

Supplementary material

Search strategy

Pubmed

Concept 1: open fracture

"Fractures, Open"[Mesh] OR open fracture*[tiab] OR compound fracture*[tiab] OR gustilo[tiab]

Concept 2: antibiotic prophylaxis

"Antibiotic Prophylaxis"[Mesh] OR antibiotic*[tiab] OR antimicrob*[tiab] OR anti biotic*[tiab] OR anti microb*[tiab] OR "Anti-Infective Agents"[Mesh:NoExp] OR "Anti-Infective Agents, Local"[Mesh] OR "Anti Infective"[tiab] OR "antiinfective"[tiab] OR "Microbicides"[tiab] OR "Cephalosporins"[Mesh] OR Cephalospor*[tiab] OR "Quinolones"[Mesh] OR Quinolones[tiab] OR "Rifampin"[Mesh] OR Rifampin[tiab] OR "Aminoglycosides"[Mesh] OR gentamicin[tiab] OR amikacin[tiab] OR tobramycin[tiab] OR "Polymethyl Methacrylate"[Mesh] OR Polymethyl Methacrylate[tiab] OR PMMA[tiab] OR Palacos R[tiab] OR Acrylic Bone Cement[tiab] OR "Hydrogel"[Mesh] OR Hydrogel[tiab] OR Collagen Fleece[tiab] OR Collagen Fleece[tiab] OR "Glycopeptides"[Mesh] OR Glycopeptide*[tiab] OR vancomycin*[tiab] OR "Daptomycin"[Mesh] OR daptomycin*[tiab] OR "Penicillins"[Mesh] OR Penicillin*[tiab] OR pre emptive[tiab] OR preemptive[tiab]

Concept 3: infection

"infection"[MeSH Terms] OR infect*[tiab] OR "bone diseases, infectious"[MeSH Terms] OR "Osteomyelitis"[Mesh] OR Osteomyelit*[tiab] OR "Bone infection"[tiab] OR bone* infect*[tiab] OR "non union"[tiab] OR non unio*[tiab] OR delayed unio*[tiab] OR nonunio*[tiab] OR Wound Infection[Mesh] OR Wound* Infect*[tiab] OR wound* drain*[tiab] OR surgi* site* infection*[tiab] OR surge* site* infection*[tiab] OR biofilm* infection*[tiab] OR Biofilm[Mesh] OR Biofil* infect*[tiab] OR implant infect*[tiab] OR sepsis[Mesh] OR sepsis[tiab] OR septicem*[tiab] OR pyemi*[tiab] OR osteit*[tiab] OR Osteitis[Mesh] OR Amputation[Mesh] OR Amputat*[tiab]

Embase

Concept 1

'open fracture'/exp OR 'open fractur*':ab,ti OR 'compound fractur*':ab,ti OR gustilo:ab,ti

Concept 2

'antibiotic prophylaxis'/exp OR antibiotic*:ab,ti OR antimicrob*:ab,ti OR 'anti biotic*':ab,ti OR 'anti

microb*':ab,ti OR 'antiinfective agent'/exp OR 'anti infective':ab,ti OR 'antiinfective':ab,ti OR 'microbicides':ab,ti OR 'beta lactam antibiotic'/exp OR cephalospor*:ab,ti OR 'quinolone derivative'/exp OR quinolone*:ab,ti OR 'rifampicin'/exp OR rifampin:ab,ti OR 'aminoglycoside'/exp OR gentamicin:ab,ti OR amikacin:ab,ti OR tobramycin:ab,ti OR 'poly(methyl methacrylate)'/exp OR 'polymethyl methacrylate':ab,ti OR pmma:ab,ti OR 'Palacos R':ab,ti OR 'acrylic bone cement':ab,ti OR 'hydrogel'/exp OR 'hydrogel':ab,ti OR 'collagen fleece':ab,ti OR 'glycopeptide'/exp OR 'glycopeptide*':ab,ti OR 'vancomycin*':ab,ti OR 'daptomycin*':ab,ti OR 'penicillin derivative'/exp OR penicillin*:ab,ti OR 'pre emptive':ab,ti OR 'preemptive':ab,ti

