

Antibiotic abuse during endodontic treatment: A contributing factor to antibiotic resistance

Ramta Bansal¹, Aditya Jain², Mehak Goyal³, Tejveer Singh³, Himanshu Sood¹,
Harjeet Singh Malviya⁴

Departments of ¹Conservative Dentistry and Endodontics and ³Oral and Maxillofacial Surgery, Desh Bhagat Dental College and Hospital, Mandi Gobindgarh, District Fatehgarh Sahib, Punjab, ²Department of Physiology, Government Medical College, Patiala, Punjab, ⁴Department of Conservative Dentistry and Endodontics, Geetanjali Dental and Research Institute, Udaipur, Rajasthan, India

ABSTRACT

Antibiotic resistance is one of our most serious global health threats. The adverse effects of overusing and misusing antibiotics are highly publicized in the health professional literature. Antibiotic abuse occurs during routine endodontic treatment and there are deficiencies in knowledge regarding prescribing antibiotic and appropriate prophylactic antibiotic use. Multidisciplinary coordination and cooperation among dentists, pharmacists, and patients is needed to curb antibiotic abuse. As endodontists, we can become part of the solution to the antibiotic resistance crisis and deal with it conclusively. This review article discusses antibiotic resistance resulting from antibiotic abuse during endodontic treatment, various factors contributing to it, and measures required for stopping antibiotic abuse in endodontic treatment. A web-based research on MedLine was performed with terms Review Articles published in the last 10 year's dental journals in English for literature researching, extracting, and synthesizing data. Relevant articles were shortlisted. Important cross-reference articles were also reviewed.

Keywords: Antibiotic, endodontic, prescription, resistance, root canal

Introduction

Antibiotics that used to be an integral part of modern medicine are now less effective or don't work at all. Antibiotic resistance now poses a serious threat to public health.^[1] Although resistance can appear spontaneously due to random mutations, overuse and misuse of antibiotics appear to promote selection for mutations.^[2] Worldwide antibiotic resistance is not completely identified, but poorer countries with weaker healthcare systems are more affected.^[3] India ranks first among all countries of the

world in total consumption of antibiotics for human use^[4] and has been referred to as "the antimicrobial resistance capital of the world."^[5] For the containment of this global threat, WHO in May 2015, adopted a Global Action Plan on Antimicrobial resistance but implementing it is proving a difficult task, especially in the low- and middle-income countries^[6] where persistent infectious diseases, easy over-the-counter access to antibiotics, and lack of access to good quality primary health care are exacerbating the problem.^[7] India has also framed its National Action Plan for Antimicrobial resistance in April 2017 but it is still at preliminary stages.^[4]

Despite all the efforts, increase in antibiotic resistance is a persistent issue and dental profession is also a contributing factor. The literature shows that there is irrational use of antibiotics in dental community.^[8,9] It is estimated that up to 10% of antibiotics

Address for correspondence: Dr. Ramta Bansal,

Department of Conservative Dentistry and Endodontics, Desh Bhagat Dental College and Hospital, Mandi Gobindgarh, District Fatehgarh Sahib, Punjab, India.

E-mail: rummybansal07@yahoo.co.in

Received: 13-09-2019

Revised: 16-09-2019

Accepted: 30-09-2019

Published: 15-11-2019

Access this article online

Quick Response Code:



Website:
www.jfmpc.com

DOI:
10.4103/jfmpc.jfmpc_768_19

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

How to cite this article: Bansal R, Jain A, Goyal M, Singh T, Sood H, Malviya HS. Antibiotic abuse during endodontic treatment: A contributing factor to antibiotic resistance. J Family Med Prim Care 2019;8:3518-24.

are prescribed in primary care dentistry^[10] for prophylaxis or therapeutic reasons. Primary care dentists are largely independent prescribers and their prescribing decisions are normally made without restriction and supervision.^[10] Studies suggest that 30% to 50% of prescribed antibiotics are unnecessary or not optimally prescribed^[11] and majority of overprescribed antibiotics are for nonindicated dental conditions and diseases.^[12-14] The most common infections treated with antibiotics in dentistry are infections related to the root canal system.^[15] In endodontics, antibiotics are used extensively not only systemically but also locally. The local mode comprises intracanal medicaments, irrigants containing antibiotics, medicated gutta percha points, medicated sealers, etc., that enable the dentist to target bacteria in every nook and corner of root canal system, which is otherwise beyond reach if targeted by conventional root canal treatment (RCT) protocols.^[16] The fundamental basis for the successful management of endodontic infection is thorough debridement of the infected root canal and drainage of involved soft as well as hard tissues.^[17] The literature also shows that collateral antibiotics are not effective in preventing or resolving signs and symptoms in endodontic infections when adequate local debridement and drainage have been achieved.^[18,19] Unfortunately, dentists still prescribe antibiotics for endodontic infections like periapical abscesses and irreversible pulpitis which require only operative measures.^[20,21]

