

Management of open fractures post debridement with standard empirical antibiotics and culture specific antibiotics: A randomized control study

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Abstract

The goals of open fracture management include preventing infection, achieving bone union, and restoring function. Current treatment strategies for the care of open fracture wounds are constantly being updated. Important principles for management include rational antibiotic usage, anti-tetanus prophylaxis, appropriate timing of initial surgical intervention, wound irrigation, antibiotic delivery methods, and type of wound closure and adjunctive therapies to aid fracture union. All patients underwent trauma assessment and appropriate treatment in the emergency department, the wounds were inspected for the size and extent of wound, both soft tissue and bone status was assessed and the amount of contamination was noted. The most common organism isolated from post-operative infected cases was *Staphylococcus aureus* (53%) a gram-positive cocci and the next common was *Pseudomonas aeruginosa* (20%) a gram negative bacilli and other gram negative bacteria, *Escherichia coli* and *Klebsiella pneumoniae*.

Keywords: Open fractures, empirical antibiotics, culture specific antibiotics

Introduction

An open fracture is defined as an injury where the fracture and the fracture hematoma communicate with the external environment through a traumatic defect in the surrounding soft tissues and overlying skin. They are also referred to as compound fractures ^[1].

Bacterial contamination is reported to occur in 60-70% of the cases which may be responsible for the infectious complications in open fracture patients. The etiology for open fractures include road traffic accidents, assault, gunshot injuries, trauma due to heavy machinery and others. Infection is a common complication that occurs in all these cases. Other complications of open fractures include malunion, non-union and even functional loss of the limb. The exposed fracture site, presence of devascularised tissue, severity of the external wound, presence of comorbid conditions, immune status of the patient, delay in arrival to the hospital

and delay in treatment are few reasons that determine the occurrence of infection ^[2].

The loss of skin integrity and exposure of subcutaneous tissue create an environment suitable for colonization and growth of microorganisms. In a traumatic fracture wound, foreign bodies, dead and devitalized tissue provide the perfect environment for microbial proliferation and infection, unless the wound is treated with prophylactic antibiotics and debridement ^[2].

In these patients, debridement of the wound and lavage along with antibiotic prophylaxis are important aspects of treatment. The goal should be to achieve a rapid healing of the soft tissues and bones ^[1].

The goals of open fracture management include preventing infection, achieving bone union, and restoring function. Current treatment strategies for the care of open fracture wounds are constantly being updated. Important principles for management include rational antibiotic usage, anti-tetanus prophylaxis, appropriate timing of initial surgical intervention, wound irrigation, antibiotic delivery methods, and type of wound closure and adjunctive therapies to aid fracture union ^[1].

As a result of the introduction of sulfonamides and penicillin in the 1930s and 1940s, specific antimicrobial resistance has been a problem. Penicillin-resistant staphylococci emerged in the 1940s and 1950s. Resistance to methicillin developed in the 1960s, and resistance to amino glycosides among *Pseudomonas aeruginosa* isolates emerged in the late 1960s and 1970s. Multidrug resistance has become more common among nosocomial pathogens (that is *Enterococcus*, *Staphylococcus* and *Enterobacter* species) over the last decade. Additionally, methicillin resistance among staphylococci, vancomycin resistance among enterococci and third generation cephalosporin and fluoroquinolone resistance among *pseudomonas*, *Enterobacter* and *Escherichia coli* species has become common in community acquired isolates ^[3].

Several factors contribute to the rise in antimicrobial resistance. A few of these factors include improper use of antimicrobials for prophylaxis and treatment of infection, prolonged hospitalization, more intensive care unit stays and multiple co-morbidities. An increase in the use of invasive devices and catheters, ineffective infection control practices and lack of compliance with infection control practices. Generally, the level of antibiotic resistance depends on the proportion of resistant organisms introduced into the hospital from the community, the proportion that become resistant spontaneously or through antibiotic use, and the proportion that is transmitted from person to person. In order to reduce the spread of antimicrobial resistance organisms in hospitals, all of these factors must be addressed ^[3,4].

Methodology

A. Study design: A Randomized control study.

B. Sample size: 35 in each group.

C. Inclusion criteria

1. Patients willing to give informed consent (Annexure 1).
2. Age above 18 years.
3. All patients with open fractures of long bones without any other foci of.
4. Infection detected clinically.

D. Exclusion criteria

1. Patients not willing to give informed consent.
2. Patients who have undergone wound debridement or surgical procedure for the Fracture.