Concept 3

'infection'/exp OR infect*:ab,ti OR 'osteomyelitis'/exp OR 'osteomyelit*':ab,ti OR 'bone infection'/exp OR 'non union':ab,ti OR 'non unio*':ab,ti OR 'delayed unio*':ab,ti OR 'nonunio*':ab,ti OR 'wound infection'/exp OR 'wound drainage'/exp OR 'wound drainage':ab,ti OR 'biofilm'/exp OR 'sepsis'/exp OR 'sepsis':ab,ti OR 'septicem':ab,ti OR 'osteitis'/exp OR 'osteitis':ab,ti OR 'amputation'/exp OR 'amputation':ab,ti OR 'pyemi*':ab,ti

Web of Science

Go to advanced search

Concept 1

ts=("open fractur*" OR "compound fractur*" OR gustilo)

Concept 2

ts=(antibiotic* OR "Prophyla*" OR antimicrob* OR "anti microb*" OR antiinfective OR "anti infectiv*" OR Microbicide OR cephalospori* OR quinolo* OR rifampi* OR aminoglycosid* OR gentamycin* OR amikacin OR tobramycin OR "poly methyl methacrylate" OR "poly methylmethacrylate" OR polymethylmethacrylate OR PMMA OR "palacos R" OR "acryl bone cement" OR Hydrogel OR "collagen fleece" OR Glycopeptides OR Vancomycin OR Daptomycin OR Penicillin* OR "pre emptive" OR preemptive)

Concept 3

ts=(infect* OR osteomyelit* OR "non unio*" OR "delayed unio*" OR nununio* OR "wound drain*" OR biofilm* OR sepsis OR septicem* OR pyemi* OR osteit* OR amputat*)

Table i. Detailed data form of primary studies eligible for quantitative analysis

Study/characteristic	Details
01_Henry et al¹³ (1990)	
Study title	The role of local antibiotic therapy in the management of compound fractures
Objective	Effect of tobramycin PMMA beads in open fracture wounds for temporary wound coverage
Setting	Single centre in the United States (Humana Hospital, University of Louisville)
Time period	August 1983 - November 1987
Funding	Not reported
Level of evidence	Low
Study design	Retrospective cohort study
Selection of participants	Consecutive
Sample-size calculation	No
Statistical analysis	Chi-squared test
Follow-up interval	Control group: 20.9 mths (6 to 50); intervention group: 17.5 mths (6 to 51)
Inclusion criteria	Open limb fractures
Exclusion criteria	None
Total number of open fractures reported	404 in 339 patients
Number of open fractures for analysis	404
Patient characteristics	Mean age: 33 yrs; gender: 62% male; mean ISS: 21
Fracture location	Clavicle, humerus, ulna, radius, hand, pelvis, femur, patella, lower leg, ankle, foot
Gustilo–Anderson	I: 127 (31%); II: 153 (39%); III: 124 (31%); equal distribution between cohort
Report of relevant prognostic factors	Partially
Systemic antibiotics in both groups	Yes, penicillin, cefazolin, tobramycin
Intervention group: local antibiotics	Tobramycin PMMA beads
Group size	Intervention group: 334; control group: 70
Control group: additional antibiotics	No
Decision to use local antibiotics	Based on surgeon's decision and/or availability of beads
Matching of cohorts	Similar case matching reported: grade open fracture, primary wound closure, ISS, age, gender, fracture location, follow-up interval
Follow-up rate	100%
Outcome parameter(s)	Wound infection and/or bone infection
Definition of infection?	Incomplete; infection = identification of pathogen in culture
Infection rate: all	7.2% (n=29)
Infection rate: intervention group	4.2% (n=14)
Infection rate: control group	21.4% (n=15)
Further results	ISS didn't show correlation with infection rate; beads reduced rate of polymicrobial infections
Osteosynthesis	No details reported
Key finding	"Prophylactic use of antibiotic beads supplemented with systemic antibiotics was of significant benefit preventing acute and chronic infections in open fractures."
General comment	Probable overlap with populations reported in the two studies by Ostermann et al ^{2,3} (same centre, overlapping study period).
Quality assessment	GRADE quality of evidence: low
02_Ostermann et al¹⁴ (1993)	
Study title	The role of local antibiotic therapy in the management of compound fractures
Objective	Effect of tobramycin PMMA beads in open fracture wounds for temporary wound coverage
Setting	Single centre in the United States (University of Louisville)
Time period	1983 - 1989
Funding	Not reported
Level of evidence	Low
Study design	Retrospective cohort study
Selection of participants	Consecutive
Sample-size calculation	No
Statistical analysis	Chi-squared test
Follow-up interval	Not reported
Inclusion criteria	Open limb fractures
Exclusion criteria	None
Total number of open fractures reported	704 in 590 patients
Number of open fractures for analysis	704
Patient characteristics	Mean age: 34 yrs; gender: 57% male
Fracture location	Not reported
Gustilo–Anderson	I: 198 (28%); II: 259 (37%); III: 247 (35%); equal distribution between cohort
Report of relevant prognostic factors	Partially; especially ISS missing
Systemic antibiotics in both groups	Yes, penicillin, cefazolin, tobramycin
Intervention group: local antibiotics	Tobramycin PMMA beads
Group size	Intervention group: 547; control group: 157
Control group: additional antibiotics	No
Decision to use local antibiotics	Not reported
Matching of cohorts	Similar case-matching reported: grade open fracture, age, gender, fracture location, follow-up interval; no matching in wound closure