The aim of the present article is to discuss antibiotic abuse during endodontic treatment, its contribution toward antibiotic resistance, and measures required to stop antibiotic abuse in endodontic treatment. A web-based research on Medline was done by using term journal article and Review published in last 10 year's dental journals in English language papers. The keywords searched on MedLine were "Antibiotics and endodontics," "Antibiotic resistance," "Antibiotic prophylaxis dental," "Antibiotic prescribing pattern," "Antibiotics abuse," "Antibiotics and dentists," and "Antibiotics over prescription." In addition, important cross-reference articles were reviewed. The present review screened about 100 articles, relevant articles were shortlisted, and facts were compiled.

Discussion

Although antibiotics are prescribed for a variety of dental concerns, they are often sought out for real or perceived endodontic problems.^[22] According to the American Association of Endodontists (AAE) guidelines 2017,^[17] the objectives for the treatment of endodontic infections are removal of the pathogenic microorganisms, their by-products, and pulpal debris from the infected root canal system and establishment of conditions that favor the lesion to heal. Antibiotics must only be used as additive therapy in patients with systemic manifestations such as fever, lymphadenopathies, etc., following adequate endodontic disinfection or abscess drainage or when spreading infections such as cellulitis are present.^[23] In addition, prophylactic measure is observed in immunocompromised patients or in predisposing conditions such as endocarditis. Administration of antibiotics in

the absence of the above-mentioned reasons has no evidence of therapeutic benefit.^[17] Despite the limited usefulness of antibiotics in endodontics, their use is common and possibly increasing.^[21] Review of literature has shown that dentists worldwide prescribe antibiotics not only inappropriately^[24] during endodontic treatment but also for nonindicated conditions, such as pulpitis.^[14,25] A study revealed that although majority of Indian dentists were aware of antibiotic resistance, still indiscriminate prescription of antibiotics was found among them.^[8] It is necessary to identify the factors responsible for the over-prescription of antibiotics so that efforts can be made to tackle this abuse.

Factors causing over prescription of antibiotics during endodontic treatment

1. **Placebo effect:** Although the literature shows conclusively that antibiotics neither control nor prevent localized endodontic pathosis,^[23,26] many patients perceive improvement in their condition after consuming antibiotics, due to a strong placebo effect that antibiotics possess.^[27] The literature contains many studies that promote prescription of antibiotics for the patient's comfort and to alleviate their apprehension.^[28,29]
2. **Prevention of spread of infection:** Antibiotics are believed to prevent the spread of infection. This belief often is a contributing factor while prescribing in cases of acute apical abscesses. The mainstay of treatment of acute apical abscesses is incision for establishing drainage and RCT or extraction of the involved tooth to eliminate the source of infection. The effectiveness of an oral antibiotic as first choice of treatment is highly questionable as there is a lack of effective circulation in a necrotic pulp system. The only exception is cellulitis, for which penicillin is recommended.^[30] However, this studies show the highest rate of antibiotic prescription during endodontic treatment occurred for cases of acute apical abscess.^[31]
3. **To prevent flare-ups:** The precautionary measures for root canal flare-up comprise of choosing instrumentation technique with the minimal extrusion of periapical debris, completion of the biomechanical preparation in a single visit, sealing of the access cavity between visits, and maintaining aseptic environment during RCT.^[32] However, some studies recommended the systemic use of antibiotics to prevent flare up during or after RCT.^[28,33] Some consider that instituting antibiotics before the commencement of RCT in teeth with necrotic pulps is therapeutic rather than prophylactic.^[34] This is because necrotic pulps show periapical radiolucencies that are invariably infected and use of antibiotics becomes therapeutically mandatory.^[35] However, studies show that prophylactic use of amoxicillin in asymptomatic nonvital teeth before RCT has no effect on the incidence of flare-up.^[32,36]
4. **Prophylaxis for patients at risk:** The AAE guidelines recommend that prophylactic antibiotics should be given for immunocompromised patients, or with a history of infective endocarditis or placement of a prosthetic joint in

previous 2 years, and patients with congenital heart disease.^[37] Antibiotic prophylaxis is not right for everyone and should only be used when the potential benefits outweigh the risks of taking them. A study reported that prophylactic antibiotics that dentists prescribe are unnecessary 81% of the time.^[38] The literature shows that there are deficiencies in knowledge regarding appropriate prophylactic antibiotic use.^[31]

