



## COMPARING THE EFFECT OF PLACEBO AND PROPHYLACTIC ANTIBIOTICS ON ASYMPTOMATIC NECROTIC TEETH.

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### Article received on:

17/04/2019

### Accepted for publication:

23/06/2019

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**ABSTRACT... Objectives:** Treatment of asymptomatic necrotic teeth is a common type of occurrence in endodontic practice. Root canal treatment of these teeth sometimes results in pain and /or swelling of varying degree. These severe symptoms upset both the patient and dentist. This study was to compare the effect of prophylactic amoxicillin and placebo in endodontic flare-up in asymptomatic necrotic teeth requiring root canal treatment. This was evaluated by using flare-up index. The influence of age, sex, was compared between flare-up and non-flare-up groups. Using a standardized technique and the same materials eliminated the variability of operator. **Study Design:** Quasi experimental study. **Setting:** Department of Operative Dentistry, Lahore Medical and Dental College, Lahore. **Period:** From January 2018 to December 2018. **Material & Methods:** 102 patients with asymptomatic necrotic teeth with periapical radiolucency were selected from the Operative Dentistry Department of Lahore Medical and Dental College. Patients were divided into two groups experimental and control, by convenient sampling. One half of the patients were given prophylactic amoxicillin and other half was given placebo one hour before treatment. **Results:** Flare-up occurred in four of the experimental and seven of the control group patients. Statistical analysis revealed no significant differences between flare-up and non- flare- up patients for age and sex. The data outcome was of qualitative in nature i.e. pain and swelling, they were subjected to Chi-Square test of significance with P value of  $\leq 0.05$ . The results demonstrated that 10.8% of the 102 patients had a flare-up. No side effects were observed in the patients who were prescribed amoxicillin. **Conclusion:** The occurrence of flare-up did not significantly influence by Prophylactic amoxicillin (P= .33).

**Key words:** Amoxicillin, Antibiotic Prophylaxis, Dental Pulp Necrosis, Follow-Up Studies, Placebos, Root Canal Therapy.

**Article Citation:** Qasim M, Anjum O, Yousaf O, Khan S, Pirvani M. Comparing the effect of Placebo and Prophylactic Antibiotics on asymptomatic Necrotic teeth. Professional Med J 2019; 26(12):2162-2168.  
**DOI:** 10.29309/TPMJ/2019.26.12.3563

## INTRODUCTION

Treatment of asymptomatic necrotic teeth is a common type of occurrence in endodontic practice. Root canal treatment of these teeth sometimes results in pain and /or swelling of varying degree. These severe symptoms upset both the patient and dentist.<sup>1-3</sup> Flare-up was defined as “moderate to severe postoperative pain or moderate to severe swelling that began 12 to 48 hours after treatment and lasts at least 48 hours”.<sup>4</sup> The causative factors of flare up may be mechanical, chemical or microbial injury to the peri radicular tissue. Mechanical and chemical injuries are usually associated with iatrogenic factors, such as over instrumentation, apical

extrusion of irrigants or medication, perforation etc.<sup>5,6</sup>

The presence of some bacteria commonly associated with clinical symptoms such as porphyromonas spp (species), prevotella spp and fusobacterium nucleatum in an asymptomatic teeth may predispose to postoperative pain provided they are extruded apically or allowed to over grow. In addition, introduction of new microorganisms into the root canal system during treatment may be another cause of postoperative pain of microbial origin.<sup>5,7,8</sup> It has been shown that bacteria can be isolated from files, which have been used for preparation of teeth with necrotic pulp.

However this is not the case in vital pulp cases.<sup>9,10</sup> In another study occurrence of bacteraemia was 31% when endodontic instrumentation remained 1 mm short of the apical foramen and 54% when instrumentation was deliberately extended 2 mm beyond the apical foramen.<sup>11,12</sup>

The use of prophylactic antibiotics to prevent an infection was advised. For antibiotics to be effective they must be present in the systems when wound is seeded with bacteria. Delay of three to four hours in antibiotic administration resulted in lesions that were identical to those receiving no prophylaxes. Clinically antibiotics must be effective against organisms encountered. It must be present in the tissue when contamination begins, continues during the period of operation (debridement of the root canal), and discontinues after the operation is complete. The dose of amoxicillin used in this study fulfilled the requirement.

