

Prophylactic use of cephradine in dental procedures: A observational study in Bangladesh

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Abstract

Bacteremia is common with manipulation of the teeth and periodontal tissues during dental procedures. Majority of dental office visits result in some degree of bacteremia that warrants antibiotic prophylaxis before a dental procedure to reduce the frequency, nature or duration of bacteremia. This study aimed to collect data on prophylactic use of cephradine which is most preferred in dental procedures in Bangladesh. A total of 2219 patients both adults and children above 5 years were enrolled to assess use of antibiotic, its dose and duration for antibiotic prophylaxis during dental procedures. Efficacy of antibiotic prophylaxis in terms of clinical cure, further dose modification and need to change antibiotic was evaluated at day 10 of antibiotic use and in case of root canal therapy at day 30. Any side effect of antibiotic use recorded within 3 days was considered for safety evaluation. This was a non-controlled, multicentre, observational study. 2016 (90.9%) of the patients received cephradine as prophylactic antibiotic with a mean dosage of 500mg (487.48+60.99) and duration of treatment was 3-7 days (5.47+1.03). Some of the dentists also preferred amoxicillin (149, 6.7%) and cephalexin (54, 2.4%) for prophylaxis. The majority of the patients (1657, 82.2%) who had prophylaxis with cephradine had no clinical sign of infection and some of the patients needed to change their initial dose or change of the antibiotic. Overall 1816 (81.8%) patients were found having no clinical sign of infection on antibiotic prophylaxis. Among the patients 239 (10.7%) needed to change the dose of prescribed antibiotic and 55 (2.4%) were required to change their prescribed antibiotic. However, the data on type of infection was not recorded. 109 (4.9%) patients were lost to follow up on Day 10. Prescribed antibiotic prophylaxis was not associated with adverse events in majority (91%) of the patients. Some of the patients reported diarrhea (104, 4.7%), stomach upset (68, 3.1%) and dizziness (31, 1.4%) during antibiotic use. However, those were self-limiting and no dose adjustment, discontinuation of therapy or withdrawal from the study was required. No serious adverse events were reported. Cephadrine 500 mg for 5 days course was preferred as prophylactic antibiotic in dental procedures in this study. Majority of the patients had no clinical sign of infection on evaluation at day 10. Cephadrine therapy was mostly not associated with adverse events in patients; however, diarrhea, stomach upset and dizziness were reported in some patients that were self-limiting.

Keywords: antibiotic prophylaxis, cephadrine dental treatment.

Introduction

Transient bacteremia is common with manipulation of the teeth and periodontal tissues, and there is wide variation in reported frequencies of bacteremia in patients resulting from dental procedures:

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tooth extraction (10-100 percent), periodontal surgery (36-88 percent), scaling and root planning (8-80 percent), teeth cleaning (up to 40 percent), rubber dam matrix/wedge placement (9-32 percent) and endodontic procedures (up to 20 percent).¹⁻⁷ Studies suggest that more than 700 species of bacteria, including aerobic and anaerobic gram-positive and gram-negative microorganisms, may be identified in the human mouth, particularly on the teeth and in the gingival crevices.^{1,8-11} Approximately 30 percent of the flora of the gingival crevice is streptococci, predominantly of the viridans group. Streptococcus viridans, staphylococcus aureus, enterococcus, pseudomonas, serratia, and candida are some of the microorganisms implicated with Infective endocarditis (IE). IE is an uncommon but life-threatening complication resulting from bacteremia. The vast majority of cases of IE caused by oral microflora can even result from bacteremia associated with routine daily activities such as tooth brushing, flossing, and chewing other than dental procedures.^{12, 13}

Because the published data suggest that the vast majority of dental office visits result in some degree of bacteremia, studies reported that antibiotic prophylaxis before a dental procedure reduced the frequency, nature or duration of bacteremia.^{14,15,16} The American Dental Association (ADA), The American Heart Association (AHA) recommended protocols for antibiotic prophylaxis against bacterial endocarditis. The ADA/AHA/AAOS (American Academy of Orthopaedic Surgeons) recommended cephalixin, cephradine or amoxicillin for prophylactic use in dental procedure.¹³ Cephradine is effective against many gram-positive bacilli and cocci (other than enterococcus) and some gram-negative bacilli. It has peak tissue concentrations within the first hour after administration and effective concentrations are maintained for at least 5 hours.

At present there is no consensus regarding prophylactic use of antibiotics in dental procedures in Bangladesh and the reference regimens are varying. Clinical experience from dentists demonstrated that for prophylaxis cephradine was used as choice of antibiotic in 60% of cases during dental procedures. Therefore this observational study was conducted to collect, analyze and disseminate data on prophylactic use of cephradine in dental procedures locally. Another purpose was to find out the guideline or reference if any followed by the physicians during and immediately after the dental procedure in order to reduce the occurrence of bacterial endocarditis, bacterial arthritis, and other soft tissue infection. Moreover the study findings might help to develop a local guidance.