5. **To reduce postendodontic pain:** According to published data, RCT induces more frequent and more severe postoperative pain than do other dental operative procedures.^[39,40] The postendodontic pain is the result of inflammatory process, which may be related to microbial irritation, mechanical or chemical factors, and its frequency is up to 40%.^[41] Controlled trials show that antibiotics are ineffective in managing dental pain;^[29] however, both general dentists and endodontists routinely prescribe antibiotics for patients with dental pain.^[24,42,43]
6. **To improve periapical healing and treatment outcome:** Review of literature showed no association between the use of antibiotics and RCT outcome.^[44,45] Clinical trials show that antibiotics are unrelated to posttreatment signs and symptoms^[46,47] and have no impact on postsurgical outcomes.
7. **Patients insist and expect antibiotics:** Studies show that patient insist for prescription of antibiotics after RCT due to a commonly held belief that antibiotics are “miracle drugs” that will resolve or minimize adverse postendodontic events.^[48]
8. **Busy dentist:** Patients with dental pain invariably present unscheduled and distressed to dentist who has sometimes already busy appointment book. In such cases, antibiotics are often prescribed to patients not for their clinical benefit but to delay appointment or to cover the referral period. Although guidelines permit prescription of antibiotics if definitive treatment has to be delayed due to referral to specialist services,^[49] prescribing antibiotics like this is totally unjustified and should not be made routine.
9. **Poor patient:** Dentists are more likely to prescribe an antibiotic for poor patients than commit more office time to surgical management.^[21] Also poor patient who cannot afford RCT and don't want to undergo extraction demand for antibiotic prescription thinking that they can save the tooth by warding off the infection. It is important for patient to understand that antibiotics are not an alternative to dental intervention; they are adjunct.^[50]

Apart from over-prescription of antibiotics, other factors that contribute to antibiotic resistance are:

Irregular dose regimens of antibiotics: Penicillin VK and amoxicillin, both beta-lactam antibiotics, are the first line of antibiotics chosen as adjunct therapeutic agents in endodontics.^[51] The recommended dosage for amoxicillin is 500 mg T.D.S for adults. Although the doses are well established based on pharmacokinetic studies,^[52] there is far less evidence to support the duration of treatment. Most clinicians prescribe antibiotics in courses of 3 to 7 days.^[17] However, the literature review indicates that shorter courses of 2–3 days duration can be effectively used

as adjuvant therapies.^[17] The British National Formulary also advocates an antibiotic course of 2–3 days for treatment of acute dental infections.^[53] Several reports have shown that patients improved significantly after 2–3 days of antibiotic therapy, thus proving that prolonged courses may not confer additional benefits.^[54,55] Moreover, therapies lasting 7 days with amoxicillin have been shown to increase the population of resistant strains.^[56]

Broad spectrum antibiotics: In dentistry, antibiotic prescription is empirical because the dentist does not know what microorganisms are causing the infection, as samples from the root canal or periapical region are not commonly taken and analyzed. Consequently, based on clinical and bacterial epidemiological data, the patient is subjected to treatment on a presumptive basis with broad-spectrum antibiotics often being prescribed.^[51] Although AAE guidelines recommend that the dentists should minimize the use of broad-spectrum antibiotics, several studies^[21,57,58] confirm that dentists prefer moderate-to-broad spectrum antibiotics over those with a more appropriate narrow spectrum. This inappropriate use of antibiotics contributes to antibiotic resistance.

Charm for newer antibiotics: Numerous patients presume that new and costly medications are more efficacious than older agents. Pharmaceutical company representatives (PCRs) actively network with healthcare providers and regularly visit providers even in remote areas to market newer antibiotics.^[59] PCRs also contribute to increasing resistance by demanding or requesting doctors to prescribe their newer antibiotics. This aids selection of resistance to these newer drugs as well as to older drugs in their class.

Patient-related factors: Patient-related factors contributing to resistance are patient's misperception about the utility of antibiotics in endodontic infections, poor compliance, interruption of treatment when patients begin to feel better, poor patients who are unable to afford the full treatment course antibiotics, and self-medication.^[52]

Suboptimal primary health centers (PHCs): Although dental care is a part of primary health care in India, dental care services are available only in few states at the primary health care level.^[60] Thus, general practitioners and health workers at PHCs function as the first point of contact for dental patients with an acute dental pain. Due to nonavailability of dentist in rural areas, patients approach these nondental practitioners to get temporary relief. In such cases, general practitioner invariably prescribes antibiotics to patients before issuing a referral mostly due to pressure or insistence from patients.^[61]

Prevention

Dentists can reduce the irrational use of antibiotics in dentistry by absorbing following pointers:

1. Conservative use of antibiotics:

Conservative use of antibiotics is indicated to minimize the risk of developing resistance to current antibiotic regimens.^[62]

They should be prescribed only in defined indications. Assure evidence-based antibiotic references are readily accessible during patient visits. Minimize the use of broad-spectrum antibiotics and use them for the shortest duration possible. Shorter courses also improve patient’s compliance which gives an added benefit. Revise empiric antibiotic regimens on the basis of patient progress and, if needed, perform culture results.

