Efficacy of Single Dose Azithromycin as Prophylactic Antibiotic in Surgical Removal of Mandibular Third Molars: A Clinical Study

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Abstract

Objective To evaluate the efficacy of single dose Azithromycin as prophylactic antibiotic in surgical removal of mandibular third molar.

Materials and Methods The study was carried out as an open clinical trial on fifty (23 males & 27 females) patients chosen from the ones referred to our Oral & Maxillofacial Surgery Department for surgical removal of mandibular third molar (SRMTM). Pre-surgical evaluation of pain, swelling, lymphadenopathy, fever and purulent discharge from the surgical site were made. All patients were administered oral Azithromycin 500mg, 1 hour prior to the procedure. The patients were followed up clinically for a minimum period of 10 days post operatively. Evaluation for pyrexia, purulent discharge from surgical site, persistent pain &/or swelling & lymphadenopathy was done on 1st, 3rd, 7th and 10th postoperative day to determine SSI (surgical site infection). All patients received same set of post-operative medications (Tab. Diclofenac sodium (50mg) TID, Tab. Ranitidine 150 mg BID for 5 days) and set of instructions.

Results Surgical site infection was seen in only one patient (2%) out of the total fifty patients included in the study when oral Azithromycin was administered one hour prior to surgical removal of mandibular third molar.

Conclusion Our study suggests that, giving antibiotics pre-operatively 1 hour before the SRMTM is beneficial to

reduce/avoid SSI. The surgeon must consider all potential factors that may contribute to the post-operative complication and decide whether the benefits of antibiotic therapy outweigh its risks.

Keywords Prophylactic antibiotic ·
Impacted mandibular third molar · Azithromycin ·
Surgical site infection

Introduction

The surgical removal of impacted third molars is one of the most commonly performed procedure by oral and maxillofacial surgeons. It may cause pain, trismus, edema, nausea, infection and alveolar osteitis. In modern hospital or outpatient operative suite, patients often believe that proper methods are consistently utilized to maintain aseptic technique and environment. However, this is not always the case and breach can occur in aseptic protocol causing negative impact on the outcome. Salivary contamination during the procedure is another cause of concern and may lead to surgical site infection (SSI) [1–5]. This study is designed to evaluate the frequency of SSI after surgical removal of mandibular third molar in subjects receiving a single oral pre-operative prophylactic dose of Azithromycin 500 mg.

Materials and Methods

The study was carried out as an open clinical trial on 50 (23 males and 27 females) patients chosen from the ones referred to our Oral & Maxillofacial Surgery Department for surgical removal of mandibular third molar (SRMTM). The Institutional Review Board approval and the informed

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written consent from all the patients was obtained. Inclusion criteria were (1) patients above 18 years of age (2) patients with partially bony impacted mandibular third molar with or without pericoronitis or caries (3) patients not receiving any antimicrobial medication for at least 6 weeks prior to SRMTM. Exclusion criteria were (1) Patients allergic to Azithromycin and allergic to standard set of medication given post-operatively (2) immunocompromised and systemically compromised patients (3) patients having local pathology such as cyst or tumor associated with impacted mandibular third molar (4) patients with previously radiated maxillofacial region (5) patients having received antibiotics for recent systemic infection 6 weeks prior to surgery (6) mentally challenged patients (7) patients unable to come for follow up visits. Laboratory investigations such as complete hemogram, bleeding time, clotting time, prothrombin time, blood sugar level-random and routine urine were carried out on all patients. Pre-surgical evaluation of pain, swelling, lymphadenopathy, fever and purulent discharge from the surgical site were made. All patients were administered oral Azithromycin 500 mg, 1 h prior the procedure. All patients were followed-up clinically for a minimum period of 10 days post-operatively. Evaluation for pyrexia, purulent discharge from surgical site, persistent pain and/or swelling and lymphadenopathy was done on 1st, 3rd, 7th and 10th post-operative days. Pain was quantified subjectively using a visual analogue scale (VAS) (Fig 1) [6]. Increase in pain from 3rd to 10th day post-operatively was considered as infective in nature. Swelling was measured using a horizontal and vertical guide with a flexible ruler [7]. The horizontal measure being the distance between the oral commissure and the lowest part of ear lobe and the vertical being the distance between the external canthus of the eye and the angle of the mandible. The average of the two determined the facial measurement (Fig 2). Swelling not commensurating with the inflicted surgical injury or showing increase, and/or not diminishing between 4th and 10th day post-operatively was considered as infective in nature. Axillary temperature was measured with a digital thermometer (Hangzhou Medical Digital Thermometer) [8]. Temperature of 100.4 °F or more, at any given time between 4th and 10th day post-operatively and not attributable to any other systemic condition was considered as pyrexia due to SSI. Purulent discharge from surgical site and lymphadenopathy seen between 4 and 10 days was considered as infective in nature. All surgical procedures for removal of impacted third molar were performed under local anesthesia by the same surgeon following the standard aseptic and surgical protocol (scrubbing with povidone iodine 7.5 % scrub followed by painting with 5 % povidone iodine solution, sterile draping and chlorhexidine 0.2 % oral rinse). “Terrance Ward” incision was used in

