Antibiotics: their use and misuse in paediatric dentistry. A systematic review

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Abstract

Aim The use of antibiotics by health care professionals has benefitted humankind to a great extent. Recent reports show an increasing trend of antibiotic prescription by paediatric dentists. This systematic review aims to address the current pattern of antibiotics prescription among the paediatric dental population according to the evidence-based literature. The question of research addressed here deals with the assessment of the correlation of the injudicious prescription of antibacterial agents and antibiotic resistance among the population of interest.

Methods Electronic search databases: PubMed, Ovid and Cochrane Library, were used to review studies as per their relevance and findings. Keywords for search were associated with population: 'paediatric patients', intervention: 'antibiotics treatment', 'prescribing behaviour', and outcomes: 'antibiotic resistance'

Results A total of 542 abstracts were identified, 45 of which met the inclusion criteria and were reviewed. A multifactorial relationship leading to increased prescription of antibiotics in paediatric dentistry was observed. Very few studies actually correlated this prescribing behaviour with resistance to these drugs. No consensus regarding the duration of antibiotic therapy or prophylaxis was found.

Conclusion Insufficient literature support necessitates the requirement of increased evidence to draw a definitive association between the prescribing trends of antibiotics in paediatric dentistry and drug resistance. The development of intervention programmes like antibiotic stewardship ensuring collaboration between patients and paediatric dentists can ensure effective antibiotic prescription.

KEYWORD Antibiotic prescription,Antibiotic resistance, Paediatric antibiotics.

Introduction

Antibiotics can be unanimously considered as drugs which have truly revolutionised healthcare by achieving adequate control of infections. Since the discovery of penicillin, the use of antibiotics has shown a tremendous rise among medical and dental professionals alike [Cohen, 2000]. In light of this increasing prescription trend, the worldwide problem of antibiotic resistance is a cause of concern. In fact, this threat has been aptly referred to as a 'ticking time bomb' requiring prompt actions [Palmer, 2014]. This phenomenon, associated with mutational or genetic changes within the bacterial strains under selective pressure, has been inevitably associated with increased consumption of these medicines. Also, in conjunction with antibiotic resistance, the incidence of side-effects and hypersensitivity reactions along with superinfections has been commonly documented with antibiotic usage [O'Donnell and Barker, 2016; Beacher et al., 2015; Da Fosenca, 2000]. In fact, recently an indirect association has been found between the early use of antibiotics in childhood and the risk of allergic asthma [Droste et al., 2000].

Unjustified use of antibiotics has also been reported in children with orofacial infections. As paediatric dentists, the awareness regarding the definitive indications of antibiotics is mandatory. When prescribed systemically, these drugs should be used as adjuncts to treat certain oral infections or for prophylaxis to prevent serious situations of bacteremia [Fine et al., 1998]. Otherwise undesired issues like resistance may ensue. Abuse by the patient or the parent and inefficient usage can also lead to this problem.

Despite extensive reports and studies concerning the use of antibiotics and the global issue of antibiotic resistance, the use of these agents amongst dental practitioners specifically is only demonstrated through questionnaires or interviews. A definite lack of scientific literature to assess the pattern of use of antibiotics in denstistry in relation to drug resistance has been noted. Hence, this review was conducted to identify the current practices of antibiotics prescription observed by dental health professionals for children with oral health care needs and the causes of their prescribing behaviour. Studies in relation to this pattern or trend with the growing problem

of antibiotic resistance are also identified through this paper. Also, the potential solutions to curb this worldwide concern have been considered as a part of this comprehensive review. The evaluation of the items summarised is as follows.

1. Prescribing behaviour of antibiotics in paediatric dentistry.
2. Factors responsible for the prescribing trends.
3. Guidelines for use of antibiotics in paediatric dentistry.
4. Future implications.