(Continued)

Table i. (Continued)

Study/characteristic	Details
Follow-up rate	100%
Outcome parameter(s)	Wound infection and/or bone infection
Definition of infection?	Incomplete; infection = identification of pathogen in culture; bone infection = "deep bony infection occurring after 6 weeks"
Infection rate: all	7.0% (n=49)
Infection rate: intervention group	4.2% (n=23)
Infection rate: control group	16.6% (n=26)
Further results	Beads reduced rate of polymicrobial infections
Osteosynthesis	No details reported
Key finding	"Prophylactic use of antibiotic-laden PMMA beads in addition to systemic antibiotics was of benefit in preventing infectious complications in compound fractures, in particular in Type IIIB open fractures."
General comment	Primary and delayed primary wound closure in less frequent in control group; probable overlap with populations reported in the Ostermann et al ³ (1995) and Henry et al ¹ (1990) (same centre, overlapping study period).
Quality assessment	GRADE quality of evidence: low
03_Ostermann et al¹⁵ (1995)	
Study title	Local antibiotic therapy for severe open fractures. A review of 1085 consecutive cases
Objective	Effect of tobramycin PMMA beads in open fracture wounds for temporary wound coverage
Setting	Single centre in the United States (University of Louisville)
Time period	May 1983 - July 1992
Level of evidence	Low
Funding	Not reported
Study design	Retrospective cohort study
Selection of participants	Consecutive
Sample-size calculation	No
Statistical analysis	Chi-squared test
Follow-up interval	Not reported
Inclusion criteria	Open limb fractures
Exclusion criteria	None
Total number of open fractures reported	1085 in 940 patients
Number of open fractures for analysis	1085
Patient characteristics	Mean age: 34 yrs; gender: 64% male
Fracture location	Clavicle, humerus, ulna, radius, hand, pelvis, femur, patella, lower leg, ankle
Gustilo-Anderson	I: 279 (26%); II: 364 (34%); III: 442 (41%); equal distribution between cohort
Report of relevant prognostic factors	Partially, especially ISS missing
Systemic antibiotics in both groups	Yes, penicillin, cefazolin, tobramycin
Intervention group: local antibiotics	Tobramycin PMMA beads
Group size	Intervention group: 845; control group: 240
Control group: additional antibiotics	No
Decision to use local antibiotics	Based on surgeon's decision and/or availability of beads
Matching of cohorts	Similar case-matching reported: grade open fracture, age, gender, fracture location, follow-up interval; no matching in wound closure
Follow-up rate	100%
Outcome parameter(s)	Wound infection and/or bone infection
Definition of infection?	Not reported
Infection rate: all	5.5% (n=60)
Infection rate: intervention group	3.7% (n=31)
Infection rate: control group	12.1% (n=29)
Further results	Beads reduced rate of polymicrobial infections
Osteosynthesis	No details reported
Key finding	"The adjuvant use of local antibiotic-laden PMMA beads may reduce the risk of infection in severe compound fractures."
General comment	Primary and delayed primary wound closure in less frequent in control group; probable overlap with populations reported in the Ostermann et al ² (1995) and Henry et al ¹ (1990) (same centre, overlapping study period).
Quality assessment	GRADE quality of evidence: low
04_Keating et al¹⁶ (1996)	
Study title	Reamed nailing of open tibial fractures: does the antibiotic bead pouch reduce the deep infection rate?
Objective	Determine whether addition of the bead pouch to a standard protocol of wound management of open fractures was associated with a concomitant reduction in the rate of deep infection
Setting	Single centre in the United Kingdom
Time period	October 1987 - June 1993
Level of evidence	Low
Funding	Not reported
Study design	Retrospective cohort study
Selection of participants	Consecutive: first control (historical group), then intervention group

