MENTORS IN ORTHOPEDICS

TREATMENT OF ORTHOPAEDIC INFECTIONS USING CONTINUOUS LOCAL ANTIBIOTIC PERFUSION

https://doi.org/10.71165/eovt-24zf

AUTHORS

Hyonmin Choe - Yokohama City University, Yokohama, Japon
Yutaka Inaba - Yokohama City University, Yokohama, Japon

SUMMARY

Background: Management of orthopedic implant-related infections is complicated by bacterial biofilms, which provide a protective environment against host immune responses and systemic antimicrobial agents. Standard systemic therapy often fails to reach the minimum biofilm eradication concentration (MBEC), necessitating local delivery strategies to address periprosthetic joint infections, fracture-related infections, and osteomyelitis.

Objective: This article evaluates the methodology, clinical applications, and current evidence regarding continuous local antibiotic perfusion (CLAP) as a technique for delivering high-concentration antimicrobials to infected orthopedic sites.

Key Points: CLAP utilizes low-flow antibiotic infusion into intramedullary (iMAP), soft tissue (iSAP), or intra-articular (iJAP) compartments combined with negative pressure wound therapy (NPWT). This dual-action system facilitates continuous drainage of exudates while maintaining high local drug concentrations targeting the MBEC. Clinical data indicate high rates of implant retention and bone union in fracture-related infections and successful outcomes in spinal surgical site infections and fungal periprosthetic joint infections. Despite these results, challenges remain regarding the standardization of infusion protocols, potential bone toxicity from high-concentration aminoglycosides, and the risk of renal impairment. Current evidence is primarily limited to retrospective cohorts and case series.

Conclusion: CLAP represents a specialized local delivery strategy that may allow for implant preservation in refractory orthopedic infections. While initial clinical outcomes are favorable, prospective trials are required to establish standardized dosing, safety benchmarks, and definitive indications for its application in musculoskeletal infection management.

KEYWORDS

Prosthesis-Related Infections; Anti-Bacterial Agents; Biofilms; Negative-Pressure Wound Therapy; Osteomyelitis

INTRODUCTION

One of the major challenges in treating orthopedic implant-related infections is the formation of bacterial biofilms, which significantly contribute to treatment resistance. Although systemic administration of antibiotics is the standard approach to managing bacterial infections, biofilms formed at the site of infection are known to protect bacteria from immune cells and confer high levels of resistance to antibiotics [1]. As a result, systemic antibiotics often fail to achieve therapeutic efficacy in periprosthetic joint infections (PJI).

The commonly used indicator for antibiotic effectiveness, the minimum inhibitory concentration (MIC), is not clinically meaningful in the context of biofilm-associated infections [1],[2]. This is because MIC represents the lowest concentration of antibiotics required to inhibit the growth of planktonic (free-floating) bacteria [2]. In contrast, to assess the efficacy of antibiotics against biofilms, the minimum biofilm eradication concentration (MBEC) must be considered. MBEC values are reported to be tens to hundreds of times higher than the MIC [3].

Achieving MBEC through systemic antibiotic administration is extremely difficult. Therefore, in many cases of implant-related infections, in addition to surgical debridement and irrigation, local administration of antiseptics or high-concentration antibiotics is required. Traditionally, antibiotic-loaded spacers, such as those made from bone cement, have been used to deliver high concentrations of antibiotics locally [2]. More recently, intra-articular catheters [4],[5], intramedullary antibiotic infusion [6], and resorbable antibiotic gels [7],[8] applied around implants have shown promise in enhancing local antibiotic delivery. Continuous local antibiotic perfusion (CLAP) , a technique developed primarily in Japan, has been increasingly reported as an effective technique for managing implant-associated infections. CLAP is a technique that enables the perfusion of high-concentration antibiotics directly at the site of infection. Since its first report in treating implant-related infections following trauma surgery, CLAP has been applied across various fields of orthopedic infections with promising outcomes [9],[10],[11],[12],[13],[14]. A key feature of CLAP is the simultaneous use of low-flow antibiotic infusion into the infected site and negative pressure wound therapy (NPWT), which facilitates continuous drainage of hematomas and exudates after surgery. This approach allows antibiotics to circulate without stagnation within the infected area. Conventional antibiotic irrigation methods often relied on high-flow systems, which led to leakage from the surgical wound and made postoperative wound management challenging. In contrast, CLAP uses low-flow perfusion combined with sustained negative pressure drainage via NPWT, resulting in improved wound control and stability (Figure 1). In Japan, the Salem Sump tube—a double-lumen catheter originally developed for gastric lavage—is most commonly used for antibiotic perfusion and hematoma drainage in CLAP procedures. However, it is important to note that this device is not originally intended for use in joints or soft tissues. Therefore, its off-label application in such cases requires institutional approval and informed consent from the patient.