Methodology

The systematic review was conducted in accordance with the Preferred Reporting Items in Systematic Review and Meta-Analysis (PRISMA) guidelines [Moher et al., 2015]. The search strategy involved an explicit search from multiple databases, namely, PubMed, Ovid Medline, and Cochrane Library. As a part of conduction of the review, the keywords that were selected included "antibiotic prescribing", "antibiotic resistance", and "antibiotic prophylaxis". The filter applied limited the selection of articles from the year 1997 until 2017. The changes in the prescription pattern in the last twenty years were included only to ensure the current scenario of antibiotic prescription and assess emergence of the phenomenon of antibiotic resistance. The inclusion criteria was formatted as per the analysis involving the paediatric population, intervention of antibiotic prescription and treatment or prophylaxis to check for the outcome in terms of antibiotic resistance (PICO analysis) [Stern et al., 2014]. The studies included were non-clinical or clinical trials, cross-sectional surveys, studies, case reports, etc. The inclusion and exclusion criteria are summarised in Tables 1 and 2.

Data were then extracted from each of the chosen review articles as per the type of study, intervention of drug therapy, its dosage, duration, and the associated outcome of resistance. The risk bias from each of the researches was considered, and only the articles with important conclusions in reference to prescribing trends of antibiotics, its factors, guidelines, and its resistance were included. Two reviewers were then selected for the implementation of this review, who independently conducted the process of search and evaluation of the articles to avoid any form of observer bias. After that, another analyst was involved to compile the individual results and record the findings.

Inclusion Criteria (as per PICO analysis)			
Population	Intervention	Comparison	Outcome
Children and adolescents below 18 years of age	Antibiotic therapy Antibiotic prophylaxis	Operative intervention or any other therapy except use of antibiotics	Antibiotic resistance or other adverse effects

TABLE 1 Inclusion criteria

Exclusion Criteria
Articles dealing with adult population, that is above 18 years of age
Studies not specific to dental profession
Articles published before the year 1997
Studies or reports in other languages than English
Non-peer reviewed articles

TABLE 2 Exclusion criteria

Results

According to the selected search criteria, an identification of a total of 542 titles and abstracts were selected from the noted databases. After application of filters and exclusion criteria, a total of 45 articles were found to be relevant. These articles were then independently reviewed by two reviewers and categorised as per the following criteria: Nationwide trends

Author and year	Study design	Region or nation assessed for prescription trends	Antibiotic used commonly	Discussion
Cherry, et al. (2012)	Survey, Cross sectional	North Carolina	Amoxicillin	Overprescription of antibiotics seen, more by general dentists Lack of adherence to guidelines (AAPD)
Dar-Odeh NS, et al. (2013)	Survey, Cross sectional	Jordan	Amoxicillin	Overprescription of antibiotics in non-indicated conditions and for non-scientific reasons
Sivaram, et al. (2013)	Survey, Cross sectional	AAPD members	Amoxicillin	Overuse of antibiotics seen Lack of knowledge of antibiotic stewardship programmes
Peric, et al. (2015)	Survey, Cross sectional	Croatia)	Penicillin analogues (Amoxicillin +Calvulanic acid)	-
Konde, et al. (2016)	Survey, Cross sectional	India	Amoxicillin	Lack of adherence to AAPD guidelines, more evident in general dental practitioners.
Al-Johani, et al. (2017)	Survey, Cross sectional	Jeddah (Saudi Arabia)	Amoxicillin	Lack of consistency in antibiotic prescription with non-adherence to guidelines (9.5-45%)
Ford, et al. (2017)	Survey, Cross sectional	Australia	Amoxicillin	Increased prescription of antimicrobials noted from 2000-2012.
Yesudian, et al. (2015)	Original Research	North England	Amoxicillin	Inappropriate prescribing of antibiotics which improved with interventions.

TABLE 3 Prescribing trends of antibiotics

associated with prescription of antibiotics in paediatric dentistry (Table 3), factors responsible for these prescribing practices, and their association with drug resistance in the population of interest. The results of each reviewer were compiled and the significant findings were presented in discussion.

