The role of postoperative prophylactic antibiotics in the treatment of facial fractures: a randomised, double-blind, placebo-controlled pilot clinical study. Part 3: Le Fort and zygomatic fractures in 94 patients

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Abstract

The aim of this study was to evaluate the difference between the effect of a 5-day and a 1-day postoperative course of antibiotics on the incidence of infection after midfacial fractures. A total of 98 patients with displaced Le Fort or zygomatic fractures that required operation were randomly assigned into 2 groups, both of which were given amoxicillin/clavulanic acid 1.2 g intravenously every 8 h from the time of admission until 24 h postoperatively. The 5-day group was then given amoxicillin/clavulanic acid 625 mg orally 8-hourly for another 4 days. The 1-day group was given placebo orally at the same time points. Patients were followed up 1, 2, 4, 6, and 12 weeks, and 6 months, postoperatively. The development of an infection of the wound was the primary end point. Ninety-four of the 98 patients completed the study. Two of the 45 patients in the 5-day group (4%) and 2/49 in the 1-day group (4%) developed postoperative wound infections. One in each group had a purulent infection, while the others had only wound breakdown. Two patients of the 5-day group and one in the 1-day group developed rashes on the trunk. There were no significant differences in the incidence of infection or side effects between the groups. In midfacial fractures a 1-day course of antibiotics postoperatively is as effective in preventing infective complications as a 5-day regimen.

Keywords: Zygoma; Zygomatic fracture; Midface fractures; Le Fort; Antibiotics; Antimicrobial agents; Infection

Introduction

In a large study of craniomaxillofacial trauma, midfacial fractures accounted for 71.5% of the facial fractures. Because of the prominent position of the zygoma in the midface, fractures of it are the most common in the midface after those of the nasal bone. Orbital and Le Fort fractures also account for a large proportion of fractures in more severe midfacial trauma.

The zygoma forms part of the bony orbit and the maxillary sinus, and displacement commonly results in opening of the non-sterile sinus, which potentially increases the risk of infection not only of the soft tissue but also of the eye. An intraoral approach is often used for reduction and fixation of both zygomatic and Le Fort I and II fractures. Because of the inevitable contamination of the surgical wounds with the bacterial flora of the oral cavity and sinuses, they are considered clean-contaminated wounds and hence at an increased risk of postoperative wound infection. Prophylactic antibiotics are therefore both justified and widely used.

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However, there are at present no clear guidelines about the duration of the postoperative antibiotic regimen. In addition, various authors such as Zachariades et al, and Chloe and Yee, have reported low infection rates (0.8% and 0, respectively) in patients treated for midfacial fractures.\textsuperscript{4,5}

The purpose of this randomised, placebo-controlled, double-blind trial was therefore to investigate the efficacy of antibiotics given after operations on midfacial fractures, and to compare a 1-day with a 5-day postoperative antibiotic regimen.

Patients and methods

This prospective, single centre, randomised, double-blinded, placebo-controlled clinical trial followed the principles outlined in the Declaration of Helsinki and was approved by the local Human Ethics Committee.

A total of 98 patients with zygomatic or Le Fort fractures, who were treated by open reduction and internal fixation at the Department of Cranio-Maxillofacial Surgery, University Hospital of Bern, Switzerland, from January 2008 to July 2011, were enrolled. Written informed consent for participation in the study was obtained from all patients.

Patients were excluded from the trial when any of the following criteria were present: need for intensive care, presence of an acute bacterial infection, gunshot wounds, pathological fracture (caused by cysts or metastases, for example), fracture of the skull base with rhinoliquorrhoea or intracranial emphysema, history of malignancy or radiation to the head and neck region, known hypersensitivity or allergy to penicillin or other β-lactam antibiotics, compromised host defence including immunosuppression, malabsorption, malnourishment, cachexia, and reduced body weight (<40 kg or body mass index (BMI) <17), severe renal insufficiency (stage ≥ 4 according to the Kidney Disease Outcomes Quality Initiative),\textsuperscript{6} or poor compliance. Those who needed postoperative maxillomandibular fixation (MMF) were also excluded.

