Is DAIR Still an Effective Way to Eradicate Acute Prosthetic Joint Infections? Our Experience in the Jordanian Royal Medical Services

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ABSTRAcT
Background: Prosthetic joint infections is estimated to occur in 1–2% of primary total joint arthroplasty. Debridement, antibiotics, irrigation and retention of prosthesis (DAIR) is the traditional treatment for acute prosthetic joint infections. Objective: To determine risk factors of treatment failure in subjects managed with debridement, antibiotics, irrigation and retention of prosthesis for acute prosthetic joint infections. Methods: Our prospective, double blind and randomized investigation included 70 subjects, of both sexes, aged 63-72 years, who were managed with debridement, antibiotics, irrigation and retention of prosthesis for total hip or total knee arthroplasty acute prosthetic joint infections at Prince Hashim military hospital and Queen Alia military hospital, Jordan, during the period October 2017-October 2020. The observation period was 3 years. Therapy success was defined as absence of infection following 3 years, retention of the prosthesis and no further antibiotics therapy. Prosthetic joint infection was defined based on one or more of: a) growth of the same microorganism in minimum 2 cultures; b) one positive culture and a purulent synovial fluid upon debridement; c) negative culture and minimum 2 of purulent synovial fluid upon debridement. A successful outcome was defined as no clinical and laboratory evidence of infection (serum C-reactive protein less than 10 mg/L) at 3 years. Subjects with chronic, suppressive antibiotics or with prosthesis removal were considered therapy failure. Parameters statistically and remarkably discrepant between success and failure groups were investigated with logistic regression. P less than 0.05 were considered statistically significant. Results: Amount of 46 subjects (65.7%) had no infection during the period of observation. Factors correlated with therapy failure were: history of Rheumatoid Arthritis, delayed infection (more than 1.5 years following arthroplasty), ESR at presentation of more than 50 mm/h and infection induced by coagulase-negative Staphylococcus. Symptoms duration of less than 5 days was associated with a better outcome. The use of Gentamicin sponges was statistically remarkably more in the success group and the use of beads was more in the failure group in the univariate but not in the logistic regression. Less surgical interventions were needed in the group managed with sponges than in the group managed with beads. Prosthetic joint infection induced by coagulase-negative Staphylococcus was associated with a less success rate and streptococcal infections were associated with an increased success rate. Conclusion: Rheumatoid arthritis, duration of symptoms of more than 5 days, ESR of more than 50 mm/h, delayed infection (more than 1.5 years following the index arthroplasty) and coagulase-negative Staphylococcus infections reduce the rate of a successful debridement, antibiotics, irrigation and retention of prosthesis therapy. Keywords: Debridement, antibiotics, irrigation, retention; Prosthetic joint infections.

1. BACKGROUND
Prosthetic joint infections is estimated to occur in 1-2% of initial total hip arthroplasties and total knee arthroplasties (1). Infected prosthetic joints are unresponsive to systemic antibiotics therapy alone because of the poor vascular supply and biofilm production. Acute prosthetic joint infections are divided in three groups according to the period of clinical picture and postoperative period: a) Early after surgery: clinical picture less than 4 weeks postoperatively; b) Delayed chronic: gradual onset of clinical picture and c) Acute hematogenous: acute onset in a previously well-functioning prosthesis (2) or early (3 months), late/low-grade (3-24 months) and delayed infection (more than 24 months) (3).
Different risk factors associated with acute prosthetic joint infections are rheumatoid arthritis, diabetes mellitus, malignancy, obesity and immunosuppressant use (4). Revision operation increases the risk of acute prosthetic joint infections. Factors associated with a worse result of acute prosthetic joint infections therapy are: infections induced by Staphylococcus spp. (5) and more by Staphylococcus aureus (6), polymicrobial acute infections (4), intra-articular purulence (5), retention of exchangeable elements (4) and a longer period between the index arthroplasty and the confirmation of infection (4).

Most acute prosthetic joint infections are caused by coagulase-negative Staphylococcus (30-41%) and S. aureus (12-47%). Streptococcus spp. and Enterococcus spp. are found in approximately 10% of cases and gram-negative bacteria such as Escherichia coli are less than 5% (7). 5–39% were polymicrobial infections (6).