3. Patients with open fracture who have been treated by iv or oral antibiotic.
4. Dressing before coming to emergency department.
5. Patients with polytrauma.
6. Patients with type 3C open fracture.
7. Patients with immunosuppression.

After obtaining approval and clearance from the institutional ethics committee, the patients fulfilling inclusion and exclusion criteria were enrolled for study after informed consent.

All patients with open fractures of long bones presenting to emergency department, a detailed history and clinical examination were done. As part of a working proforma the following details will be noted from the patient and his attenders-demographic details, date and time of injury, the mode of injury.

All patients underwent trauma assessment and appropriate treatment in the emergency department, the wounds were inspected for the size and extent of wound, both soft tissue and bone status was assessed and the amount of contamination was noted.

All wounds were classified based on Gustilo Anderson classification of open fractures. Patients were randomized into two groups by computer generated codes.

Patients in group 1, culture sample was not sent and empirical antibiotics were given for 5-10 days depending on open fracture type. The empirical antibiotics used are Ceftriaxone (3rd generation cephalosporin) for type I & type II open fractures, for type III ceftriaxone & amikacin (aminoglycoside), metronidazole was added in cases with gross organic, soil or faecal contamination in type 3 fractures.

Patients in group 2, under aseptic precaution swab or tissue sample was taken from open fracture wound and sent for culture & sensitivity and empirical antibiotics were given for 2 days (till we get culture report), patients with positive culture report antibiotics were changed to culture specific antibiotics and patient with negative culture report same antibiotics were continued, antibiotics were given for 5-10 days depending on open fracture type.

For all patients tetanus prophylaxis was given, thorough wound irrigation and debridement was carried out.

Bony injuries were stabilized with intramedullary nail or plate and screws or external fixator, depending on factors like soft tissue coverage, contamination, comminution and periosteal stripping.

The soft tissue wounds were addressed by primary closure or delayed primary closure or by coverage procedure such as split skin grafting or rotational flap.

Patients were followed up clinically during hospital stay and till six months by follow up visits or via phone call if patients are not able to make it to hospital to extract maximum data possible.

Wound infection was suspected by the presence of symptoms and signs of wound infection like Fever with chills, erythema and local rise of temperature, tenderness, serosanguinous discharge, frank pus, abscess collection, foul smell and necrosis of graft or flap. The cases in which infection occurred, deep culture of wound or soft tissue were obtained to determine the infecting organism.

Patient with negative initial culture were excluded from group 2(culture specific antibiotic) for comparing the rate of infection in both groups.

Results

Table 1: Wound Management

| | Group 1 | | Group 2 | | Total | |
|-------------------------|---------|--------|---------|-------|-------|--------|
| | n | % | n | % | n | % |
| Primary Closure | 23 | 65.71 | 26 | 74.28 | 49 | 70 |
| Delayed Primary Closure | 5 | 14.28 | 2 | 5.71 | 7 | 10 |
| Flap | 5 | 14.28 | 3 | 8.57 | 8 | 11.42 |
| SSG | 2 | 5.72 | 4 | 11.43 | 6 | 8.57 |
| Total | 35 | 100.00 | 35 | 100.0 | 70 | 100.00 |

55% of total cases fracture stabilized with interlocking nail.

Table 2: Fracture Stabilization

| Fracture Stabilization | Group 1 | Group 2 | Total n | % |
|------------------------|---------|---------|---------|-----|
| ILN | 22 | 17 | 39 | 55 |
| Plating | 4 | 4 | 8 | 11 |
| EXFIX | 9 | 13 | 22 | 31 |
| CC Screws | | 1 | 1 | 1 |
| Total | 35 | 35 | 70 | 100 |

In group 2 (culture specific antibiotic group) 85% of initial culture from open fracture showed positive report and 13% were negative.

Table 3: Initial Culture from Open Fracture Wound in Group 2(n=35)

| | n | % |
|----------|----|-------|
| Positive | 30 | 85.72 |
| Negative | 5 | 14.28 |
| Total | 35 | 100.0 |

In positive cultures, *Staphylococcus aureus* was isolated in 37% of cultures, 63 % Gram negative bacteria, among which *Pseudomonas aeruginosa* was the commonest, accounting for 23% of the cultures. Other members of gram-negative bacteria isolated were, *Escherichia coli* (14%) *Klebsiella pneumoniae* (6%), *Klebsiella oxytoca* (6%), *Acinetobacter baumannii* (6), *Proteus mirabilis* (3%), and *Proteus vulgaris* (3%).