Patients were then randomly assigned into 2 groups according to a computer-generated protocol (RandList\textsuperscript{8}, Version 1.0, DatInf GmbH, Tübingen, Germany). The ratio of penicillin:placebo was 1:1. The list with the computer-generated numbers was kept by the pharmacist responsible. Details of the list were not known by any of the attending surgeons or nurses. The antibiotics and placebo were prepared by the pharmacy using identical gelatin capsules. The surgeons, nurses, and patients were unaware of which postoperative prophylaxis was being given. The main investigator found out the code only at the end of the trial.

Antimicrobial prophylaxis

From admission until 24 h postoperatively, all patients were given 1.2 g amoxicillin/clavulanic acid (GlaxoSmithKline AG, Münchenbuchsee, Switzerland) intravenously every 8 h as prophylaxis. Patients in the 5-day group were then given oral amoxicillin/clavulanic acid 625 mg 3 times daily for an additional 4 days.

Patients in the 1-day antibiotic group were given an oral placebo 3 times a day for the same period. Patients who had intraoral surgical approaches were also given 0.1% chlorhexidine mouthwash (Chlorhexamed\textsuperscript{®}, GlaxoSmithKline, Münchenbuchsee, Switzerland) postoperatively.

Surgical technique

All operations were done under general anaesthesia by senior staff and trainees.

Zygomatic complex/Le Fort III fractures

The frontozygomatic fracture was routinely exposed through a lateral eyebrow incision, and it was then reduced using a malar hook. In cases of comminution of the bone, difficult reduction, or insufficient stability, we obtained additional surgical access (intraoral or transconjunctival). After verification of the correct position of the zygoma, the fracture was fixed using standard titanium miniplates and screws (Synthes, Oberdorf, Switzerland or Medartis, Basel, Switzerland) where necessary.

Le Fort I and II fractures

After arch bars had been placed, we made an intraoral vestibular incision and dissected subperiosteally. In Le Fort II fractures we made additional transconjunctival incisions. The fracture was exposed then reduced, teeth were wired into the intermaxillary fixation, and the fracture was fixed using standard titanium miniplates and screws (Synthes or Medartis). In cases in which the nasal bone and septum were involved, they were repositioned by closed reduction, and stabilised using septal splints and a nasal cast.

Involvement of orbital floor

Exposure was achieved through a transconjunctival approach. The herniated tissue was repositioned and the defect in the orbital floor was covered using resorbable implants of polyglandin/polydioxyanone (Ethisorb, Johnson & Johnson, New Brunswick, USA) or poly-L/DL lactide (Polimax, Synthes, Oberdorf, Switzerland) if necessary. Wounds were closed with polyglandin 910 (Vicryl) and polypropylene (Prolene) sutures.

Outcome measures

The surgeons evaluated all participants for infection within a 6-month period postoperatively according to the criteria for infections of the surgical site published by the Centres for Disease Control (CDC).\textsuperscript{7} These included: purulent discharge (with or without microbiological confirmation), spontaneous
wound dehiscence, abscess formation, or deliberate opening of the wound by a surgeon in the presence of signs and symptoms of infection such as localised pain, tenderness, or fever (>38 °C). Any possible adverse or allergic reactions were recorded. Patients were evaluated daily during their hospital stay. After discharge, they were followed up at 1, 2, 4, 6, and 12 weeks, and 6 months.

**Treatment of infection**

If there were signs of postoperative wound dehiscence or superficial purulent infection, patients were treated with local measures including drainage and daily wound irrigation with povidone iodine (Betadine®; Mundipharma Medical Company, Basel, Switzerland). In cases of deeper infection, the treatment included the immediate use of a broad-spectrum antibiotic with subsequent modification if needed, depending on the results of culture and sensitivity tests.