Fig. 1 VAS scale to evaluate pain reference values given to patients: **A** Score 0—No pain, patient feels well. **B** Score 1—Slight pain. If the patient is distracted he/she does not feel pain. **C** Score 2—Mild pain. The patient feels pain even if concentrating on some activity. **D** Score 3—Severe pain. The patient is very disturbed but nevertheless can continue with normal activities. **E** Score 4—Very severe pain. The patient is forced to abandon normal activities. **F** Score 5—Extremely severe pain. The patient must abandon every type of activity and feel the need to lie down

all the cases [9]. Constant copious irrigation with refrigerated saline was used during the bone removal and odontectomy to prevent thermal necrosis. Sectioning of the tooth was done when indicated. Primary closure was accomplished using a 3-0 Mersilk (Johnson & Johnson, Manufacturer product code:W502H) after hemostasis. Pom-pom was used as a pressure pack post-operatively. Surgical time was calculated from placement of incision to the last suture given. All patients received same set of post-operative medications (Tab. Diclofenac sodium (50 mg) TID, Tab. Ranitidine 150 mg BID for 5 days) and set of

Fig. 2 Vertical and horizontal measurement to determine facial measurement **A** Vertical measure corresponds to the measure between the external canthus of the eye and the angle of the mandible. **B** Horizontal measure corresponds to the measure between the commissure and the ear lobe

instructions. Any evidence of infection seen on the follow-up visits was managed either medically by starting appropriate antibiotics or surgically by removal of sutures and dressing, depending on the severity of the infection.

Results

Average age of the patients included in the study was 32 years (range from 19 to 50). Average duration of the surgery was 29 min (range from 25 to 35 min). Paired *t* test was used for statistical analysis of facial measurement on the 1st, 3rd, 7th and 10th day post-operative days with the pre-operative measurement. Post-operative SSI was seen in only one patient (2 %). Analysis showed that there was a significant increase in facial measurement till the third post-operative day. From the third day onwards there was a remarkable decrease in swelling. The measurement on the tenth day was comparable to pre-operative measurement (Graph I). Wilcoxon Signed Rank test was used to compare pain score on different post-operative days. Statistical analysis showed highly significant ($P < 0.001$) decrease in the amount of pain from the first to tenth day post-operatively (Graphs II, III). However only one case showed persistent pain on the 7th post-operative day (Graphs II, III). Pyrexia,

Graph I Comparison of facial measurement on different days

Graph II Pain and swelling on third post-operative day

Graph III Pain scores on different post-operative days

Graph IV Post-operative complications seen

purulent discharge from surgical site, pain and swelling with lymphadenopathy were all seen in the same patient on the 7th post-operative day (Graph IV).