Objectives

Primary objective of the study was to assess the prophylactic use of cephradine in dental procedures. Secondary objectives were to evaluate the clinical cure rate with cephradine prophylaxis in dental procedures and also to find out the guideline or reference if any followed by the physicians during and immediately after the dental procedure in order to reduce infections.

Materials and methods

Adults and children of 5 years and above visiting dentist's office for whom dental procedure having a risk of bleeding or producing high levels of bacteria in blood e.g. Root Canal Therapy (RCT), dental extraction, periodontal surgery and periodontal scaling was planned and antibiotic prophylaxis with cephradine was prescribed were included in this study. Patients required dental procedures but having infection prior to surgical intervention and those had severe medical conditions e.g.

complicated heart disease, uncontrolled diabetes, carcinoma etc. were excluded to participate in this study. Patients with very severe infection who required hospitalization were also excluded from this study.

Methods

This non-controlled, multicenter, observational study was carried out between September 2011 and October 2012 by 31 dentists to assess the prophylactic use of cephradine in dental procedures at their office. Though initially 40 dentists were planned and invited to participate in this study 9 dentists did not enroll patients and were excluded from the study.

Patient demographics, dental examination, investigations, treatment plan, related diseases or risk factors, antibiotic prescribed for prophylaxis with its dose and duration of therapy, any guideline followed by the investigators were collected at baseline. Follow-up data of clinical outcome in terms of clinical cure (in those with previous infection), dose modification of cephradine or change of antibiotic was recorded after 10 days of prophylactic therapy. In case of root canal therapy patient follow-up was continued till 30 days of prophylaxis. Any adverse event reported by the patient within 3 days of therapy was recorded by the investigators. Patient data were collected by the investigators using paper copy of Data Collection Forms (DCF) provided for each patient. The completed DCFs were collected from the investigators by the study monitor at the end of study.

Primary endpoints of this study was to assess demographics, indications, risk factors/ co-morbidities, dosage and duration of antibiotic use in patients who were prescribed cephradine for prophylaxis in dental procedures. Secondary endpoints evaluation aimed percentage of patients who would be clinically cured or needed dose modification or change of antibiotic within 10 days or 30 days in case of specific procedure such as Root Canal Therapy. Percentage of patients who reported side effects within three days was considered for safety evaluation.

All the patients enrolled were considered for primary endpoint analysis and data of the patients available at day 10 of antibiotic use was considered for evaluation of efficacy of antibiotic prophylaxis. Statistical analysis was done using SPSS 17.0 and was mainly descriptive and was summarized as mean, median, standard deviation, minimum, maximum and percentages.

Results

A total of 2219 patients had antibiotic prophylaxis with cephadrine for dental procedures were included in this study. Among the enrolled patients 1180 (53.2%) were males and 1039 (46.8%) were females. The median age of the patients was 35 years, the youngest one 5 years and the oldest one 88 years. There were 234 (10.5%) children (<18 years) and 1985 (89.5%) adults in this study. Majority of the patients (90.6%) were urban residents, 8.7% of the patients were from rural areas and a very few (0.7%) represented from slum areas. About half (47.9%) of the adult patients completed graduation or even higher education whereas 143 (7.2%) of them did not have any educational background. Among the adults 1732 (87.3%) were employed in different professions and the rest were unemployed.

Table 01: Patients characteristics at baseline

	Children (<18 years) (n=234)	Adults (≥18 years) (n=1985)	Total (n=2219)
Age (years)			
Median	9	37	35
Gender			
Male/Female	113/121	1067/981	1180/1039
Locality [n (%)]			
Urban	220 (94.0)	1791 (90.2)	2011 (9.6)
Rural	13 (5.6)	179 (9.0)	192 (8.7)
Slum	1 (0.4)	15 (0.8)	16 (0.7)
Dental examination status			
Gingivitis	54 (23.1)	1069 (53.9)	1123 (50.6)
Periodontitis			
- Mild (<3mm)	50 (21.4)	539 (27.2)	589 (26.5)
- Moderate (3-5mm)	12 (5.1)	457 (23.0)	469 (21.1)
- Severe (>5mm)	0	78 (3.9)	78 (3.5)
Gum recession	8 (3.4)	612 (30.8)	620 (27.9)
Decayed teeth	165 (70.5)	1538 (77.5)	1703 (76.7)
Missing teeth	27 (11.5)	663 (33.4)	690 (31.1)
Filling teeth	44 (18.8)	692 (34.9)	736 (33.2)
Ulcer/white lesion			
- Tongue	1 (0.4)	50 (2.5)	51 (2.3)
- Oral cavity floor	0	33 (1.7)	33 (1.5)
- Palate	1 (0.4)	30 (1.5)	31 (1.4)
- Gingival mucosa	0	63 (3.2)	63 (2.8)
Investigations			
CBC	5 (2.1)	67 (3.4)	72 (3.2)
Xray	50 (21.4)	754 (38.0)	804 (36.2)
Others	0	4(0.2)	4 (0.2)