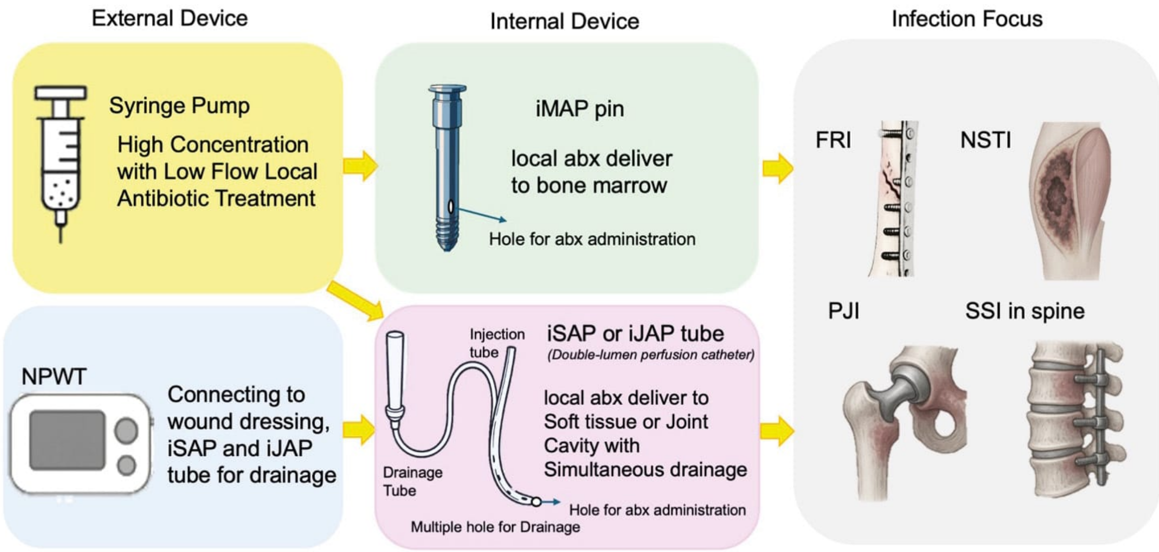

Figure 1

BASIC PRINCIPLES AND METHODOLOGY OF CLAP

Continuous Local Antibiotic Perfusion (CLAP) is a therapeutic technique designed to deliver high concentrations of antibiotics locally, targeting the MBEC. This method involves low-flow antibiotic perfusion into the intramedullary canal (intra-Medullary Antibiotics Perfusion: iMAP), soft tissue (intra-Soft tissue Antibiotics Perfusion: iSAP), or joint space (intra-Joint Antibiotics Perfusion: iJAP)(Table 1). By connecting a continuous negative pressure device to the iJAP or iSAP tube, sustained drainage is achieved at the infected site or within the joint, creating a negative pressure gradient that facilitates directed antibiotic perfusion (Figure 1).

iMAP Pin	A bone marrow needle that is inserted into the infected bone to deliver high-concentration antibiotics directly into the intramedullary space.
iSAP tube	A double-lumen drain that is placed within the soft tissue infection site, allowing simultaneous high-concentration antibiotic delivery and drainage.
iJAP tube	A double-lumen drain is placed intra-articularly to enable continuous antibiotic perfusion along with drainage from the joint cavity.
NPWT	NPWT provides continuous suction and drainage from the infected area by connecting to the iSAP or iJAP tubes.
Syringe Pump	Used to continuously deliver high-concentration antibiotics such as gentamicin (typically at 1200 mg/mL) at a low infusion rate (e.g., 2 mL/hr)

Table 1: Items used for CLAP iMAP: Intra-Medullary Antibiotics Perfusion, iSAP: Intra-Soft tissue Antibiotics Perfusion, iJAP: Intra-Joint Antibiotics Perfusion, NPWT: Negative Pressure Wound Therapy

For the appropriate use of CLAP, preoperative and intraoperative evaluation of the infection site is crucial. Preoperative imaging, including CT, MRI, and nuclear medicine studies, should be used to identify abscess formation, the extent of osteomyelitis, and other relevant findings. During surgery, it is important to assess for the presence of subcutaneous pockets and delineate the extent of dead space. During debridement, care should be taken to preserve as much healthy tissue as possible, and anatomical reconstruction of the soft tissue should be performed at wound closure to ensure effective perfusion with CLAP. Postoperatively, the CLAP system should be monitored daily. Based on intraoperative assessment, daily flushing of the antibiotic perfusion system should be performed as needed.