**Statistical analysis**

Based on the prevalence of infection after surgical treatment of facial fractures in previous studies, we estimated that a sample size of 110 in each group would be needed for a power of 80% and type I error of 5% (one-tailed) (Power and Precision 3.2, Biostat Inc., Nova Jersey, USA). We studied only 94 patients and therefore this needs to be viewed as a pilot study for future research.

**Results**

Between January 2008 and July 2011, 213 patients with a fractured zygoma or Le Fort type fracture were treated surgically, of which 98 met the criteria to be included in this study. Three patients with fractured zygomas withdrew from the study – one developed an allergic rash to the drugs, and two failed to attend postoperative appointments. One patient from the Le Fort fracture group was unable to swallow the tablets provided. A total of 94 patients therefore completed the study.

There were 35 in the Le Fort fracture group (30 of whom were male) and 59 in the zygomatic fracture group (44 of whom were male), and their ages ranged from 14 to 77 years. After randomisation, there were 45 patients in the 5-day group and 49 in the 1-day group (Table 1). The groups were comparable.

Fifty patients with fractures of the zygoma were treated by plating of the frontozygomatic region, or the infraorbital region, or both, of which 4 also had the zygomaticomaxillary buttress fixed. Seven patients were deemed not to require fixation with plates after reduction, and 2 required only plating of the zygomaticomaxillary buttress. The orbital floor was reconstructed with absorbable polyglactin/polydioxanone (Ethibond) patches in 19 cases, and poly-L/DL lactide (Polymax) plates in 8 cases (Table 2). In the Le Fort fracture group,
Table 2
Details of patients who had reconstruction of fractures of the zygoma (data are number of patients).

<table>
<thead>
<tr>
<th></th>
<th>5-Day group (antibiotic)</th>
<th>1-Day group (placebo)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plating:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No plating</td>
<td>3</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>Intraoral approach</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>and plating alone</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extraoral approach</td>
<td>22</td>
<td>24</td>
<td>46</td>
</tr>
<tr>
<td>and plating alone</td>
<td></td>
<td></td>
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<td>Intraoral and</td>
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<td>extraoral approaches and</td>
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</tr>
<tr>
<td>plating</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Orbital reconstruction:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No implant</td>
<td>16</td>
<td>16</td>
<td>32</td>
</tr>
<tr>
<td>Ethisorb patch</td>
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<td>10</td>
<td>19</td>
</tr>
<tr>
<td>Polymax plate</td>
<td>3</td>
<td>5</td>
<td>8</td>
</tr>
</tbody>
</table>

Table 3
Details of Le Fort fractures (data are number of patients).

<table>
<thead>
<tr>
<th></th>
<th>5-Day group (antibiotic)</th>
<th>1-Day group (placebo)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isolated Le Fort I</td>
<td>9</td>
<td>10</td>
<td>19</td>
</tr>
<tr>
<td>Isolated Le Fort II</td>
<td>2</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Isolated Le Fort III</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Multiple levels (I–III)</td>
<td>6</td>
<td>4</td>
<td>10</td>
</tr>
<tr>
<td>Total</td>
<td>17</td>
<td>18</td>
<td>35</td>
</tr>
</tbody>
</table>

19 patients had isolated Le Fort I fractures, 6 had isolated Le Fort II fractures, and none had isolated Le Fort III fractures. However, 10 patients had fractures at multiple levels, including 4 with Le Fort III fractures (Table 3).

Two patients in each group (4%) developed postoperative infections – one from each group had a purulent infection, of which the one in the 5-day group spontaneously discharged from a small wound dehiscence. The other 2 patients had only breakdown of the wound (Table 4). All the patients with postoperative infections in the Le Fort fracture group had Le Fort I fractures only.

All patients with wound breakdown including the patient with concurrent purulent discharge were successfully treated with local measures alone. The other patient with a purulent infection was prescribed amoxicillin/clavulanic acid 1 g twice daily for 5 days, over and above the local measures, which resolved the infection. Two patients in the 5-day group and 1 in the 1-day group developed skin rashes over the trunk. There were no significant differences between the groups in the incidence of infection or side effects.