Table 4: Organisms Isolated from initial culture in group 2

| Organisms | n | % |
|--------------------------------|----|-----|
| <i>Acinetobacter baumannii</i> | 2 | 6% |
| <i>Escherichia coli</i> | 4 | 13% |
| <i>Klebsiella oxytoca</i> | 2 | 6% |
| <i>Klebsiella pneumoniae</i> | 2 | 6% |
| <i>Pseudomonas aeruginosa</i> | 7 | 23% |
| <i>Proteus mirabilis</i> | 1 | 3% |
| <i>Proteus vulgaris</i> | 1 | 3% |
| <i>Staphylococcus aureus</i> | 11 | 36% |
| Total | 30 | |

21% of total cases reported post-operative infection.

Table 5: Total incidence of infection

| | n | Infection | Percentage |
|---------|----|-----------|------------|
| Group 1 | 35 | 8 | 22% |
| Group 2 | 35 | 7 | 20% |
| Total | 70 | 15 | 21% |

Post-operative infection in group 1 with 35 cases of open fractures treated with empirical antibiotics 8(22%) cases developed infection and in group 2, 30 cases treated with culture specific antibiotics 7(28%) cases developed infection.

Patient with negative initial culture were excluded from group 2 (culture specific antibiotic) for comparing the rate of infection in both groups.

Rate of infection in both groups are compared for statistical significance using chi-square test (table 13), the p obtained was 0.9637, suggest that no statically significance in rate of infection in both groups as p value is >.05.

Table 6: Chi square test for statistical significance of infection rate between two groups

| | Infected | Not infected | Marginal Row Totals |
|------------------------|--------------|----------------|---------------------|
| Group 1 | 8 (8.08) [0] | 27 (26.92) [0] | 35 |
| Group 2 | 7 (6.92) [0] | 23 (23.08) [0] | 30 |
| Marginal Column Totals | 15 | 50 | 65 (Grand Total) |

The chi-square statistic is 0.0021. The p-value is .963768. Not significant at $p < 0.05$.

The infection rates in the post-operative period were correlated with the fracture grading and it was observed that 8% of type I, 19% type 2, 27% type 3 and 28% type 3b fractures developed infection.

Table 7: Analysis of Infection Based on Fracture Grading

| | Group | | Total | | |
|---------|---------|---------|-------|-----------|------------|
| | Group 1 | Group 2 | N | Infection | Percentage |
| Type 1 | 1 | 0 | 12 | 1 | 8% |
| Type 2 | 3 | 2 | 26 | 5 | 19% |
| Type 3A | 2 | 3 | 18 | 5 | 27% |
| Type 3B | 2 | 2 | 14 | 4 | 28% |
| Total | 8 | 7 | 70 | 15 | |

The most common organism isolated from post-operative infected cases was *Staphylococcus aureus* (53%) a gram-positive cocci and the next common was *Pseudomonas aeruginosa* (20%) a gram negative bacilli and other gram negative bacteria, *Escherichia coli* and *Klebsiella pneumoniae*.

Table 8: Organisms Isolated in Infected Cases

| | Group | | Total | |
|-------------------------------|---------|---------|-------|-----|
| | Group 1 | Group 2 | N | % |
| <i>Staphylococcus aureus</i> | 5 | 3 | 8 | 53% |
| <i>Klebsiella pneumoniae</i> | 1 | 1 | 2 | 13% |
| <i>Escherichia coli</i> | 1 | 1 | 2 | 13% |
| <i>Pseudomonas aeruginosa</i> | 1 | 2 | 3 | 20% |

Table 9: Culture Specific Antibiotics Used in Group 2

| Culture specific antibiotic used for | Ceftriaxone | Cefotaxime | Ciprofloxacin | Cefoperazone | Piptaz | Amoxi clav | Cefuroxime | Amikacin | Ceftazidime | Vanco mycin |
|--------------------------------------|-------------|------------|---------------|--------------|--------|------------|------------|----------|-------------|-------------|
| | | | | | | | | | | |

| specific organism (No. of cases) | | | | | | | | | | |
|-------------------------------------|---|---|---|---|---|---|---|---|---|---|
| Acinetobacter baumannii (2) | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |
| E coli (4) | 0 | 1 | 0 | 0 | 0 | 0 | 2 | 1 | 0 | 0 |
| K oxytoca (2) | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| K pneumonia (2) | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 0 |
| P aeruginosa (7) | 0 | 0 | 2 | 2 | 0 | 0 | 0 | 1 | 2 | 0 |
| P mirabilis (1) | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| P vulgaris (1) | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Staph aureus (11) | 0 | 0 | 2 | 0 | 2 | 3 | 3 | 0 | 0 | 1 |

Discussion

In group 2 (culture specific antibiotic group) 85% of initial culture from open fracture showed positive report. Lee *et al.* [5] conducted a retrospective study on 245 open fractures to determine the role of bacterial wound cultures in open fracture and observed that, 53% of the initial cultures from open fracture were positive, According to Gustilo and Anderson in their series 70.3% of open wounds yielded positive results. Therefore, they consider the routine use of antibiotics in open fractures as therapeutic rather than prophylactic and a subsequent change should be guided by the sensitivity of the organism isolated.