Prophylactic administration of antibiotics has been considered for preventing flare-up. Mores and co-workers concluded that prophylactic antibiotics significantly reduced the flare-up.<sup>13,14</sup> Udoye found that antibiotics were less effective than analgesic in reducing inter appointment emergencies.<sup>6</sup> Walton and Chiappnelli concluded that post treatment symptoms of flare-up were not affected by prophylactic administration of antibiotics.<sup>15</sup> Various studies have concluded that prophylactic dose of antibiotics may be used to prevent infections. They argued that if bacteria were responsible for endodontic flare-up, prophylactic antibiotic could prevent their occurrence.<sup>4,16</sup> Gram negative anaerobic bacterias are commonly responsible for the development of post-operative symptoms.<sup>17</sup> Amoxicillin was used in this study because it is effective against bacteria commonly present in the root canal system. It provides high serum level initially and is maintained for 10 to 12 hours thus making it excellent choice for single dose regime.<sup>4,18</sup> This study attempts to see if any advantage exists for prophylactic administration of antibiotics in asymptomatic necrotic teeth as measured by flare up index.

The purpose of this study was to assess the

flare-up postoperatively after prophylactic administration of amoxicillin and compare it with placebo effect.

## METHODOLOGY

This study was conducted in Operative Dentistry Department of Lahore Medical and Dental College Lahore from January 2018 to December 2018. The study was approved by the college ethics committee. The initial sample size was calculated based on the power of 0.9 and the type 1 error of 0.05, with 51 patients in each group. Total 102 patients with asymptomatic necrotic teeth with periapical radiolucency were included in the study. Participants were included in the study if they were healthy and have asymptomatic necrotic restorable teeth, non-endodontically treated teeth with negative pulp response to electric pulp tester and no bleeding from pulp chamber on opening. Patients of age ranging from 18 to 60 were included in the study. Patients were divided into two groups experimental and control by convenient sampling, one half of the patients were given 2 gm of amoxicillin and other half was given 2 gm of placebo one hour before treatment. Study design was Quasi experimental.

Patient's prior use of antibiotics within one month, allergic to penicillin/amoxicillin, on steroid therapy, physical and mental conditions that prevent the jaw opening; symptomatic necrotic teeth with periapical radiolucency and endodontically treated teeth were excluded from the study.

The pulp status was recorded as vital if the tooth responded to electric pulp tester and non-vital vital or necrotic did not respond to electric pulp tester. Percussion sensitivity was assessed by light tapping the tooth with the handle of mirror. History and dental examination was conducted and all postoperative of the patients were recorded. Dental history and consent forms were available both in English and Urdu.

Access was gained to the canal orifice and initial radiograph were taken with K file in canal. Cleaning and shaping of canal was done with 2.5 % sodium hypochloride. The canals were dried and no intracanal medication was placed. Teeth

were temporarily sealed with cavite. Each patient was given five-day diary (Appendix B) to record postoperative symptoms. The symptoms were recorded for consecutive five days before going to bed. The diary contained a flare-up index on which the patient marked the degree of pain and swelling. Each patient was given Brufen 400-mg tablet according to verbal and written instructions. Patients returned the diary after five days.

The data was entered and analyzed on SPSS version 20. Since the outcome was of qualitative nature for example pain and swelling, they were subjected to Chi-Square test of significance with P value of ≤ 0.05.

**RESULTS**

Average age of patients in flare-up and non-flare-up group

102 subjects were included in this study. They were divided in two groups experimental (antibiotic prescribed) and control (placebo) in equal halves (51 each group). Two patients from both groups who did not return the five-day diary for recording postoperative symptoms were dropped from the study.

