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Original Research

A double-blind, randomized, placebo-controlled trial of short- and extended-regime antibiotics in infection rates after open reduction and internal fixation of uncomplicated single mandibular fractures

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ABSTRACT

Purpose: To compare short- and extended-regimen post-operative antibiotic prophylaxis after open reduction internal fixation (ORIF) of single uncomplicated mandibular fractures.
Subjects and methods: A prospective, single centre, randomized, double-blinded, placebo-controlled study was carried out where 39 patients with single uncomplicated mandibular fractures were treated by an intra-oral approach. They were divided into two groups: group 1 (20 patients) and group 2 (19 patients). Each group received injection amoxicillin + clavulanic acid (30 mg/kg/day) pre-operatively, intra-operatively and for 24 h post-operatively. Group 1 then received placebo and group 2 received oral amoxicillin + clavulanic acid (30 mg/kg/day) in two divided doses for the next 4 days. The patients were evaluated on the 3rd and 7th post-operative day for signs of clinical infection and suture site aspirates were collected for culture. Microbial load was evaluated against the presence or absence of clinical infection in both the groups.
Results: Two patients (10%) in group 1 and three patients (15.7%) in group 2 had clinical signs of infection. No statistically significant difference ($p = 0.58$) was seen in the incidence of infection in both the groups. Microbial load was positive in seven patients (35%) and six patients (30%) in group 1; four patients (21%) and three patients (15.8%) in group 2 on the 3rd and 7th post-operative day respectively. No statistical significance was seen with the presence of microbial load and clinical signs of infection in both groups.
Conclusion: After ORIF of single uncomplicated mandibular fractures, infection rates are the same with either short- or extended-antibiotic regimen.

1. Introduction

Infection of mandibular fractures is a significant problem when compared to other facial fractures [1]. Mandibular fractures in the dentate segment are frequently contaminated as they are vulnerable to seepage of oral flora through the periodontal ligament or mucosal tears leading to infection. With the frequent use of open reduction and internal fixation (ORIF) for management of these injuries, infection rate further increases when compared to closed treatment [2]. Micro-organisms often attributed to maxillofacial infections are staphylococci, streptococci, peptostreptococci and bacteroides [3]. While using a trans-oral approach, streptococci, anaerobic Gram-positive cocci, and anaerobic Gram-negative rods predominate; whereas staphylococci poses an additional risk while using a trans-cutaneous approach [4]. The presence of these bacteria at the operated site as they overcome the host resistance is important for the establishment of infection.

The use of pre-operative and peri-operative antibiotics to decrease the incidence of infection during ORIF of mandibular fractures has been well established [1,5]. The problem is how long post-operative antibiotics should be administered so as to prevent infection of the suture site. Long-term antibiotics increase the risk of superinfections, allows microbes to develop resistant strains endangering the entire community and additionally they account for a significant financial burden on the health care system. The current problem has been recognized by many researchers and a

☆ Asian AOMS: Asian Association of Oral and Maxillofacial Surgeons; ASOMP: Asian Society of Oral and Maxillofacial Pathology; JSOP: Japanese Society of Oral Pathology; JSOMS: Japanese Society of Oral and Maxillofacial Surgeons; JSOM: Japanese Society of Oral Medicine; JAMI: Japanese Academy of Maxillofacial Implants.

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number of protocols have been used while studying infection rates after treatment of mandibular fractures. Investigators have compared 1 shot, 1 day with a 3-day regimen [6], less than 2 days with more than 2 days [7], and 1 day with a 5-day regimen [8]. Unfortunately, however, only a few double-blinded randomized control trials have attempted to answer the problem.

The present study was designed to determine if extended regimen of antibiotic is necessary to reduce the incidence of infection after trans-oral ORIF of mandibular fractures. Also evaluated was whether the presence of microbial load at the suture site corresponds to clinical signs of infection.

2. Subjects and methods

A prospective, single centre, randomized, double-blinded, placebo-controlled study was designed wherein all healthy males and females reporting with single uncomplicated mandibular fracture between 1st October 2010 and 31st June 2011 were included. Prior institutional ethical clearance and informed written consent was obtained from every patient. Exclusion criteria were (1) infected fractures at the time of treatment, (2) comminuted mandibular fractures, (3) gunshot mandibular fractures, (3) condylar fractures, (4) extra-oral approach required to treat the fracture, (5) associated midface or systemic injuries, (5) immunocompromised medical status, (6) patients allergic to penicillin, (7) non-compliance in taking post-operative medication, (8) pregnant patients, and (9) patients less than 12 years of age.