2. Being responsible while prescribing antibiotics:

Dentists should avoid prescribing antibiotics based on nonevidence-based historical practices, patient demand, convenience, or pressure from colleagues, to delay appointment, or to retain the patient.

3. Educating our patients:

A didactic discussion with the patient is indispensable to change the overprescribing phenomenon. We must ensure patients understand, and are supported in adhering to, the planned duration of therapy. We can educate our patients to take antibiotics exactly as prescribed, take antibiotics prescribed only for them, and not to save antibiotics for future illness. Many dentists may not be highly concerned about their antibiotic prescribing habits since many patients expect to get an antibiotic for an issue patients perceive as bacterial. Patients should be educated that the key to successful management of endodontic infection is definitive treatment and prescription of antibiotics in these circumstances is futile. Patients should be taught to avoid pressuring the dentist for an antibiotic prescription. Briefing patients about anticipated postendodontic pain and specifying analgesics to manage it will not only increase the faith of patients in their dentists, but also increase patients’ pain threshold, and change their attitude toward placebo role antibiotic plays in managing dental pain.

4. Educating our referring dentists:

Dealing with the issue of overprescribing of antibiotics is difficult and requires a group effort. General dentists are part of the remedy as well. Discuss antibiotic use and prescribing protocols with referring dentists. Further, the senior dentists, when supervising the work of junior dentists, need to be cautious in examining the antibiotic prescribing patterns during the management of endodontic cases.

Measures required for curbing antibiotic abuse

The problem of antibiotic resistance cannot be scaled down without substantial constraints in antibiotic use. This can be done by

1. Issuing antibiotic prescribing guidelines: Appropriate antibiotic prescribing guidelines must be issued by the government. In this regard, Government of South Australia has furnished guiding principles for antimicrobial therapy referred as MINDME^[63]: an acronym for “antimicrobial creed” Table 1. Analogous clinical guidelines on the use of antibiotics in India will ensure that clinicians prescribe antibiotics appropriately and optimally. In April 2017, the

Indian government has also adopted the National Action Plan (NAP) for containing Antimicrobial resistance.^[64] This 5-year NAP (2017–2021) outlines the priorities and implementation strategies for curbing Antimicrobial resistance in India.^[65] The government can adopt computerized decision support systems that are designed to improve antibiotic use by providing treatment recommendations to clinicians at the time of prescribing. Implementation of this system has been associated with reduced use of broad-spectrum antibiotics, improved antibiotic selection and dosing, fewer prescribing errors, antibiotic cost, and reduced antibiotic resistance.^[66]

2. **Antimicrobial Stewardship Program:** These Programs are devised to enhance the relevant use of antimicrobials by encouraging the selection of the optimal antimicrobial drug regimen, dose, duration of therapy, and route of administration.^[67] Strategic approaches^[66] to antimicrobial stewardship are outlined in Table 2. Antimicrobial Stewardship Program has been well emphasized in the medical field, but not in the dentistry.^[68] These programs should be well promoted and must include the evidence-based education for dentists about appropriate antibiotic drug, dose, dosing interval, and duration to make them more confident in the prudent use of antibiotics.
3. **Addressing “over the counter” sale of antibiotics:** In most developing countries, there is little regulation on the retail of pharmaceuticals. Antibiotics are available often without a physician’s prescription^[69] and this nonprescription use and ease of availability of antibiotics has major contribution in escalating the danger of antibiotic resistance. It varies from 19% to 90% in countries outside U.S. and Europe.^[70] The rule of “prescription-only medicines” should be composed according international guidelines and should be strictly reinforced. The creation of centralized computer applications monitoring antibiotic manufacture and supply

Table 1: Antimicrobial Creed

M	Microbiology guides therapy wherever possible
I	Indications are evidence based
N	Narrowest spectrum required
D	Dosage which is appropriate according to the site and type of infection
M	Minimize duration of therapy
E	Ensure monotherapy in most cases