Debridement, antibiotics, irrigation and retention of the prosthesis (DAIR) is used for acute infections with no risk factors such as remarkable co-morbidities. DAIR has a success rate between 14% and 100% (8). Success of more than 70% can be expected in cases with a short period of symptoms (less than 3-4 weeks), a stable implant and a healthy soft tissues around the prosthesis are selected (9). In chronic infections, implant retention is rarely successful.

Local antibiotics with aminoglycosides in beads or sponges achieve increased local concentrations with no toxic serum levels. Beads have a lengthened release in comparison to sponges but with no increased concentrations, acting as foreign bodies, to which bacteria can adhere.

2. OBJECTIVE

The aim of this study was to determine the risk factors in patients managed with debridement, antibiotics, irrigation and retention of prosthesis for acute prosthetic joint infections and the results of DAIR for total hip and knee.

3. METHODS

Our prospective, double blind and randomized investigation included 70 subjects, of both sexes, aged 63-72 yrs. and managed with debridement, antibiotics, irrigation and retention of prosthesis for total hip arthroplasty or total knee arthroplasty acute prosthetic joint infections at Prince Hashim military hospital and Queen Alia military hospital, Jordan, during the period October 2017 - October 2020, after obtaining written informed consent from all subjects and approval from our local ethical and research board review committee of the Jordanian Royal medical services. The observation period was 3 years. Absence of infection following 1.5 years, retention of the prosthesis and no further antibiotics therapy was regarded as therapy success.

Prosthetic joint infection was defined based on one or more of (8): a) growth of the same microorganism in minimum 2 cultures (before surgery joint aspiration and/or during surgery, intracapsular); b) one positive culture and intracapsular purulence in debridement, acute inflammation upon histological study of tissue taken intraoperatively and/or an actively draining sinus tract; c) negative culture and minimum 2 of intra-articular purulence upon debridement, acute inflammation upon histological study of tissue taken intraoperatively and an actively draining sinus tract.

The decision to do DAIR or not was made according to the clinical picture, kind of infection and whether the prostheses were loose. DAIR was repeated following 2 weeks if the clinical and laboratory picture worsened. Antibiotic therapy based on bacterial antibiogram was given for a minimum 6 weeks. The joint was opened via the old scar or incision, tissues were samples for three cultures from synovium, capsule and interfaces, and the joint was debrided with synovial resection. Following debridement, the joint and overlying soft tissues were irrigated with saline using lavage, and primarily closed. Removal of Gentamicin beads was with debridement. After surgery, antibiotics were started, either with a broad coverage such as Vancomycin, or an agent according to antibiogram. Enoxaparin 4000 IU SC was given daily in the hospital. Before debridement, antibiotic holiday and aspirating the joint to define the offending organism before operation is recommended. Removal of skin margins, excision of any sinuses, radical synovectomy and exchange of modular parts of the implant (polyethylene inlay, femoral head, polyethylene tibial insert) follows. The joint should have a full lavage. A suction drain can be left inside for couple of days. If drainage or infection continue, then a second debridement is advised. Continuous closed irrigation was not more efficient than standard technique with initial closure and in situ drain.

A proper treatment outcome was defined as no clinical and laboratory picture of inflammation (serum C-reactive protein less than 10 mg/L) at 3 years. Subjects with chronic, suppressive antibiotics or with prosthetic removal were therapy failure.

Statistical analysis

Independent t-tests were done for continuous parameters and the non-parametric Mann-Whitney U-test was used for continuous parameters. For categorical variables, chi-square and Fisher’s exact tests were done. Parameters statistically and remarkably discrepant between success and failure groups were investigated with logistic regression. P less than 0.05 were considered statistically significant.

4. RESULTS

Amount of 70 patients with prosthetic joint infections (48 hips and 22 knees) were managed with DAIR, of whom 46 subjects were infection-free after treatment without the need for further resection arthroplasty or administration of suppressive antibiotics (65.7% success rate). Patients’ data analyzed for the Success and failure groups risk factors are shown in Table 1.