(Continued)

Table i. (Continued)

Study/characteristic	Details
Sample-size calculation	No
Statistical analysis	Chi-squared test, Fisher's exact test
Follow-up interval	23 mths (12 to 50)
Inclusion criteria	Grade II and III open tibial fractures
Exclusion criteria	None
Total number of open fractures reported	81 in 79 patients (3 amputations)
Number of open fractures for analysis	78
Patient characteristics	Mean age: 35 yrs; gender: 81% male; mean ISS: 13
Fracture location	Tibia
Gustilo–Anderson	II: 38 (49%); III: 40 (51%)
Report of relevant prognostic factors	Partially
Systemic antibiotics in both groups	For 72 hrs: cefazolin every 8 hrs; grade III fracture: additional gentamicin
Intervention group: local antibiotics	Tobramycin PMMA beads
Group size	Intervention group: 53; control group: 25
Control group: additional antibiotics	No
Decision to use local antibiotics	First control, then intervention group
Matching of cohorts	Similar case-matching reported: fracture comminution, age, gender, mean time to wound coverage
Follow-up rate	90% (78/87) (lost to follow-up, n=6; amputation, n=3)
Outcome parameter(s)	Deep infection and/or nonunion
Definition of infection?	Incomplete: "presence of a purulent discharge, with bony involvement evident at the time of surgical debridement"
Infection rate: all	7.4% (n=6)
Infection rate: intervention group	3.8% (n=2)
Infection rate: control group	16.0% (n=4)
Further results	Comparable nonunion rate in both groups
Osteosynthesis	Uniform surgical procedure: nailing
Key finding	"The introduction of the bead pouch coincided with a reduced infection rate with no other change in protocol to explain the difference."
General comment	Control group: wound coverage with saline dressing; no amputation due to infection.
Quality assessment	GRADE quality of evidence: low

05_Moehring et al¹⁷ (2000)