Table 2: Strategic approaches to antimicrobial stewardship

Strategic approaches to antimicrobial stewardship	
1.	Appropriate antimicrobial therapy.
2.	Optimizing antimicrobial prophylaxis for operative procedures.
3.	Developing and implementing an antibiotic policies and standard treatment guidelines.
4.	Prospective auditing and providing feedback and timely intervention in streamlining the antibiotic prescriptions.
5.	Formulary restriction/preauthorisation.
6.	Improving antimicrobial prescribing by educational and administrative means.

record throughout India can go a long way to tackle with this issue.^[66]

4. **Education Programs:** Passive educational activities such as lectures or informational pamphlets should be used to complement stewardship activities. Academic dental hospitals should integrate education on fundamental antibiotic stewardship principles into their curriculum. The dental curriculum needs to include a clear protocol of therapeutic treatment during endodontic management. E-mailing lectures to dentist as a part of continuing education program is essential to update practitioner knowledge about endodontic pharmacology. Other options that can help to facilitate education on antibiotic use include presentations, posters, flyers, newsletter, or electronic communication to dental staff along with a variety of web-based education resources.^[67]
5. **Role of primary health care in curbing antimicrobial resistance:** The challenge of reducing antibiotic resistance can be advanced through effective primary health care. There is urgent need to develop primary oral health care programs all over the world, especially in developing countries like India to promote rational dental care.^[71] There should be sufficient skilled health workers with good antibiotic prescribing practice to provide primary dental care. Mobile applications and other such new technologies to support health education, case diagnosis and management^[72] have potential to improve rational antibiotic use. Drug shortages lead to use of inappropriate antibiotic in primary care settings.^[73] This can be corrected by improved supply chain management, especially in peripheral facilities.^[74] Rapid diagnostic technologies for primary care could improve both the accuracy of diagnosis and treatment.^[75] Many countries having national action plans for antibiotic resistance are initially targeting tertiary care. These should be expanded to the primary care level. WHO approach “AWaRe”-Access, Watch, Reserve for tackling antibiotic resistance should be properly implemented to primary care.

Conclusion

Lack of knowledge on rational use of antibiotics among dental practitioners is one of the contributing factors to antibiotic resistance. Antibiotic resistance is a multifaceted problem and its containment requires a holistic approach. Endodontists should stop injudicious use of antibiotics. Health professionals, government as well as general public have to come together to reduce the inappropriate use of antibiotics. Countries need to develop Primary dental health care program to address this global issue and these programs need to be better reflected in national plans.

Acknowledgments

None

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Cassini A, Högberg LD, Plachouras D, Quattrocchi A, Hoxha A, Simonsen GS, *et al.* Attributable deaths and disability-adjusted life-years caused by infections with antibiotic-resistant bacteria in the EU and the European Economic Area in 2015: A population-level modelling analysis. *Lancet Infect Dis* 2019;19:56-66.
2. Goossens H, Ferech M, Vander Stichele R, Elseviers M. Outpatient antibiotic use in Europe and association with resistance: A cross-national database study”. *Lancet* 2005;365:579-87.
3. Swedish work on containment of antibiotic resistance - Tools, methods and experience. Stockholm: Public Health Agency of Sweden. 2014. pp. 16-7, 121-8. Available from: www.folkhalsomyndigheten.se. [Last assessed on 2019 Sep 20].
4. Taneja N, Sharma M. Antimicrobial resistance in the environment: The Indian scenario. *Indian J Med Res* 2019;149:119-28.
5. Chaudhry D, Tomar P. Antimicrobial resistance: The next big pandemic. *Int J Community Med Public Health* 2017;4:2632-6.
6. Turning plans into action for antimicrobial resistance (AMR). Working paper 2.0: implementation and coordination. Geneva: World Health Organization; 2019 (WHO/WSI/AMR/2019.2).
7. Singh PK. A universal good: How increased health coverage can help beat back antimicrobial resistance. World Health Organization, Regional Office for South-East Asia, 2017. Available from: <http://www.searo.who.int/mediacentre/features/2017/howincreased-health-coverage-can-help-beat-back-amr-resistance/en/>.
8. Puranik MP, Sabbarwal B, Bose S. Dental practitioner's knowledge and practices regarding antibiotic prescription and development of resistance: A cross-sectional study. *J Indian Assoc Public Health Dent* 2018;16:144-8.
9. Ramachandran P, Rachuri NK, Martha S, Shakthivel R, Gundala A, Battu TS. Implications of overprescription of antibiotics: A cross-sectional study. *J Pharm Bioall Sci* 2019;11(Suppl S2):434-7.
10. Sanderson OBE S, Williams D. The need for global guidance on antibiotic stewardship in dentistry. *AMR Control* 2019-20 (online edition);107-8.
11. Demirjian A, Sanchez GV, Finkelstein JA, Ling SM, Srinivasan A, Pollack LA, *et al.* CDC Grand Rounds: Getting smart about antibiotics. *MMWR Morb Mortal Wkly Rep* 2015;64:871-3.
12. Wasan H, Gupta P, Mathur A, Mutneja E, Mathur VP, Gupta YK. Influence of qualification and practice settings of dental practitioners on antimicrobial prescribing in Delhi and National Capital Region, India. *J Nat Sci Biol Med* 2017;8:229-34.
13. Löffler C, Böhmer F. The effect of interventions aiming to optimize the prescription of antibiotics in dental care-A systematic review. *PLoS ONE* 2017;12:e0188061.
14. Segura-Egea JJ, Martín-González J, Jiménez-Sánchez MDC, Crespo-Gallardo I, Saúco-Márquez JJ, Velasco-Ortega E. Worldwide pattern of antibiotic prescription in endodontic infections. *Int Dent J* 2017;67:197-205.