Age was divided into following four groups. Less or equal to 20 years, 21 –30 years, 31-40 years and greater than 40 years (Table-I). Out of the 26 patients, aged less or equal to 20 years, three (11.5%) experienced a flare-up. Out of 35 patients, aged 21-30 years, six (14.6%) experienced a flare-up. Out of 21 patients, aged 31-40 years, one (4.8%) experienced a flare-up. Out of fourteen patients, aged above 40 years one (7.1%) experienced a flare-up. Distribution of patients with flare-up was more in age group 21-30 years as compared to other groups. (Table-I) Age 31-40 years experienced the least flare-ups as compared to the other groups. However using Chi Square analysis, age was not found to be a significant factor in predisposing a patient to develop flare-ups (p value 0.86).

Distribution of male and female patients in both experimental and control was almost same as given in Table-II. Out of the 53 female patients,

six (11.3%) experienced a flare-up. Out of the 49 male patients five (10.2%) experienced a flare-up. However by using Chi Square analysis age was not found to be a significant factor causing flare up (p value=0.86).

Study Groups			
Patient Age	Flare-up (%)	No Flare-up (%)	Total (%)
≤ 20 Years	3(11.5)	23(88.5)	26(100)
21- 30 Years	6(14.6)	35(85.4)	41(100)
31- 40 Years	1(4.8)	20(95.5)	21(100)
> 40 Years	1(7.1)	13(92.9)	14(100)
<b>TOTAL</b>	11(10.8)	91(89.2)	102(100)

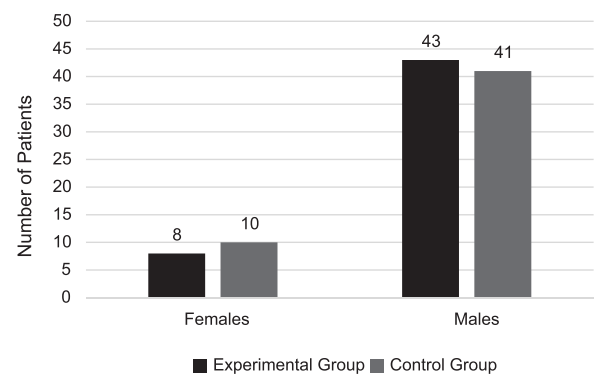
**Table-1. Age comparison of the patients in flare-up and non flare-up groups**

Statistical Test	Chi-squared	df	P-Value
	1.63	3	0.65

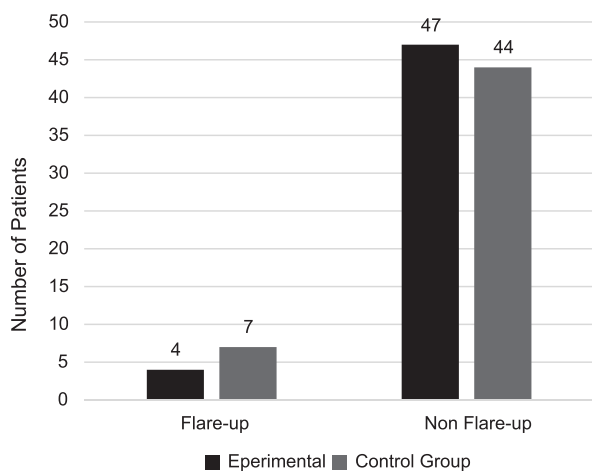
STUDY GROUPS			
Patient Age	Flare-up (%)	Non Flare-up (%)	Total (%)
Female	6(11.3)	47(88.7)	53(100)
Male	5(10.2)	44(89.8)	49(100)
Total	11(10.8)	91(89.2)	102(100)

**Table-II. Gender comparison of the patients in flare-up and non flare-up groups**

Statistical Test	Chi-squared	df	P-Value
	0.03	1	0.86



**Figure-1. Showing distribution of patients according to their age (experimental and control group)**



**Figure-2. Showing distribution of flare-up and non flare-up cases in experimental and control group.**

**DISCUSSION**

Postoperative pain and swelling are displeasing for both the patient and clinician. Asymptomatic necrotic teeth requiring root canal treatment were selected for this study. They have greater rate of flare-up than vital teeth.<sup>19</sup> In this study effect of prophylactic amoxicillin and placebo was determined on age, sex, by flare-up index. In the flare-up group, 10.8% of the amoxicillin and placebo patients had moderate to severe pain or moderate to severe swelling. These symptoms persisted at least 48 hours.