2.1. Study design

Routine blood investigations and oral prophylaxis was carried out pre-operatively. An antibiotic sensitivity testing was carried out by sub-cutaneous deposition of 0.1 ml of injection amoxicillin + clavulanic acid in the patients' forearm. In case of sensitivity, patient was excluded from the trial. Prophylactic antibiotic was administered prior to surgery in the form of intra-venous injection of amoxicillin + clavulanic acid (30 mg/kg/day) to all patients and continued through the intra-operative period and for 24 h post-operatively. After 24 h, randomization was carried out for the administration of post-operative antibiotic. Forty similar drug-dispensing bottles were sequentially numbered for concealed allocation of patients to the trial groups. Each bottle contained the post-operative medication for a single patient which was predetermined by a computer generated random number table. Tablet amoxicillin + clavulanic acid and lactulose powder dispensed in hard gelatin capsules of similar colour by the hospital pharmacist were pre-packed in these bottles. Using this method of randomization, the patients according to their sequence of enrolment received their post-operative medication in the corresponding pre-packed bottle. Thereby assigning them into two groups – Group 1 received placebo and Group 2 received tab amoxicillin + clavulanic acid (30 mg/kg/day) in two divided doses for the next 4 days. The randomization code was secured with the head of the department in a sealed envelope to be broken as per Good Clinical Practice (GCP) guidelines or in case of serious adverse outcome. The code was revealed to the investigator at the end of the trial. The operating surgeon, investigator, statistician and patients were blinded with regard to which patient received what medication.

2.2. Surgery

ORIF was carried out for all mandibular fractures under general/local anaesthesia via an intra-oral vestibular approach by a single surgeon using same set of instruments. Pre-operative maxillo-mandibular fixation (MMF) was done for all patients at the time of admission. Local anaesthetic with adrenaline was infiltrated at the incision site. Fracture site exposure and reduction was carried out. Fracture segments were fixed using titanium osteosynthesis plates and screws (Synthes-Stratec, Oberdorf, SwitzerLand). Two plates were used for treating symphysis and parasymphysis fractures. For body fractures a single miniplate was fixed just below the tooth roots while for angle fractures, Champy's technique for superior border plating was used. Primary closure was done with 3-0 Vicryl® sutures (Ethicon, Somerville, NJ, USA). Compression dressing was applied extra-orally for 2 days. Ice pack was applied for 24 h. Analgesics were given as required and chlorhexidine mouthwash was prescribed to every patient for 2 weeks post-operatively. Suture removal was carried out after 1 week.

2.3. Follow-up evaluation

Patients were examined by a single blinded investigator on the 3rd and 7th post-operative day. The following signs of infection were looked out for:

1. Purulent discharge from the surgical/fracture site.
2. Fever with or without swelling, erythema, tenderness and dehiscence.
3. Fistula formation with drainage from surgical/fracture site.

The suture site was considered infected if any of these signs were present. Also, suture site aspirate was collected using a needle and syringe where 2 ml sterile saline solution was injected into the soft tissue incision site and aspirated back. Adequate topical anaesthesia was provided before collecting the aspirate so as to minimize patient discomfort. In case of extremely un-cooperative patients, the aspirate was collected under a regional nerve block. The primary objective was to evaluate and compare the incidence of infection in the placebo group and the antibiotic group. The secondary objective was to evaluate the local microbial load in both the groups on the 3rd and 7th post-operative day and establish whether local microbial load corresponds to clinical outcome.

2.4. Statistical analysis

Data collected for every patient included: age, sex, past medical history, mode of trauma, fracture site whether there was an anterior mandibular fracture (symphysis and parasymphysis) or a posterior mandibular fracture (body and angle), time elapsed from injury to treatment, whether the patient received post-operative antibiotics or not, signs of infection and presence or absence of microbial load in the post-operative period. Data was tabulated in Microsoft Excel (Microsoft, Redmond, WA, USA) analyzed for statistical difference between the two groups by 2-tailed Fisher's exact test with a 95% confidence interval using Stata, version 8 (Statacorp, College Station, TX, USA).

3. Results

Out of 85 patients assessed for eligibility, 40 patients met the inclusion criteria, out of which 1 was lost to follow-up leaving a total of 39 patients in the study. The age distribution of the sample was between 15 and 70 years with a mean of 29.2 years. Out of 39 patients, 33 were men and 6 were women. Group 1 (placebo group) included 20 patients and group 2 (antibiotic group) included 19 patients. There was no statistical significant difference between the two groups in terms of any patient characteristic (Table 1). Infection was present in two patients (18.2%) in group 1 and three patients (15.7%) in group 2. There was no statistically significant difference ($p = 0.58$) in the incidence of infection in both the groups. Of the infected cases, one was a women and the rest were men. Erythema