Among the adult males 364 (18.3%) were habituated with smoking cigarettes and 195 (9.8%) were used to with chewable smokeless tobacco like betel leaf with jarda and gul. The demographic and clinical characteristics of study patients are presented in Table 01. Among the patients 214 (10.8%) of the adults had diabetes mellitus and 86 (4.3%) had history of cardiovascular diseases. A small portion of them also had history of rheumatoid arthritis (0.8%), prosthetic heart valves (0.6%), and drug-induced immunosuppression medical conditions (0.2%). On dental examination, periodontitis was found in 51.1% of patients, gingivitis in 50.65 % and gum recession in 27.9% of patients. Decayed teeth were found in 76.7% of patients, 33.2% had filling teeth and 31.1% had missing teeth. 91 (4.1%) patients had ulcer or white lesion on their tongue, floor of the mouth, palate or gingival mucosa.

Root canal therapy (54%), scaling (52.2%), tooth extraction (36.1%) and dental filling were the most common dental procedures done by the investigators. Other procedures like deep curettage, polishing, root planning and flap, gingivectomy, apicectomy and cyst or any kind of operation were also done in some cases. Table 02 shows detail of the dental procedures advised for the patients.

Table 02: Dental procedures planned for the patients

	Children (<18 years)	Adults (≥18 years)	Total
Scaling	57 (24.4)	1101 (55.5)	1158 (52.2)
Deep curettage	13 (5.6)	260 (13.1)	273 (12.3)
Gingivectomy	8 (3.4)	22 (1.1)	30 (1.4)
Polishing	6 (2.6)	135 (6.8)	141 (6.4)
Root planning & Flap surgery	2 (0.9)	48 (2.4)	50 (2.3)
Tooth extraction	74 (31.6)	727 (36.6)	801(36.1)
Apicectomy	4 (1.7)	19 (1.0)	23 (1.0)
Root canal therapy	100 (42.7)	1099 (55.4)	1199 (54.0)
Filling			
Anterior	8 (3.4)	99 (5.0)	107 (4.8)
Posterior	47 (20.1)	389 (19.6)	436 (19.6)
Cyst or any kind of operation	2 (0.9)	20 (1.0)	22 (1.0)

During dental procedures the investigators prescribed cephadrine (Sefrad®) per oral to 2016 (90.9%) patients as prophylactic antibiotic with a mean dosage of 500mg (487.48±60.99) and duration of treatment was 3-7 days (5.47±1.03). Cephadrine prophylaxis was prescribed to 86.3% (202) of the children and 91.3% (1814) of the adults. For prophylaxis the dentists also prescribed amoxicillin to 149 (6.7%) patients and cephalixin to 54 (2.4%) patients. Table 03 shows antibiotic prophylaxis in children and adults. The investigators followed either text book, international or local guidelines in 318 (14.3%) cases, as reference in prescribing prophylactics.

Table 03: Antibiotic prophylaxis in patients

Antibiotic	Children (n = 234)	Adults (n=1985)	Total (n=2219)
Cephadrine	202 (86.3)	1814 (91.3)	2016 (90.9)
Cephalixin	2 (0.8)	52 (2.6)	54 (2.4)
Amoxicillin	30 (12.8)	119 (5.9)	149 (6.7)

The majority of the patients (1657, 82.2%) who had prophylaxis with cephadrine had no clinical sign of infection and some of the patients needed to change their initial dose or change of the antibiotic. Overall 1816 (81.8%) patients were found having no clinical sign of infection on antibiotic prophylaxis. Among the patients 239 (10.7%) needed to change the dose of prescribed antibiotic and 55 (2.4%) were required to change their prescribed antibiotic. However, the data on type of infection was not recorded. 109 (4.9%) patients were lost to follow up on Day 10. Clinical outcome of antibiotic prophylaxis has been shown in Table 04.