15. AboAlSamh A, Alhussain A, Alanazi N, Alahmari R, Shaheen N, Adlan A. Dental students' knowledge and attitudes towards antibiotic prescribing guidelines in Riyadh, Saudi Arabia. *Pharmacy (Basel)* 2018;6:42.
16. Bansal R, Jain A. Overview on the current antibiotic containing agents used in endodontics. *N Am J Med Sci* 2014;6:351-8.
17. AAE Position Statement. AAE guidance on the use of systemic antibiotics in endodontics. *JOE* 2017;43:1409-13.
18. Matthews DC, Sutherland S, Basrani B. Emergency management of acute apical abscesses in the permanent dentition: A systematic review of the literature. *J Can Dent Assoc* 2003;69:660.
19. Nagle D, Reader A, Beck M, Weaver J. Effect of systemic penicillin on pain in untreated irreversible pulpitis. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2000;90:636-40.
20. Demirbas F, Gjermo PE, Preus HR. Antibiotic prescribing practices among Norwegian dentists. *Acta Odontol Scand* 2006;64:355-9.
21. Marra F, George D, Chong M, Sutherland S, Patrick DM. Antibiotic prescribing by dentists has increased. Why? *J Am Dent Assoc* 2016;147:320-7.
22. Walton RE. Antibiotics: A Risky Prescription. *Pharmacology (AAE publication)* August 19, 2016. [Last assessed on 2019 Mar 21].
23. Aminoshariae A, Kulild JC. Evidence-based recommendations for antibiotic usage to treat endodontic infections and pain: A systematic review of randomized controlled trials. *J Am Dent Assoc* 2016;147:186-91.
24. Yingling NM, Byrne BE, Hartwell GR. Antibiotic use by members of the American Association of Endodontists in the year 2000: Report of a national survey. *J Endod* 2002;28:396-404.
25. Bolfoni MR, FG Pappen, Pereira-Cenc Ti, Jacinto RC. Antibiotic prescription for endodontic infections: A survey of Brazilian Endodontists. *Int Endod J* 2018;51:148-56.
26. Agnihotry A, Fedorowicz Z, van Zuuren EJ, Farman A, Al-Langawi J. Antibiotic use for irreversible pulpitis. *Cochrane Database Syst Rev* 2016;2:CD004969.
27. Tilburt JC, Emanuel EJ, Kaptchuk TJ, Curlin FA, Miller FG. Prescribing "placebo treatments": Results of national survey of US internists and rheumatologists. *BMJ* 2008;337:a1938.
28. Abbott AA, Koren LZ, Morse DR, Sinai IH, Doo RS, Furst ML. A prospective randomized trial on efficacy of antibiotic prophylaxis in asymptomatic teeth with pulpal necrosis and associated periapical pathosis. *Oral Surg Oral Med Oral Pathol* 1988;66:722-33.
29. Fouad AF. Are antibiotics effective for endodontic use? An evidence-based review. *Endod Topics* 2002;3:52-66.
30. Siqueira JF, Rôças IN. Microbiology and treatment of acute apical abscesses. *Clin Microbiol Rev* 2013;26:255-73.
31. AlRahabi MK, Abuong ZA. Antibiotic abuse during endodontic treatment in private dental centers. *Saudi Med J* 2017;38:852-6.
32. Akbar I. Efficacy of prophylactic use of antibiotics to avoid flare up during root canal treatment of nonvital teeth: A randomized clinical trial. *J Clin Diagn Res* 2015;9:ZC08-11.
33. Mata E, Koren LZ, Morse DR, Sinai IH. Prophylactic use of penicillin V in teeth with necrotic pulps and asymptomatic periapical radiolucencies. *Oral Surg Oral Med Oral Pathol* 1985;60:201-7.