OVERVIEW OF RESEARCH ON CONTINUOUS LOCAL ANTIBIOTIC PERFUSION (CLAP)

In recent years, CLAP has attracted increasing attention as a novel treatment strategy for refractory infections in the field of orthopedic surgery. This approach enables the continuous local delivery of high-concentration antibiotics to infected sites, including those with biofilm formation, such as implant-associated infections, osteomyelitis, and deep soft tissue infections. By doing so, CLAP aims to achieve the Minimum Biofilm Eradication Concentration (MBEC), a therapeutic threshold that is difficult to attain with systemic antibiotic administration alone.

Published reports on CLAP span a wide range of clinical scenarios, including fracture-related infections (FRI), periprosthetic joint infections (PJI), postoperative spinal infections, necrotizing fasciitis, pediatric Brodie abscesses, and infections following frozen bone grafts. The technique has been applied in both acute and chronic infections, as well as in bacterial and fungal infections, including those caused by multidrug-resistant organisms such as MRSA. Many studies emphasize the preservation of implants, even in cases where implant removal or revision surgery would have been considered necessary under conventional treatment approaches. Favorable clinical outcomes have also been reported in retrospective cohort studies on chronic osteomyelitis, multicenter studies on postoperative spinal infections, and fungal PJIs.

The application of Continuous Local Antibiotic Perfusion (CLAP) for fracture-related infections (FRI) has gained momentum as a treatment strategy aimed at achieving both bone union and implant retention. Particularly in diaphyseal infections and nonunions—common and challenging scenarios—CLAP has shown promising results. Maruo et al. reported a bone union rate of 95% and an implant retention rate of 88% using iMAP for early FRI, demonstrating its effectiveness in avoiding reoperations [12]. Furthermore, Sawauchi et al. described successful healing of a tibial nonunion using a combination of CLAP and bone grafting [15]. In the treatment of periprosthetic joint infections (PJI), CLAP has been increasingly adopted as an adjunct to the Debridement, Antibiotics, and Implant Retention (DAIR) procedure, including for fungal infections [9],[14]. Choe et al. were the first to report the successful use of CLAP in combination with antifungal therapy for fungal PJI, suggesting its potential in infection control and implant preservation [9],[14],[16],[17],[18],[19]. Additional reports include Zenk et al., who demonstrated the utility of CLAP combined with DAIR in chronic TKA PJI [9],[14],[20].

CLAP has also drawn attention as a treatment option for surgical site infections (SSI) following spinal instrumentation surgery [21],[13]. It has shown high rates of implant retention and reduced need for reoperation, with early intervention identified as a key factor for success. Takahashi et al. reported that CLAP enabled implant preservation and demonstrated its effectiveness as an initial treatment strategy. A multicenter retrospective study further confirmed an 82% infection control rate, highlighting early introduction as a predictor of success [13].

Efficacy of CLAP has been demonsotrated in several case reports including refractory spondylitis [22], post-open fracture infections [23] and chronic osteomyelitis [24], necrotizing fasciitis [25], gas-forming vertebral osteomyelitis [26], frozen bone autograft infection [27], and Brodie's abscess in pediatric patients [28], confirming its flexibility and scalability as a strategy for localized infection control.

As indications for CLAP continue to expand, evaluating its safety—particularly regarding bone toxicity and renal function of high concentration gentamycin—has become an urgent priority. Yamamoto et al. conducted in vitro assessments of the cytotoxic effects of high-concentration antibiotics on osteocytes [29], while Fujihara et al. investigated risk factors for renal impairment during CLAP therapy [30]. These studies represent ongoing efforts to establish safety benchmarks through both basic and clinical research. Furthermore, with the accumulation of

Japanese case reports and review articles, international dissemination of knowledge on CLAP is beginning to emerge.