Table 04: Clinical outcome of antibiotic prophylaxis in patients at Day 10

Clinical outcome	Cephadrine (n=2016)	Cephalixin (n=54)	Amoxicillin (n=149)	Overall (n=2219)
Cured	1657 (82.2)	32 (59.2)	127 (85.2)	1816 (81.8)
Change of dose	211 (10.4)	14 (25.9)	14 (9.4)	239 (10.7)
Change of antibiotic	45 (2.2)	5 (9.2)	5 (3.3)	55 (2.4)
Lost to follow up	103 (5.1)	3 (5.5)	3 (2.0)	109 (4.9)

Any adverse event reported by the patients within 3 days of therapy was recorded by the investigators. 2015 (91%) of the patients reported no adverse event with the prescribed antibiotic prophylaxis.

Diarrhea was the common adverse event reported in 104 (4.7%) patients. Stomach upset other than diarrhea was reported in 68 (3.1%) patients and 31 (1.4%) patients reported dizziness. Reported adverse events were self-limiting, no dose adjustment, discontinuation of therapy or withdrawal from the study was required. No serious adverse events were reported. Adverse events reported in the patients have been shown in Table 05.

Table 05: Adverse events reported in patients with antibiotic prophylaxis

Adverse events	Cephadrine (n=2016)	Cephalixin (n=54)	Amoxicillin (n=149)	Overall (n=2219)
None	1831 (90.8)	52 (96.3)	132 (88.6)	2015 (90.8)
Stomach upset	60 (3.0)	1 (1.9)	7 (4.7)	68 (3.1)
Diarrhea	97 (4.8)	1 (1.9)	6 (4.0)	104 (4.7)
Dizziness	27 (1.3)	0	4 (2.7)	31 (1.4)
Other	1 (0.0)	0	0	1 (0.0)

Discussion

The purpose of this open label non comparative study was to collect, analyse and disseminate data on prophylactic use of cephadrine in dental procedures in Bangladesh. The American Dental Association (ADA), The American Heart Association (AHA) and The American Academy of Orthopaedic Surgeons (AAOS) recommended cephalixin, cephadrine or amoxicillin for prophylactic use in dental procedures where patients have cardiac conditions like prosthetic cardiac valve or prosthetic material used for cardiac valve repair, previous IE, congenital heart diseases (CHD).

A total of 2219 patients were enrolled in this study and had undergone different dental procedures. There were 234 (10.5%) children (<18 years) and 1985 (89.5%) adults with the median age of 35 years (range 5~88 years). Periodontitis, gingivitis, dental caries, gum recession were found common on oral examination. Some of the patients had ulceration or white lesion on tongue, floor of the mouth, palate or gingival mucosa. Root canal therapy, scaling, tooth extraction and dental filling were the most common dental procedures done by the investigators. Other procedures like deep curettage, polishing, root planning and flap, gingivectomy, apicectomy and cyst or any kind of operation were also done in some cases.

Cephadrine (Sefrad®) was prescribed to 2016 (90.9%) patients as antibiotic prophylaxis during their dental procedures with a mean dosage of 500mg (487.48±60.99) and average duration of treatment was 5 days. The investigators also prescribed amoxicillin or cephalixin to some of the patients as prophylaxis. The investigators followed either text book or Key Opinion Leaders' or local guidelines as reference in prescribing prophylactic antibiotic in 318 patients. Generally oral hygiene is not properly maintained in Bangladesh which put the patients at more risk of infection during dental procedures. Therefore, although guidelines do not recommend antibiotic prophylaxis for the patients who are not at the risk but the use of antibiotic is a routine practice in Bangladesh to avoid any chance of infection. However, there is a need of creating more awareness among the dentists about rationale use of antibiotics.

At the end of study an evaluation on Day 10 the majority (82.2%) of the patients having prophylaxis with cephradine had no clinical sign of infection, only 2.2% of the patients needed to change their antibiotic prescribed initially. In this study safety reports within 3 days were planned to record as most of the related events occur in early days of antibiotic therapy and are self-limiting might be ignored if asked to notice later. Majority (90.8%) of the patients did not report any adverse events. Diarrhea (4.6%) was the common adverse event and mostly reported in children. Some of the patients reported stomach upset (3.1%) other than diarrhea and dizziness (1.4%). The reported adverse events were self-limiting, no dose adjustment, discontinuation of therapy or withdrawal from the study was required. No serious adverse event was also reported.

Conclusion

Although guidelines do not recommend use of antibiotic prophylaxis for the patients undergoing dental procedures who are not at risk but the use of antibiotics were significant in this study as this is a routine practice in Bangladesh. Cephadrine (Sefrad®) 500 mg dosage and a 5 days course was preferred as prophylactic in dental procedures in this study. Majority of the patients had no clinical sign of infection on evaluation at day 10. Cephadrine therapy was mostly not associated with adverse events in patients; however, diarrhea, stomach upset and dizziness were reported in some patients that were self-limiting.

Acknowledgement

The study was supported by a Sanofi Bangladesh Limited.

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