Discussion

Prescribing trends of antibiotics in paediatric dentistry

Most of the evidence regarding the prescribing behaviour of antibiotics in paediatric dentistry was through cross-sectional surveys and studies conducted nationwide or regionally to identify the pattern of antibiotic prescription. An overall assessment of the prescribing practices revealed use of antibiotics by dental practitioners to be approximately 7–11% of the total antibiotic consumption globally [Cleveland and Kohn, 1998]. This suggests that although the major contributors to the global issue of antibiotic resistance are general physicians and paediatricians, some contribution from paediatric dentists has also been noted [Rapkin, 1997]. An initial assessment and search of literature disclosed as much as 252 articles and reports, out of which most of them were excluded as a result of an unclear evidence in the population of interest, that is the paediatric age group. As a result, only seven cross-sectional studies that analysed the current practices of antibiotic prescription among the paediatric population by dental professionals were reviewed. Most of the studies assessed the nationwide or regional prescribing behaviour of these drugs. Most studies assessed these prescribing trends through questionnaires sent to practising dentists, asking for personal information and open- and closed-ended questions through case scenarios. The responses to these questions were then analysed to check for correct prescription of antibiotics. Prudent usage of antibiotics, in most of the studies, was considered only after a few common findings. These included prescriptions of antibiotics after any form of systemic evidence of infection spread like facial swelling, radiographically evident pathology and, most importantly, considering a definite or clinical examination of the patient before any form of antibiotic prescription. Nationwide and area-specific results have been tabulated (Table 3).

A study by Cherry et al. [2012] was one of the pioneer studies which effectively undertook a wide-scale survey of practising dentists for the paediatric dental population in North Carolina. As a result, a definite lack of adherence to the guidelines set by the American Academy of Paediatric Dentistry (AAPD) was noted (10–42%) and this behaviour tended to increase over weekends (14–17%). An important finding was that paediatric dentists showed a comparatively better adherence to the guidelines as compared to general dental practitioners which was statistically significant. The most commonly prescribed antibiotic was amoxicillin followed by penicillin derivatives and clindamycin, which was prescribed in case of allergy to penicillin. Another important survey which was undertaken in India on hundred dentists and hundred paediatric dental specialists revealed an overprescription of antibiotics by both dental professionals with general dental practitioners showing a higher incidence of antibiotic overusage. This study reported the use of amoxicillin or the combined usage of amoxicillin and clavulanic acid with metronidazole commonly in cases of suspected aerobic and anaerobic prescription respectively [Konde et al., 2016]. Another important finding derived from this survey suggested that though the awareness regarding prophylaxis of antibiotics and resistance was adequate, a general lack of knowledge was observed regarding the guidelines for a judicious drug use.

Similar studies and surveys conducted in Jordan [Dar Odeh, et al. 2013], Croatia [Peric et al., 2015], and Jeddah (Saudi Arabia) [Al-Johani et al., 2017] also reported a definite overprescription and overusage of drugs by practising dentists and non-adherence to guidelines. Similarly, the most commonly prescribed drug was amoxicillin, and other penicillin derivatives was a common finding in these studies. A retrospective study to assess the changes in antibiotic prescription during the past 12 years in Australia showed an increased dispensing of antimicrobial agents suggesting an inappropriate use of these drugs [Ford et al., 2017]. To assess the overprescription of antibiotics for prophylaxis, a study conducted in Brazil revealed not only an incorrect usage of drug but also an inappropriate prescription in terms of the generic name, dosage, and duration of antibiotic therapy [Lisboa et al., 2015].

Another important study assessed the pattern of antibiotic use amongst the members of AAPD [Sivaram et al., 2015]. The survey reported a tendency to overprescribe and overuse antibiotics in certain conditions like irreversible pulpitis and abscess with or without sinus tract and draining fistula. On the other hand, the importance of educational intervention as a marker for improvement in prescription pattern was highlighted in a study by Yesudian et al. [2015]. The study was conducted in paediatric dentistry department of three centres of the United Kingdom and the results reported an overuse of antibiotics which gradually improved with subsequent cycles through interventions like "aide memoire" to improve awareness of drug use. In fact, as a part of general practice in the United Kingdom, as high as 57% of the consultations involving oral problems over a period of 10 years were resolved with an antibiotic prescription, rather than a referral to a dentist for treatment [Cope et al., 2016].

All these studies also revealed an interesting deduction that is: none of these studies, surveys, and reviews checking for prescribing practices showed use of antimicrobial sensitivity testing or microbial culture reports before the actual antiobiotic prescription. Another inference from the replete review was the absence of consensus or clear-cut specification regarding the age or weight-specific dosages and duration of antibiotic therapy.