Study title	Comparison of antibiotic beads and intravenous antibiotics in open fractures
Objective	Efficacy of antibiotic-impregnated beads compared with conventional intravenous antibiotics in the treatment of open fractures
Setting	Single centre in the United States (University of California)
Time period	July 1993 - December 1995
Level of evidence	Moderate
Funding	Not reported
Study design	Randomized prospective study
Selection of participants	Consecutive enrolment not possible because patients declined to consent or inadvertently were omitted
Sample-size calculation	No (this is meant as a pilot study enabling sample size calculation for larger trials)
Statistical analysis	Chi-squared test
Follow-up interval	15 mths (12 to 27)
Inclusion criteria	Grade II and IIIA/B open long-bone fracture
Exclusion criteria	Grade I and IIIC, intraarticular injuries, open physis, pregnancy, or systemic immunocompromise
Total number of open fractures reported	75 in 67 patients (enrolled patients initially: 113)
Number of open fractures for analysis	62
Patient characteristics	Mean age: 34 yrs; gender: 75% male
Fracture location	Femur, tibia, humerus, radius
Gustilo–Anderson	I: 0; II: not reported; III: not reported
Report of relevant prognostic factors	No
Systemic antibiotics in both groups	Cefazolin + aminoglycoside or anaerobic coverage or both added for Grade IIIA/B fractures
Intervention group: local antibiotics	Tobramycin PMMA beads; no further systemic antibiotics
Group size	Intervention group: 24; control group: 38
Control group: additional antibiotics	Yes, intravenous cephalosporin and gentamicin until wound coverage
Decision to use local antibiotics	Randomization
Matching of cohorts	Similar case-matching reported: fracture comminution, age, gender, time to wound coverage
Follow-up rate	59% (67/113 patients)
Outcome parameter(s)	Infection
Definition of infection?	Incomplete: "Persistent drainage, that was positive on culture, from an open fracture site or wound that had broken down"
Infection rate: all	6.5% (n=4)
Infection rate: intervention group	8.3% (n=2)
Infection rate: control group	5.3% (n=2)
Osteosynthesis	Details reported; beads exchanged in every debridement
Key finding	Higher infection rate in patients treated with local antibiotics

(Continued)

Table i. (Continued)

Study/characteristic	Details
General comment	A third group of 13 fractures was not randomized and received both local and systemic antibiotics (due to limb saving or other reasons). This group was not taken into consideration for this meta-analysis. Systemic antibiotics were not continued in the intervention group.
Quality assessment	GRADE quality of evidence: moderate
06_Ziran et al²⁰ (2004)	
Study title	Intramedullary nailing in open tibial fractures: a comparison of two techniques
Objective	Comparison of reamed and unreamed tibial nailing in terms of union and infection rate; subgroup analysis: effect of antibiotic beads in IIIB open tibial fractures
Setting	United States, not reported if single or multicentre trial
Time period	Four-year period (no further details)
Level of evidence	Very low
Funding	Not reported
Study design	Retrospective cohort study
Selection of participants	Consecutive
Sample-size calculation	No
Statistical analysis	Fisher's exact test
Follow-up interval	Not reported
Inclusion criteria	Grade IIIB open tibial fractures for subgroup analysis
Exclusion criteria	None
Total number of open fractures reported	51
Number of open fractures for analysis	28
Patient characteristics	Not reported for subgroup IIIB
Fracture location	Tibia
Gustilo–Anderson	III: 28 (100%)
Report of relevant prognostic factors	No
Systemic antibiotics in both groups	Penicillin, cefazolin, and gentamicin
Intervention group: local antibiotics	Tobramycin PMMA beads
Group size	Intervention group: 12; control group: 16
Control group: additional antibiotics	No
Decision to use local antibiotics	Decision surgeon
Matching of cohorts	Similar case-matching for all 51 fractures stated but no detailed information given
Follow-up rate	100%
Outcome parameter(s)	Infection
Definition of infection?	None
Infection rate: all	25.0% (n=7)
Infection rate: intervention group	16.7% (n=2)
Infection rate: control group	31.3% (n=3)
Further results	Comparable nonunion rate in both groups
Osteosynthesis	Nailing: intervention group: reamed; control group: unreamed
Key finding	Due to small sample size, no valid conclusion possible to determine if local antibiotics reduce infection rate
General comment	In total, 51 open tibial fractures investigated: 22 reamed and 29 unreamed. In reamed IIIB open tibial fractures, PMMA beads were applied to wound. Just 28 IIIB open tibial fractures are considered in this systematic review. Level of evidence rated very low because prophylactic effect of local antibiotics in open fractures was investigated in just a small cohort.
Quality assessment	GRADE quality of evidence: low - very low (for subgroup of local antibiotics)
07_Singh et al¹⁸ (2015)	
Study title	Surgical site infection in high-energy periarticular tibial fractures with intra-wound vancomycin powder: a retrospective pilot study
Objective	Assess the efficacy of intraoperative vancomycin powder administration on preventing deep surgical site infection
Setting	Single centre in the United States (Vanderbilt Orthopaedic Institute)
Time period	January 2012 - December 2012
Level of evidence	Very low
Funding	Not reported
Study design	Retrospective cohort study
Selection of participants	Consecutive
Sample-size calculation	No
Statistical analysis	Fisher's exact test, Student's <i>t</i> -test, and Mann–Whitney U test
Follow-up interval	Average not reported (minimum 6 mths)
Inclusion criteria	Articular tibial fractures, adult, staged fixation with > 5 days after injury
Exclusion criteria	Follow-up < 6 mths
Total number of open fractures reported	93
Number of open fractures for analysis	26
Patient characteristics	Mean age: 47 yrs; gender: 66% male
Fracture location	Tibia
Gustilo–Anderson	Not reported
Report of relevant prognostic factors	Partially