Discussion

Surgical removal of impacted mandibular third molar is usually carried out in a clean and contaminated environment where a large amount of bacteria exist and infective post-operative complications are usually associated with bacterial contamination. For antibiotics to be effective in reducing SSI, the timing of its administration is very important. Mehran et al [11] concluded that the risk of post-operative infection in clean and contaminated wound, such as surgical removal of impacted third molar is around 10 % and that for contaminated and dirty wounds is between 20 and 40 %. Thus antibiotic prophylaxis is recommended for clean-contaminated, contaminated and dirty wounds. Adequate minimum inhibitory concentration (MIC) levels of antibiotic must be achieved before the first incision is made to allow its effect on microbes that contaminate the surgical wounds and blood clots. This requires that the antibiotic be given approximately 1 h before the procedure [1, 2].

The result obtained in our study is comparable to a similar study carried out by Ishihama et al. [10] where Azithromycin was used as a prophylactic antibiotic and the incidence of SSI was 2.2 %.

Yan-Fang [12] reviewed 12 published clinical trials on 2,396 patients for the effectiveness of antibiotic prophylaxis. 1,110 subjects received prophylactic systemic antibiotics and 1,286 subjects received placebo. Post-operative SSI occurred in 4 % of antibiotic group and 6.1 % of placebo group. In another similar study on 118 subjects (59 antibiotic and 59 placebo group) by Leslie Halpern [3] there was no post-operative inflammatory complication in subjects who received intravenous Penicillin or Clindamycin 1 h before the procedure but in placebo group, SSI was seen in 8.5 % of the subjects. Classen et al [13] in their randomized prospective trial carried out on 2,847 patients, observed that in the first group where antibiotic was given 2–24 h prior to surgery (n=369) the SSI was 6.7 % and in the second group where the antibiotic was administered within 2 h before the surgery (n=1708) the SSI was 1 %. In the third group where antibiotics were administered perioperatively (n=282) the SSI was 2.4 %, and in the fourth group which received antibiotics only post-operatively, the SSI was 5.8 %. The highest rate of infection occurred in the group that received antibiotic therapy more than 3 h before the surgery followed by the group that received antibiotic post-operatively. It is suggested that the ideal timing for administering prophylactic antibiotic therapy is 30 min–2 h prior to surgery with additional coverage extending for one to two and a half, half lives of the prescribed antibiotic for the length of the operation [14].

Administration of a single dose prophylactic antibiotic in third molar surgery makes sense from cost-effective perspective also. However the risks of potential antimicrobial resistance and severe adverse reactions are difficult to estimate and cannot be entirely ruled out in clinical decision making [3]. The choice whether to give oral or parenteral antibiotics is based on factors such as indications, convenience and facilities available. Whatever the route, the goal must be to achieve adequate tissue levels of antibiotic before the first incision is made. Antibiotics, such as Azithromycin, having a long serum half life, also encourage better patient compliance. Giving post-operative antibiotic without pre-operative administration, in minor oral surgery such as surgical SRMTM is questionable. This practice does not achieve the first goal of antibiotic prophylaxis which is to achieve adequate tissue levels and MIC [10].

However some authors are of the opinion that the incidence of post-operative infections after SRMTM (1–5 %) is too low to justify routine antibiotics [15]. The blind use of antimicrobials can result in adverse outcomes, and there is a general trend to overprescribe antimicrobials [16]. The

risks of indiscriminate prescribing include development of resistant organisms, secondary infection, toxicity, and the development of allergic reactions [17]. It is estimated that 6–7 % of patients who are given antibiotics have some kind of adverse reaction [8]. The estimated rate of infection after removal of an impacted third molar is less than 1 %, so the usage of such drugs is questionable [4, 18]. An important point in the debate about usage of prophylactic antibiotics is its timing of administration. There is significant evidence that giving antibiotics preoperatively may reduce the incidence of post-operative wound infections [19].

Our study suggests that, giving antibiotics pre-operatively 1 h before the SRMTM is beneficial to reduce/avoid SSI. However the occurrence of SSI also depends on other factors like aseptic working environment, adherence to basic principles of surgery, patient compliance and maintenance of good oral hygiene. So the decision of using antibiotic prophylaxis in SRMTM is ultimately the responsibility of the surgeon. The surgeon must consider all potential factors that may contribute to the post-operative complication and decide whether the benefits of antibiotic therapy outweigh its risks.

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Conflict of interest Nil

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