Different age groups showed statistically insignificant difference in this study. These results are similar to Clem and Morse.<sup>14,20</sup> However our results are different from Balban who found that there was a greater tendency in patients less than 50 years of age to develop an acute exacerbation than in patents over 50 years.<sup>21</sup> It is also interesting that the patient’s response in 50 years old and older was decreasing. This may be related to reduced pulp canal size (therefore reducing the volume of necrotic debris); reduced alveolar blood flow and reduced inflammatory responses in older patients.<sup>22</sup> This influence is not supported by Toosy who treated necrotic teeth and found no difference in flare-up rate of age groups except in those patients who were above 50 years. One possibility could be the transportation of radiographic apex coronally which may be due to the reason of deposition of secondary cementum

as the age progresses. This may end up in the determination of improper working length that would result in debris extrusion.<sup>23</sup>

The flare-up rate was slightly higher in females than males in this study. It is not statistically significant. This study found no gender difference for flare-up. These results are similar to Yeh who found that patient’s sex had no significant effect on the frequency of flare up.<sup>24</sup> Balban also found that there was no significant difference in the number of acute exacerbation between males and females.<sup>21</sup> On the other hand, Morse found a greater incidence of flare-up for females.<sup>14</sup> Eleazer and Matusow found no gender difference. Pickenpaugh had the same results in both experimental and control groups.<sup>25</sup>

However, difference between the experimental lesions in different studies is that the endodontic lesions have existed for a long time in nature in a freshly seeded wound and endodontic lesion. Hence, the flare-up may also be involved in an immunological factor of a chronic pre-existed lesion. The fundamental outcome is that the incidence of flare up was low. Data of this study reinforces similar perception. However it is not certain that the antibiotics are effective in reducing or preventing the severity of infection. The drug administration with the potential of mortality and morbidity along with other undesirable side effects would contrast our results.<sup>16,26,27</sup> Prospective survey of Walton and Faud revealed that flare-ups were not reduced significantly by taking antibiotics.<sup>28</sup> Additional argument besides prescribing prophylactic antibiotic for a pre-existing bacterial infection in current clinical situation is relatively ineffective. Goodman and Gillman’s pharmacological bases of therapeutics say that “an antibiotic is most effective when administered to control specific bacteria introduced rather than against bacteria already present in the patient or at the surgical site”.<sup>29</sup> So in endodontic cases prophylactic antibiotics would be likely to fail. Another recognized pharmacotherapeutics fact is that the best effectiveness of prophylactic antibiotics is when blood and tissues have adequate levels and are present on surgery or injury site.<sup>30</sup> If

Amoxicillin is prescribed prophylactically before the appointment and microorganisms are pushed past the apical foramen by armamentarium, there will be inadequate levels of drug in the tissues. Although the American Heart Association and British Society of Antimicrobial Chemotherapy recommended dosage is high. Pickenpaugh used amoxicillin prophylactically and was ineffective.<sup>4</sup> A number of clinicians may debate that to protect themselves that antibiotics should be administered prophylactically for medical purposes, in case of any adverse medical condition. This is in attempt to save the clinician against a lawsuit. This study and related trial suggest that it is not justified to prescribe antibiotics prophylactically in those conditions and it may also result in the possible undesirable side effects for the patient.<sup>4,13,18</sup> The dentist may face legal action for prescribing antibiotics for non-beneficial situation which places a patient at risk for any unwanted reaction of the drug. Particularly, in case of penicillin, which results in anaphylactic reactions, which resulted in a yearly mortality of approximately 400 to 800 patients and also has a higher incidence of morbidity. Most patients died by anaphylactic and/or other allergic reactions, resulted in patients with no history of penicillin allergy as it is difficult to diagnose it by health history.<sup>30</sup> Oral administration can provoke these adverse reactions.<sup>31</sup>

Strengths of this study was the number of follow-ups which was around 96%. It is also suggested that trials should aim to investigate the preoperative conditions as possible confounders, which was carefully taken care of in the inclusion and exclusion criteria of the study. Limitations included that the study should be double blinded to reduce the risk of selection and detection bias, but it is understandable that the blinding patients and operators is not possible in such trials. Also these kind of trials results better with a longer follow-up periods.