LIMITATIONS, CHALLENGES, AND FUTURE DIRECTIONS

Despite the promising results of CLAP in treating orthopedic infections, several limitations and challenges remain. First, there is currently a lack of standardized protocols regarding antibiotic selection, dosage, duration of administration, and infusion rate. In addition, the use of CLAP requires close monitoring of renal function and serum antibiotic concentrations to ensure patient safety. The placement of iMAP pins or iSAP/iJAP catheters demands careful preoperative planning and a high level of technical expertise, along with sufficient knowledge of CLAP itself. Most importantly, the current evidence supporting CLAP is primarily based on retrospective studies, and randomized controlled trials have yet to be conducted. Therefore, future research should focus on establishing a consensus on appropriate antibiotic agents, optimal concentrations, treatment duration, and clear indications for implant retention.

In summary, CLAP represents a promising therapeutic option for managing refractory orthopedic infections. It offers several advantages, including implant retention, targeted local therapy with reduced systemic toxicity, continues drainages. However, most of the current evidence is based on case reports and retrospective studies. Future challenges include the need for prospective clinical trials, standardization of treatment protocols, and long-term safety assessments.

REFERENCES

1. Saeed K, McLaren AC, Schwarz EM, Antoci V, et al.,2019.2018 international consensus meeting on musculoskeletal infection: Summary from the biofilm workgroup and consensus on biofilm related musculoskeletal infections. J Orthop Res,37 5: 1007-1017.

2. Schwarz EM, McLaren AC, Sculco TP, Brause B, et al.,2020.Adjuvant antibiotic-loaded bone cement: Concerns with current use and research to make it work. J Orthop Res.

3. Ceri H, Olson ME, Stremick C, Read RR, et al.,1999.The Calgary Biofilm Device: new technology for rapid determination of antibiotic susceptibilities of bacterial biofilms. J Clin Microbiol,37 6: 1771-1776.

4. Whiteside LA, Roy ME, Nayfeh TA,2016.Intra-articular infusion: a direct approach to treatment of infected total knee arthroplasty. Bone Joint J,98-B 1 Suppl A: 31-36.

5. Whiteside LA, Roy ME,2017.One-stage Revision With Catheter Infusion of Intraarticular Antibiotics Successfully Treats Infected THA. Clin Orthop Relat Res, 475 2: 419-429.

6. Park KJ, Chapleau J, Sullivan TC, Clyburn TA, Incavo SJ,2021.2021 Chitranjan S. Ranawat Award: Intraosseous vancomycin reduces periprosthetic joint infection in primary total knee arthroplasty at 90-day follow-up. Bone Joint J,103-B 6 Supple A: 13-17.

7. Casadidio C, Butini ME, Trampuz A, Di Luca M, et al.,2018.Daptomycin-loaded biodegradable thermosensitive hydrogels enhance drug stability and foster bactericidal activity against Staphylococcus aureus. Eur J Pharm Biopharm,130 260-271.

8. Tsikopoulos K, Bidossi A, Drago L, Petrenyov DR, et al.,2019.Is Implant Coating With Tyrosol- and Antibiotic-loaded Hydrogel Effective in Reducing Cutibacterium (Propionibacterium) acnes Biofilm Formation? A Preliminary In Vitro Study. Clin Orthop Relat Res,477 7: 1736-1746.

9. Choe H, Maruo A, Hieda Y, Abe K, et al.,2023.Novel Local Antifungal Treatment for Fungal Periprosthetic Joint Infection With Continuous Local Antibiotic Perfusion: A Surgical Technique. Arthroplast Today,24 101245.

10. Himeno D, Matsuura Y, Maruo A, Ohtori S,2022.A novel treatment strategy using continuous local antibiotic perfusion: A case series study of a refractory infection caused by hypervirulent Klebsiella pneumoniae. J Orthop Sci,27 1: 272-280.

11. Maruo A, Oda T, Mineo R, Miya H, et al.,2022.Continuous local antibiotic perfusion: A treatment strategy that allows implant retention in fracture-related infections. J Orthop Surg (Hong Kong),30 2: 10225536221111902.

12. Maruo A, Oda T, Miya H, Muratsu H, et al.,2021.Intra-medullary antibiotics perfusion (iMAP) for the control of fracture-related infection early after osteosynthesis. J Orthop Surg (Hong Kong),29 3: 23094990211051492.

13. Takahashi H, Okuyama K, Toki Y, Funayama T, et al.,2025.Efficacy and Limitations of Continuous Local Antibiotic Perfusion in Treating Surgical Site Infections Following Instrumented Spinal Surgery: A Retrospective Multicenter Study. Infect Dis Ther,14 2: 421-431.