Five factors were correlated with failure: rheumatoid arthritis, delayed infection, ESR more than 50 mm/h, clinical picture period more than 5 days before the be-
Table 2. Clinical features according to success or failure of management.

| Parameter                        | Success group | Failure group | P (univariate) | P (multivariate) |
|----------------------------------|---------------|---------------|----------------|------------------|
| Number                           | 46            | 24            |                |                  |
| Average age (years)              | 68            | 67            | 0.5            |                  |
| Gender M                         | 16            | 11            | 0.4            |                  |
| Gender F                         | 30            | 13            |                |                  |
| Hip arthroplasty                 | 31            | 20            | 0.1            |                  |
| Knee arthroplasty                | 15            | 4             | 0.3            |                  |
| Infection post revision          | 9             | 2             | 0.4            |                  |
| Arthroplasty with cement         | 17            | 16            | 0.05           | 0.6              |
| Co-morbidities                   |               |               |                |                  |
| Lung disease                     | 3             | 4             | 0.1            |                  |
| Diabetes mellitus                | 5             | 4             | 0.3            | 0.05             |
| Rheumatoid arthritis            | 2             | 5             | 0.05           |                  |

Table 1. Subjects data based on success or failure of management.

| Parameter                        | Success group | Failure group | P (univariate) | P (multivariate) |
|----------------------------------|---------------|---------------|----------------|------------------|
| Number                           | 46            | 24            |                |                  |
| Average period of symptoms (days)| 2             | 5             | 0.05           |                  |
| Symptoms <5 days.                | 34            | 12            | 0.05           | 0.05             |
| Symptoms <15 days.               | 42            | 19            | 0.2            |                  |
| Average period from arthroplasty to presentation (days) | 18 | 39 | 0.05 |                  |
| Infection presentation           |               |               |                |                  |
| Early <3 months                  | 39            | 16            | 0.05           |                  |
| Delayed (3-24 months)            | 6             | 5             | 0.3            |                  |
| Late >1.5 yrs.                   | 1             | 3             | 0.05           | 0.05             |
| Infection type                   |               |               |                |                  |
| I                                | 32            | 11            | 0.3            |                  |
| II                               | 1             | 2             | 0.3            |                  |
| III                              | 13            | 11            | 0.4            |                  |
| ESR >50 mm/hr.                   | 15/36         | 16/19         | 0.005          | 0.005            |

Table 2. Clinical features according to success or failure of management.

| Parameter                        | Success group | Failure group | P (univariate) | P (multivariate) |
|----------------------------------|---------------|---------------|----------------|------------------|
| Number                           | 46            | 24            |                |                  |
| Average operations               | 2.2           | 2.6           | 0.2            |                  |
| DAIR                             |               |               |                |                  |
| One                              | 14            | 8             | 0.9            |                  |
| multi                            | 32            | 16            | 0.9            |                  |
| Gentamicin                       |               |               |                |                  |
| Sponges                          | 37            | 13            | 0.005          | 0.3              |
| Beads                            | 5             | 7             | 0.05           | 0.9              |
| Sponges and beads                | 4             | 4             | 0.3            | 0.9              |

5. DISCUSSION

Prosthetic joint infection is a serious complication in total joint replacement and is the second most frequent cause of revision of joint replacement. Management choices are: non-surgical methods with long period of antibiotics, debridement followed by a period of antibiotics and implant retention (DAIR), 1 or 2-stage revision, joint fusion and amputation. Implant retention with infection treatment is optimum and DAIR had different success percentages based on the patient, period of infection, the offending microorganisms, technique, number of debridements performed, arthroscopic or open, and the period of antibiotic administration. Risk factors of DAIR failure are: immunocompromised host, a long period between the start of infection and surgical debridement, the presence of a sinus, Staphylococcal infection (especially Methicillin Resistant Staphylococcal Aureus), multi-debridements, short antibiotic period and retention of exchangeable parts.

Of 70 subjects in our study, 46 were managed successfully with DAIR. Revision arthroplasty was a risk factor for prosthetic joint infection, but was not linked to therapy failure. Only rheumatoid arthritis had more therapy failure rate (8). Only three subjects with Rheumatoid Arthritis were using immunosuppressive agents (one in the success group and two in the failure group).