In group 2 out of 30 positive cultures, Staphylococcus aureus was isolated in 37% of cultures, 63% Gram negative bacteria, among which Pseudomonas aeruginosa was the commonest, accounting for 23% of the cultures. Other members of gram-negative bacteria isolated were, Escherichia coli (14%) Klebsiella pneumoniae (6%), Klebsiella oxytoca (6%), Acinetobacter baumannii (6), Proteus mirabilis (3%), and Proteus vulgaris (3%) (Table 11). This trend was in concordance with the study by Gupta *et al.* [6] which reported that Gram negative bacteria dominated the pre-debridement cultures. About 10-30% of healthy persons and the patients themselves may be carriers of Staphylococcus aureus, especially in the anterior nares. Bedsheets, instruments and dressing materials may also act as reservoirs, contributing to its pathogenicity and increased isolation in traumatic fracture wounds [1].

Post-operative follow up was done for 6 months. 21 % of total cases reported post-operative infection. The infection rates in the post-operative period were correlated with the fracture grading and it was observed that 8% of type I, 19% type 2, 27% type 3 and 28% typ3b fractures developed infection. (Table 14). In the study by Gupta *et al.* [6]. 34.3% of patients with Grade IIIB fractures got infected and 8.3% with Grade I fractures developed infection. Reports from around the world such as that of Weitz-Marschall *et al.* reported a 0% infection rate in type I, up to 12% in type II and up to 50% in type III fractures [7]. Numerous studies support the fact that the incidence of infection in open fractures correlates directly with the amount of soft tissue, bony injury and fracture classification.

Post-operative infection in group 1 with 35 cases of open fractures treated with empirical antibiotics, 8(22%) cases developed infection and in group 2, 30 cases treated with culture specific antibiotics 7(28%) cases developed infection. Rate of infection in both groups are compared for statistical significance using chi-square test (table 13), the p obtained was 0.9637, suggest that no statically significance in rate of infection in both groups as p value is >.05.

In our study the most common organism isolated from post-operative infected cases was Staphylococcus aureus (53%) a gram-positive cocci and the next common was Pseudomonas aeruginosa (20%) a gram negative bacilli and other gram negative bacteria, Escherichia coli and Klebsiella pneumoniae. These findings are in agreement with the extensive study of Arciola *et al.* [8] and Khosravi *et al.* [9] as they noticed most common organism isolated from infected orthopaedic implants was Staphylococcus aureus and other significant pathogen being *Pseudomonas aeruginosa*. This is further supported by the study done by Ralte Lalremruata *et al.* [10] on bacterial pathogen prevalent amongst orthopaedic patients noticed that S aureus is the most common organism isolated. The reason for this could be about 10-30% of healthy people act as carriers and bed sheets, instruments and dressings act as

reservoir, have their presence as nosocomial pathogens in hospital. Bergqvist *et al.* and Dan *et al.*, found that 29.8% of hospitalized patients and 26.6% of hospital staff are carriers [11, 12]. Hence keeping the above observations in mind it's important to select the antibiotic that is effective for prophylaxis.

Gustilo and Anderson in their study of open fractures found that the most common organism that was encountered in open tibial fractures was *Staphylococcus aureus*. Other organisms encountered were *Klebsiella*, *enterobacter*, *E Coli*, *proteus* and coagulase negative staphylococcus [13]. In another study by Patzakis and coworkers it was found that the most common infecting organism was *Staphylococcus Aureus* and followed by mixed gram-positive bacillus which included coagulase positive staphylococcus [14].

Conclusion

Most common pathogen which initially contaminates open fracture in our study is *Staphylococcus aureus* and *Pseudomonas aeruginosa* which constitute half of the cases. There is no significant difference in infection rate between open fractures of long bones treated with empirical antibiotics and culture specific antibiotics from initial culture from open fracture, so initial culture from open fracture does not have any extra advantage and not recommended routinely in management of open fractures.

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