34. Sjogren U, Figdor D, Persson S, Sundqvist G. Influence of infection at the time of root filling on the outcome of endodontic treatment of teeth with apical periodontitis. *Int Endod J* 1997;30:297-306.
35. Walton RE. Interappointment flare-ups: Incidence, related factors, prevention, and management. *Endod Topics* 2002;3:67-77.
36. Lindeboom JA, Frenken JW, Valkenburg P, van den Akker HP. The role of preoperative prophylactic antibiotic administration in periapical endodontic surgery: A randomized, prospective double-blind placebo-controlled study. *Int Endod J* 2005;38:877-81.
37. Hossaini-zadeh M. Current concepts of prophylactic antibiotics for dental patients. *Dent Clin North Am* 2016;60:473-82.
38. Suda KJ, Calip GS, Zhou J, Rowan S, Gross AE, Hershov RC, *et al.* Assessment of the appropriateness of antibiotic prescriptions for infection prophylaxis before dental procedures, 2011 to 2015. *JAMA Netw Open* 2019;2:e193909.
39. Levin L, Amit A, Ashkenazi M. Post-operative pain and use of analgesic agents following various dental procedures. *Am J Dent* 2006;19:245-7.
40. Ashkenazi M, Blumer S, Eli I. Post-operative pain and use of analgesic agents in children following intrasulcular anaesthesia and various operative procedures. *Br Dent J* 2007;202:E13.
41. Konagala RK, Mandava J, Pabbati RK, Anupreeta A, Borugadda R, Ravi R. Effect of pretreatment medication on postendodontic pain: A double-blind, placebo-controlled study. *J Conserv Dent* 2019;22:54-8.
42. Segura-Egea JJ, Velasco-Ortega E, Torres-Lagares D, Velasco-Ponferrada MC, Monsalve-Guil L, Llamas-Carreras JM. Pattern of antibiotic prescription in the management of endodontic infections amongst Spanish oral surgeons. *Int Endod J* 2010;43:342-50.
43. Al-Maslmani MJ, Sedeqi FA, Moule AJ. Prescription pattern of antibiotic and analgesic in endodontic treatment in Kuwaiti population: A self-administered Survey. *Saudi Endod J* 2014;4:128-34.
44. Ranta H, Haapasalo M, Ranta K, Kontiainen S, Kerosuo E, Valtonen V, *et al.* Bacteriology of odontogenic apical periodontitis and effect of penicillin treatment. *Scand J Infect Dis* 1988;20:187-92.
45. Ng YL, Mann V, Gulabivala K. A prospective study of the factors affecting outcomes of nonsurgical root canal treatment: Part 1: Periapical health. *Int Endod J* 2011;44:583-609.
46. Fouad AF, Rivera EM, Walton RE. Penicillin as a supplement in resolving the localized acute apical abscess. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1996;81:90-5.
47. Henry M, Reader A, Beck M. Effect of penicillin on postoperative endodontic pain and swelling in symptomatic necrotic teeth. *J Endod* 2001;27:117-23.
48. Jayadev M, Karunakar P, Vishwanath B, Chinmayi SS, Siddhartha P, Chaitanya B. Knowledge and pattern of antibiotic and non narcotic analgesic prescription for pulpal and periapical pathologies-a survey among dentists. *J Clin Diagn Res* 2014;8:10-4.
49. Scottish Dental Clinical Effectiveness Programme (SCDEP). *Drug Prescribing for Dentistry. Dental Clinical Guidance.* 2nd ed. Dundee; SDCEP; 2011.
50. Ramu C, Padmanabhan TV. Indications of antibiotic