(Continued)

Table i. (Continued)

Study/characteristic	Details
Systemic antibiotics in both groups	Cefazolin every 8 hrs for 24 hrs
Intervention group: local antibiotics	1 g vancomycin powder into surgical wound at time of definitive fixation
Group size	Intervention group: 3; control group: 23
Control group: additional antibiotics	No
Decision to use local antibiotics	Decision surgeon
Matching of cohorts	Similar case-matching for age, gender, smoking, diabetes, fracture location (of all 93 cases)
Follow-up rate	87% (93/107); no details about follow-up in this group
Outcome parameter(s)	Deep surgical site infection
Definition of infection?	Surgical site infection not specified
Infection rate: all	33.3% (n=1)
Infection rate: intervention group	30.4% (n=7)
Infection rate: control group	31.3% (n=3)
Further results	None
Osteosynthesis	Staged procedure, details not reported
Key finding	In all articular tibia fractures, no significant difference was found in the rate of when intrawound vancomycin powder was administered. In open articular fractures, due to the low number of patients, no conclusion was possible.
General comment	In total, 93 tibial fractures analyzed. For this review, only the 26 open fractures were taken into account. Level of evidence rated very low because prophylactic effect of local antibiotics in open fractures was investigated in just a small cohort.
Quality assessment	GRADE quality of evidence: very low (for subgroup of open fractures)
08_Lawing et al¹⁹ (2015)	
Study title	Local injection of aminoglycosides for prophylaxis against infection in open fractures
Objective	Determine efficacy of local aminoglycosides (gentamicin and tobramycin), in conjunction with systemic antibiotics, to lower the prevalence of infection in patients with open fractures
Setting	Single centre in the United States (University of North Carolina)
Time period	January 2008 - August 2013
Level of evidence	Moderate
Funding	Yes, for statistics
Study design	Retrospective cohort study
Selection of participants	Consecutive
Sample-size calculation	No
Statistical analysis	Fisher's exact test, chi-squared-test, and Mann-Whitney U test; logistic regression model
Follow-up interval	Control group: 12.5 mths; intervention group: 11.3 mths
Inclusion criteria	Open fractures
Exclusion criteria	Metacarpal/phalangeal fractures, systemic or pre-existing local infection, operative care > 36 hrs, age < 10 yrs
Total number of open fractures reported	351
Number of open fractures for analysis	351
Patient characteristics	Mean age: 38 yrs; gender: 65% male
Fracture location	No details reported
Gustilo-Anderson	I: 44 (12%); II: 139 (40%); III: 168 (48%)
Report of relevant prognostic factors	Yes (very detailed)
Systemic antibiotics in both groups	Cefazolin; in grade III fractures gentamicin added; in contaminated fractures penicillin added
Intervention group: local antibiotics	Local aminoglycoside injection after wound closure
Group size	Intervention group: 168; control group: 183
Control group: additional antibiotics	No
Decision to use local antibiotics	Decision surgeon
Matching of cohorts	Similar case-matching for age, gender, polytrauma; multivariate analysis was performed to adjust for potential differences for confounding variables
Follow-up rate	100%
Outcome parameter(s)	Infection
Definition of infection?	CDC definition of superficial and deep infection
Infection rate: all	14.8% (n=52)
Infection rate: intervention group	9.5% (n=16)
Infection rate: control group	19.7% (n=36)
Further results	Nonunion rate 15% and equally in both groups
Osteosynthesis	Details reported
Key finding	"After multivariate analysis to adjust for possible confounding factors, the administration of local antibiotics was found to be an independent predictor of lower infection rates."
General comment	In some grade II/III fractures, a catheter was placed in the wound and irrigation with aminoglycoside every 6 hrs; these wounds were covered with negative pressure wound therapy.
Quality assessment	GRADE quality of evidence: moderate (upgrading due to large effect, matching of cohorts, and multivariate analysis to adjust possible confounding factors)