In most subjects (46/70), intervention was started during 5 days of presentation with more favorable outcome. The therapy success with early infections and infections of short period of symptoms is frequently caused by lack of biofilm formation (1), and it is indicated that DAIR must only be used for subjects with a short period of symptoms (not more than 15 days) or period with successful therapy. Prosthetic joint-correlated infection induced by coagulase-negative Staphylococcus was correlated with a reduced success incidence and streptococcal infections were correlated with an increased success incidence. All streptococcal infections were managed during 5 days of clinical picture. Five subjects had a polymicrobial prosthetic joint-correlated infection with successful therapy.
following index surgery of less than 30 days (9). Clinical picture of less than seven days was correlated with therapy success. Six subjects with a period of clinical picture of more than 4 weeks were managed with DAIR. Early prosthetic joint infection was recorded during 3 months following index operation (3). Period of clinical picture of more than 4 weeks was not a factor associated with therapy outcome. An ESR of more than 50 mm/h was associated with therapy failure. A reduced ESR might indicate a shorter period of infection, and might be an antici-pative of an increased success. These markers (CRP and ESR) can confirm prosthetic joint infection (10), although increased CRP was anticipative of failure (4).

During revision, Gentamicin beads were used to fill the dead space following arthroplasty removal (8). The use of Gentamicin sponges in management of prosthetic joint infection was used (11). An increased success incidence for sponges and a reduced success incidence for beads was recorded. The collagen-Gentamicin sponges used are biodegradable, but not beads. Sponges attain more local antibiotic concentrations than beads. Beads are foreign bodies and sustain infection.

This study was small and beads were used in severe infection. Coagulase-negative Staphylococcus infection was linked with therapy failure. Staphylococcal or S. aureus infection had more risk of failure (5) due to the ability of the species to produce an early biofilm. The virulence of coagulase-negative Staphylococcus is low, which may delay the confirmation of infection. Management of streptococcal infections had an increased success percentage during 5 days following clinical picture. The increased success percentage is due to the short period of clinical picture. There was an association between streptococcal infections and good outcome (12). Three of 70 subjects experienced a polymicrobial infection, but were with no infection later on. Polymicrobial infections was in the range of 5 and 10% (13, 14) and more percentages of multi-organism prosthetic joint infection of 19-39% (6). More failure for polymicrobial infection was recorded with a hazard ratio of 1.8 (4).

Not exchanging the polyethylene insert in TKA or the PE inly and femoral head in THR was an independent risk factor for failure. Modular exchangeable parts should always be exchanged.

The methods of irrigation and debridement and culture were not identical in all subjects. There was possible bias in the use of Gentamicin beads and sponges. DAIR must be performed in the acute phase after surgery during one month or in acute late haematogenous infections of TKA during ten days of onset. The debridement must be open and not arthroscopic and the modular parts should be exchanged. Antibiotics after surgery must be administered for at least 3 months and followed up by clinical inflammatory markers. Immunocompromised patients, MRSA infection, the failure of one DAIR and poor status of surrounding soft tissues usually end up in one or two-stage revision arthroplasty. During lavage, there was a tendency toward using chlorhexidine gluconate 0.05%. Chlorhexidine gluconate was most efficient in decreasing bacterial growth and hence was superior to jet saline lavage.

### 6. CONCLUSION

Multiple factors were related with DAIR failure: rheumatoid arthritis, period of clinical picture more than 5 days, delayed infection (more than 1.5 years following arthroplasty), ESR of more than 50 mm/h and coagulase-negative Staphylococcus. If one or more of these factors are found in a patient, the chances of successful DAIR therapy reduces. Gentamicin sponges had outcome similar to those of beads.

| Parameter                          | Success group | Failure group | P(univariate) | P(multivariate) |
|------------------------------------|---------------|---------------|---------------|-----------------|
| Coagulase-negative Staphylococcus  | 3             | 8             | 0.005         | 0.05            |
| Staphylococcus aureus              | 30            | 15            | 0.5           |                 |
| Streptococcus spp.                 | 9             | 1             | 0.05          |                 |
| Enterococcus faecalis              | 4             | 0             | 0.3           |                 |

Table 4. Microbiology and success or failure of management.

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