- prophylaxis in dental practice- review. *Asian Pac J Trop Biomed* 2012;2:749-54.
51. Segura-Egea JJ, Gould K, Şen BH, Jonasson P, Cotti E, Mazzoni A, *et al.* Antibiotics in Endodontics: A review. *Int Endod J* 2017;50:1169-84.
 52. Suchi K, Praveen J. Antibiotics in dentistry a boon or bane. *J Dent App* 2015;2:132-7.
 53. Longman LP, Preston AJ, Martin MV, Wilson NHF. Endodontics in the adult patient: The role of antibiotics. *J Dent* 2000;28:539-48.
 54. Kuriyama T, Absi EG, Williams DW, Lewis MAO. An outcome audit of the treatment of acute dentoalveolar infection: Impact of penicillin resistance. *Br Dent J* 2005;198:759-63.
 55. Martin MV, Longman LP, Hill JB, Hardy P. Acute dentoalveolar infections: An investigation of the duration of antibiotic therapy. *Br Dent J* 1997;183:135-7.
 56. Lacey RW, Lord VL, Howson GL, Luxton DE, Trotter IS. Double-blind study to compare the selection of antibiotic resistance by amoxicillin or cephadrine in the commensal flora. *Lancet* 1983;2:529-32.
 57. Teoh LSK, Marino R, McCullough M. Part 1. Current prescribing trends of antibiotics by dentists in Australia from 2012 to 2016. *Aust Dent J* 2018;63:329-37.
 58. Ford PJ, Saladine C, Zhang K, Hollingworth SA. Prescribing patterns of dental practitioners in Australia from 2001 to 2012. *Antimicrobials Aust Dent J* 2017;62:52-7.
 59. Nair M, Tripathi S, Mazumdar S, Mahajan R, Harshana A, Pereira A, *et al.* "Without antibiotics, I cannot treat": A qualitative study of antibiotic use in Paschim Bardhaman district of West Bengal, India. *PLoS One* 2019;14:e0219002.
 60. Simon AK, Rao A, Rajesh G, Shenoy R, Pai MB. Oral health care availability in health centers of mangalore taluk, India. *Indian J Community Med* 2014;39:218-22.
 61. Barnett T, Hoang H, Stuart J, Crocombe L. Non-dental primary care providers' views on challenges in providing oral health services and strategies to improve oral health in Australian rural and remote communities: A qualitative study. *BMJ Open* 2015;5:e009341.
 62. Costelloe C, Metcalfe C, Lovering A, Mant D, Hay AD. Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: Systematic review and meta-analysis. *BMJ* 2010;340:c2096.
 63. Antimicrobial Prescribing Clinical Guideline v1.1 (Public)-1-A2. Clinical Guideline No.: CG168. Government of South Australia. Approval date: 21 November 2018.
 64. National Action Plan on Antimicrobial Resistance (NAP-AMR) [Internet]. [Cited 2019 Mar 23]. Available from: http://www.searo.who.int/india/topics/antimicrobial_resistance/nap_amr.pdf.
 65. Ranjalkar J, Chandy SJ. India's National Action Plan for antimicrobial resistance – An overview of the context, status, and way ahead. *J Family Med Prim Care* 2019;8:1828-34
 66. Antimicrobial Stewardship Program Guideline. Prof. Balram Bhargava Secretary, Department of Health Research Director General, Indian Council of Medical Research. Published 15-11-2018. Available from: <https://icmr.nic.in/sites/default/files/guidelines/AMSP.pdf>.
 67. Dellit TH, Owens RC, McGowan JE, Gerding DN, Weinstein RA, Burke JP, *et al.* Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. *Clin Infect Dis* 2007;44:159-77.
 68. Cope AL, Francis NA, Wood F, Chestnutt IG. Antibiotic prescribing in UK general dental practice: A cross-sectional study. *Community Dent Oral Epidemiol* 2016;44:145-53.
 69. Chokshi A, Sifri Z, Cennimo D, Horng H. Global contributors to antibiotic resistance. *J Glob Infect Dis* 2019;11:36-42.
 70. Morgan DJ, Okeke IN, Laxminarayan R, Perencevich EN, Weisenberg S. Non-prescription antimicrobial use worldwide: A systematic review. *Lancet Infect Dis* 2011;11:692-701.
 71. Haque M, Sartelli M, Haque SZ. Dental infection and resistance-global health consequences. *Dent J (Basel)* 2019;7:22.
 72. Frost I, Laxminarayan R, McKenna N, Chai S. Technical series on primary health care. Antimicrobial resistance and primary health care. Available from: https://www.who.int/docs/default-source/primary-health-care-conference/amr.pdf?sfvrsn=8817d5ba_2. [Last accessed on 2019 Sep 20].
 73. Årdal C, Outtersson K, Hoffman SJ, Ghafur A, Sharland M, Ranganathan N, *et al.* International cooperation to improve access to and sustain effectiveness of antimicrobials. *Lancet* 2016;387:296-307.
 74. Kotwani A, Ewen M, Dey D, Iyer S, Lakshmi PK, Patel A, *et al.* Prices and availability of common medicines at six sites in India using a standard methodology. *Indian J Med Res* 2007;125:645-54.
 75. World Malaria Report 2017. Geneva: World Health Organization; 2017. Available from: <http://www.who.int/malaria/publications/world-malaria-report-2017/report/en/>. [Last accessed on 2018 Sep 17].