PMMA, poly(methyl methacrylate); ISS, Injury Severity Score; GRADE, Grading of Recommendations Assessment, Development and Evaluation; CDC, Centers for Disease Control and Prevention

Table ii. Characteristics of eligible studies for qualitative analysis: case series and case reports

Author (year)	Study design/ setting	Population (inclusion criteria)	Open fractures, n	Gustilo- Anderson grade	Local AB/ systemic AB	Infection rate, % (n)	Outcome parameter(s)	Mean follow-up (range)	Key finding	Comment
Eckman et al⁹ (1985)	Prospective case series; single centre in the United States	Open tibial or femoral fracture	70	Not reported	Tobramycin PMMA beads; systemic antibiotics not reported	0% (0)	Acute wound infection (no definition mentioned)	Not reported	Significant levels of tobramycin can be achieved in the extracellular fluid at the fracture site when tobramycin- impregnated PMMA beads are placed in the wound after irrigation and debridement.	Local and systemic tobramycin levels measured
Henry et al¹⁰ (1993)	Retrospective case series; single centre in the United States	Open limb fracture (excluding hand fractures)	227	I: 16; II: 83; IIIA: 48; IIIB: 65; IIIC: 15	Tobramycin PMMA beads (applied if primary wound closure not possible); systemic antibiotics: penicillin, cefazolin, tobramycin for 5 days	9.2% (21); I: 0%; II: 2.4%; IIIA: 4.2%; IIIB: 7.7%; IIIC: 0%	Wound infection; bone infection (no definition mentioned)	Not reported	The bead pouch is a temporary solution for the problem of compromised soft-tissue coverage of the fracture. Reduced infection rate compared with literature data.	
Wright et al¹¹ (2007)	Retrospective case series; single centre in the United States	Not reported	125	Not reported	Not reported	3.2% (4)	Not reported	31 wks (6 to 134)	The use of antibiotic beads is justified to prevent active infection in open fractures.	Full text not available
Gardner et al¹² (2008)	Retrospective case series; single centre in the United States	Open AO/OTA type C3 pilon tibial fractures with reconstructive approach	10	IIIA: 7; IIIB: 3	PMMA beads with gentamicin, vancomycin, or both; systemic antibiotics not reported	20% (2)	Deep infection (no definition mentioned)	19 mths (3 to 53)	In some carefully selected patients, a 3-stage protocol using antibiotic beads and internal fixation is possible and safe.	
Hutson et al¹³ (2010)	Retrospective case series; single centre in the United States	IIIB open tibial shaft fractures	19	IIIB: 19	PMMA spacer with tobramycin and vancomycin; systemic antibiotics not reported	0% (0) (2 soft- tissue infections reported, but not rated as deep bone infections)	Infection; nonunion (no definition mentioned)	58 mths (16 to 135)	The use of antibiotic spacers and flaps to construct a soft tissue combined with distraction osteogenesis is an effective technique to salvage complex open tibial fractures with segmental bone loss.	Bone union in 23/26