In this study, there were no unwanted side effects in 51 patients who were prescribed amoxicillin. Considering the fact that a huge amount of antibiotics are prescribed in medicine and dentistry overall incidence of an adverse reaction

is low although it could be serious.

## CONCLUSION

The results of this study have shown prophylactic amoxicillin has no effect on the occurrence of flare-up as compared with placebo in asymptomatic necrotic teeth. No correlation between flare-up and age, sex, was found.

## CONFLICT OF INTEREST

The authors certify that they have NO affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript.

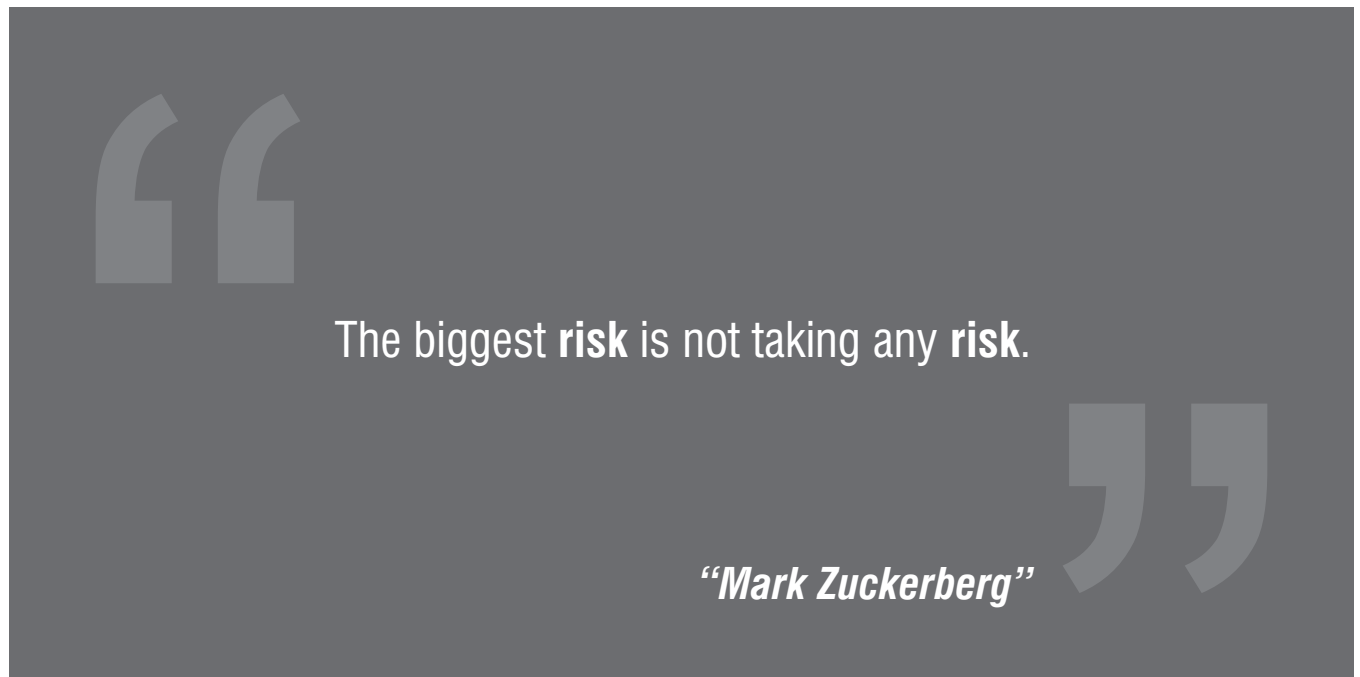
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3	Omer Yousaf	Data collection and Literature review.	
4	Shoaib Khan	Proof reading and editing.	
5	Madiha Pirvani	Discussion and references.	