14. Zenke Y, Motojima Y, Ando K, Kosugi K, et al.,2024.DAIR in treating chronic PJI after total knee arthroplasty using continuous local antibiotic perfusion therapy: a case series study. BMC Musculoskelet Disord,25 1: 36.

15. Sawauchi K, Fukui T, Oe K, Kuroda R, et al.,2024.Management of Infected Tibial Nonunion: Combining Synthetic Bone Grafting with Continuous Local Antibiotic Perfusion (CLAP). Am J Case Rep,25 e945023.

16. Iwamoto K, Yamamoto N, Saiga K, Maruo A, et al.,2024.Prosthetic joint infection after total talar replacement: An implant-retained case treated with combined continuous local antibiotic perfusion (CLAP). J Orthop Sci,29 1: 349-353.

17. Miyake Y, Takagi T,2024.Treatment experience with continuous local antibiotic perfusion for periprosthetic joint infection. J Orthop Sci,29 6: 1469-1476.

18. Suzuki Y, Iwasaki K, Joutoku Z, Onodera T, et al.,2024.High-concentration continuous local antibacterial perfusion therapy: safety and potential efficacy for acute and chronic periprosthetic knee joint infection. SICOT J, 10 51.

19. Mashiko R, Hatta T, Nagashima C,2023.Periprosthetic Joint Infection Following Reverse Shoulder Arthroplasty Treated With Continuous Local Antibiotic Perfusion: A Case Report. Cureus,15 11: e49193.

20. Yamaguchi S, Ueda S, Ichiseki T, Soma D, et al.,2024.Effective Management of Methicillin-Resistant Shoulder Septic Arthritis Using Continuous Local Antibiotic Perfusion: A Case Study and Long-Term Follow-Up. Am J Case Rep,25 e944491.

21. Takahashi H, Koda M, Funayama T, Noguchi H, et al.,2021.Continuous local antibiotic perfusion for patients with surgical site infection after instrumented spinal surgery; a novel technique to retain the implants. J Clin Neurosci,93 70-74.

22. Ohyama S, Inoue M, Toshi N, Okuyama K, et al.,2023.Retroperitoneal Continuous Local Antibiotic Perfusion for Refractory Pyogenic Vertebral Osteomyelitis: A Case Report. Cureus,15 12: e50636.

23. Takahara S, Maruo A, Takayama H, Harada T,2022.Continuous Local Antibiotics Perfusion Therapy for Acute Deep Infections after Open Fractures. Case Rep Orthop,2022 2563939.

24. Oe K, Maruo A, Fukui T, Muratsu H, et al.,2021.Treatment of Chronic Osteomyelitis of the Femur by Intramedullary Antibiotic Perfusion (iMAP): A Case Report. J Orthop Case Rep,11 12: 35-38.

25. Tomaru N, Nakamura H, Makiguchi T, Yamada Y, Yokoo S,2024.Necrotizing Fasciitis of the Lower Extremity Treated With Continuous Local Antibiotic Perfusion. Cureus,16 8: e66865.

26. Nagatani S, Kato S, Yokogawa N, Shimizu T, et al.,2024.Surgical Treatment for Emphysematous Osteomyelitis of the Lumbar Spine: A Case Report. Spine Surg Relat Res,8 5: 540-543.

27. Ito K, Murata H, Wasa J, Katagiri H,2025.Efficacy of continuous local antibiotic perfusion therapy for post-operative infections in frozen bone autografts treated with liquid nitrogen. BMJ Case Rep,18 6:.

28. Sawauchi K, Oe K, Fukui T, Kumabe Y, et al.,2025.Innovative Management of Brodie's Abscess: Continuous Local Antibiotic Perfusion in a 14-Year-Old Patient. Am J Case Rep,26 e947099.

29. Yamamoto Y, Fukui T, Sawauchi K, Yoshikawa R, et al.,2024.Effects of high antibiotic concentrations applied to continuous local antibiotic perfusion on human bone tissue-derived cells. Bone Joint Res,13 3: 91-100.

30. Fujihara Y, Uchibori K, Yoshimoto Y, Ota H, et al.,2025.Prognostic factors influencing the occurrence of drug-induced renal dysfunction during continuous local antibiotic perfusion therapy. J Orthop Sci