad spectrum antibiotics. Though broad  
108 spectrum, anti-microbial therapy at the time of induction is given, that helps to cut the risk of  
109 infection at the surgical site [8]. These benign microorganisms tend to become pathogenic taking  
110 advantage of suppressed immune system, associated co-morbidities along with sterile surgical  
111 sites making certain individuals more vulnerable to infections.

112 Here, we present a case report of PJI treated successfully with initial therapy of  
113 meropenem + colistin, and de-escalation therapy of CSE-1034. The patient responded well to the  
114 treatment and was discharged on 18<sup>th</sup> day of admission with the advice to continue CSE-1034 for  
115 2 weeks. Hence the present report highlights the importance of CSE-1034 in deep infections  
116 usually treated with only last resort antibiotics. The normal course of antibiotic treatment for PJIs  
117 extends from 4-6 weeks. Moreover, drug induced thrombocytopenia is reported in patients

Comment [VS18]: Researchers

118 undergoing meropenem treatment for more than 10 days[9]. Thus, in deep infection cases where  
119 carbapenems are used empirically and the treatment duration extends from 4-6 weeks, CSE-1034  
120 can be used as deescalating antibiotic to complete the treatment course and cure the infection  
121 without observing any side effects associated with prolonged meropenem therapy and  
122 compromising the safety of patients. In support of our outcome, various studies in the past have  
123 documented CSE-1034 as an effective treatment for MDR bacterial infections alone or as  
124 combination therapy with colistin [10][11]. |This unique case study highlights the safety and  
125 efficacy profile in prolonged duration treatment modules along with dramatic reduction in  
126 treatment-related costs, if CSE-1034 is used in de-escalation therapy in treating PJI.

Comment [VS19]: Conclusion

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## 128 **References**

Comment [VS20]: Rechecked

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