Discussion

The Surgical Infection Prevention Guideline Writers Workgroup in the United States issued a consensus paper in 2005 that advised that antimicrobial prophylaxis should be given within 60 min before the incision is made, and then discontinued within 24 h postoperatively, as prolonged use of prophylactic antimicrobial agents showed no additional benefit, and is associated with emergence of resistant bacterial strains. However, we could find little published information about antimicrobial prophylaxis in the management of midfacial fractures, and few papers that deal with open reduction of these fractures actually mention the duration of postoperative prophylaxis. Kneip and Loukota retrospectively reviewed 134 patients from various centres concerning their infection rates after repair of zygomatic fractures. They highlighted the wide variation in the prescription of prophylactic antibiotics, with postoperative regimens ranging from 4 doses or fewer to courses of 5–7 days. They reported just 2 infections of the surgical site in the 134 patients (1.5%), and these resolved with oral courses of antibiotics.

A more recent retrospective cohort study by Lauder et al. suggested that there was no significant difference in the infection rate between patients with complex trauma of the midface and frontal sinuses who were given only perioperative antibiotics, and those who received additional antibiotics before or after operation. The overall infection rate was 9% in their study.

Our results are in agreement with theirs, as we found no significant difference in the incidence of infection between the group given antibiotics before, during, and up to 24 h after operation, and the other group who were given a 5-day course. Our overall infection rate was 4/94 (4.3%) which was lower than that study, but higher than some of the earlier studies, possibly because most of our patients were treated by internal fixation with miniplates rather than reduction without plating, and the broader CDC criteria for infections of the surgical site that we adopted included cases of wound dehiscence, which is often difficult to elicit accurately retrospectively. If we exclude cases with spontaneous wound dehiscence, our rate of infection drops to 2.1%, which is closer to the rates reported by the earlier studies of antimicrobial prophylaxis.

We previously published Part 1 of our series on antibiotic prophylaxis in orbital fractures, in which we found no significant difference in the incidence of infection between the groups given 1 and 5 days of postoperative antibiotic prophylaxis. The overall infection rate in that study was 5%, which is consistent with the present study of the midfacial skeleton.

Of the 4 patients who developed postoperative infections, 3 were in the Le Fort fracture group, and tellingly, all of them had Le Fort I fractures and so had been treated by reduction and fixation through an intraoral approach. These infections might have been related to the contamination of the surgical site with the facultative pathogenic mixed flora of the oral cavity. The patient in the 1-day group had long intervals between trauma and starting preoperative antibiotics, and also between trauma and operation, which might have been contributory. The remaining patient who developed an infection had a comminuted fracture of the zygoma and orbital floor.
Reduction and fixation of the zygoma, infraorbital rim, and reconstruction of the orbital floor with a PolyMax orbital plate was done through a lateral eyebrow and transconjunctival approach, aided by a percutaneously-placed malar hook. No intraoral incision was made. Nonetheless, the degree of bone comminution and the relatively long operation (2 h) could have contributed to the subsequent development of a postoperative infection. On top of this, the patient was in the placebo group and so was not given a prolonged postoperative course of antibiotics.

Other potential confounding factors such as smoking, BMI, multiple fractures, and type of implant had no significant impact on the likelihood of postoperative infection.

Our study has certain limitations. First, the duration of preoperative antibiotic prophylaxis was not the same for all, as our patients were brought in as emergencies, and such operations cannot always be scheduled like elective cases. Secondly, with the low number of postoperative infections in the midface, our sample size may not have been large enough to detect significant differences in infection rates. With this in mind it should be viewed as a pilot study on which future research can be based. Larger randomised, double-blind, placebo-controlled studies will be necessary to provide further evidence. However, we hope that our results will contribute to future guidelines on the use of prophylactic antibiotics after repair of zygomatic and Le Fort fractures.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.bjoms.2014.01.010.

References