Cai et al¹⁴ (2010)	Prospective case series; single centre in China	Open limb fractures (tibia, femur, humerus)	26	I: 0; II: 13; IIIA: 11; IIIB: 0; IIIC: 2	Calcium sulphate with vancomycin; systemic antibiotics given for 2 to 5 days (no further details)	0% (0) (2 patients presented with drainage but cultures were negative)	Infection: active search of erythema, inflammation, warmth, and purulent drainage.	11 mths (6 to 16) (2 patients lost to follow-up)	The combination of internal fixation and calcium sulphate impregnated with vancomycin is safe and effective in the treatment of open fractures of long bones.	
Raschke et al¹⁵ (2010)	Case report; single centre in Germany	Tibial fracture	1	IIIC: 1	Intramedullary nail coated with gentamicin (UTN PROtect, DePuy Synthes, Oberdorf, Switzerland); systemic antibiotics: cefuroxime and meropenem for 10 days	0% (0)	Deep infection; nonunion	2 yrs	Gentamicin-coated nail is an option for IIIC open fractures.	
Fuchs et al¹⁶ (2011)	Prospective case series; single centre in Germany	Open or closed tibial shaft fracture total	12 (21 fractures in total)	I: 3; II: 2; IIIA/B: 4; IIIC: 3	Intramedullary nail coated with gentamicin (UTN PROtect, DePuy Synthes); systemic antibiotics: cefuroxim 3 to 30 days	0% (0) (1 wound healing disorder)	Deep wound infection; nonunion (no definition mentioned)	6 mths	Antibiotic coating of implants might minimize the risk of infections and improve clinical and radiological outcomes.	At follow- up serum gentamicin levels: negative; no nonunion, but 8 (42%) partially healed fractures
Chaudhary et al¹⁷ (2011)	Case series; single centre in India	IIIA open limb fractures treated by immediate open reduction and internal fixation	35	IIIA: 35	Gentamicin-impregnated equine collagen sponge; systemic antibiotics given (no further details)	6.5% (2/31) (3 wound healing disorders (9.7%))	Deep infection; nonunion (no definition mentioned)	40 wks (15 to 160) (4 patients lost to follow-up)	Local antibiotic-impregnated collagen sponges along with systemic antibiotics offer promising results in open fracture management	Delayed union in 5 patients (16.1%)
Metsemakers et al¹⁸ (2015)	Retrospective case series; single centre in Belgium	Tibial fracture	9 (16 fractures in total with 2 closed fractures and 5 revision cases)	II: 4; IIIA: 2; IIIB: 3	Intramedullary nail coated with gentamicin (ETN PROtect, DePuy Synthes); systemic antibiotics: cephalosporin for 5 days	0% (0)	Superficial/deep infection; nonunion (CDC guidelines definition)	18 mths	Antibiotic-coated implants seem a potential option for prevention of deep infections in trauma patients.	30% (3/9) nonunions

References

1. **Henry SL, Ostermann PA, Seligson D.** The prophylactic use of antibiotic impregnated beads in open fractures. *J Trauma* 1990;30:1231-1238.
2. **Ostermann PA, Henry SL, Seligson D.** The role of local antibiotic therapy in the management of compound fractures. *Clin Orthop Relat Res* 1993;295:102-111.
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