Factors associated with the prescribing trends

The cause of prescribing behaviour among various regions and nations has been assessed and a number of factors have been highlighted in various studies. One of the most frequent and significant cause of this increased use of antibiotics is the lack of knowledge regarding the definite indications and need of antibiotics [Peedikayil, 2011; Koyuncuoglu et al., 2017; Oberoi et al., 2015]. Overprescription in non-indicated situations like irreversible pulpitis, dentoalveolar abscesses with localised abscesses, simple traumatic conditions of intrusion, and extrusion were observed in these studies. It can be inferred that symptomatic conditions of pain and inflammation determine usage of antibiotics rather than actual infections. An inadequate clinical judgement in assessing the use of antibiotics is also responsible for the negligent use of these drugs. This misuse can also be considered a result of inappropriate, inadequate or extended use of the antibacterial agents to avoid any form of recurrence of infection [Pallash, 2000].

A special cause of the observed prescribing behaviour in reference to paediatric dentistry could be a result of the

pressure or requirements of the parent and the patient. This parental pressure has been reported as one of the main causes leading to unwarranted prescription [Dar-Odeh et al., 2010; Wong et al., 2016]. Other non-clinical situations acting as determinants for antibiotic use include uncertain diagnosis of the case, need for delay of treatment owing to unavailable appointments, and social relations etc. [Chidambaram, 2016; Hills-Smith and Schuman, 1983]. Studies suggest that the practitioners assume that using antibiotics is the quickest way to resolve any form of consultation [Avon and Solomn, 2000]. These non-scientific reasons along with avoidance of any form of negligent claims as a result of problems like ineffective sterilisation can be important factors responsible for the overuse of these drugs [Marra et al., 2016; Lewis, 2008]. The compilation of these barriers of knowledge, attitude, and external factors are accountable for the observed prescribing trends [Cope and Chestnut, 2014].

Guidelines for antibiotic use in paediatric dentistry

One of the major factors responsible for the overprescription and overusage of antibiotics could be attributed to the lack of guidelines regarding the definite use and indications of these drugs in paediatric dentistry. Different nations worldwide have published their own guidelines to assure effective usage of these drugs. These include the National Institute of Health and Care Excellence-United Kingdom (NICE) guidelines and guidelines by the American Dental Association, Canadian Dental Association, and Scottish Dental Clinical Guidelines. However, the only guidelines available to address the indications of antibiotics for the paediatric dental population are the guidelines suggested by the AAPD. The revised AAPD guidelines suggest use of antibiotics as adjuncts in certain prophylactic and therapeutic conditions after adequate assessment of systemic spread of infection and the risk factors of the patient. An important consideration of these guidelines is the avoidance of antibiotics in the case of localised infection and swelling owing to the compromised circulation of pulp thereby avoiding any form of beneficence of systemic antibiotic use. The guidelines, however, lack data regarding use of antibiotics in traumatic situations though certain trials suggest efficacy of doxycycline as a part of adjunctive therapy and for topical application of drugs. The use of antibiotics is also recommended for bacterial infections of salivary glands and facial swelling of dental origin.

Resistance to antibiotics

Very few studies were found to indicate the presence of drug resistance in the paediatric population. Two long-term clinical trials suggest a high incidence of antibiotic resistance in children as a result of chronic drug therapy in blood cancer and respiratory tract infection [Bruckner et al., 2002; Larrson et al., 2000]. Another research suggested the presence of Streptococcus sanguis resistant strains in the dental plaque of the patients as a result of long-term antibiotic therapy for otitis media [Erickson and Herzberg, 1999]. Reports by Suzuki et al. [1997] suggest the presence of resistant strains in the oral microflora of healthy individuals acting as a source of nosocomial infections. However, there is an insufficient evidence regarding the correlation of the current trends of antibiotic prescription with the causation of drug resistance.

Future implications

To account for future interventions, an extension to the review was undertaken to assess the implications for practice and research so that the impending global concern can be addressed by the oral health care professionals.

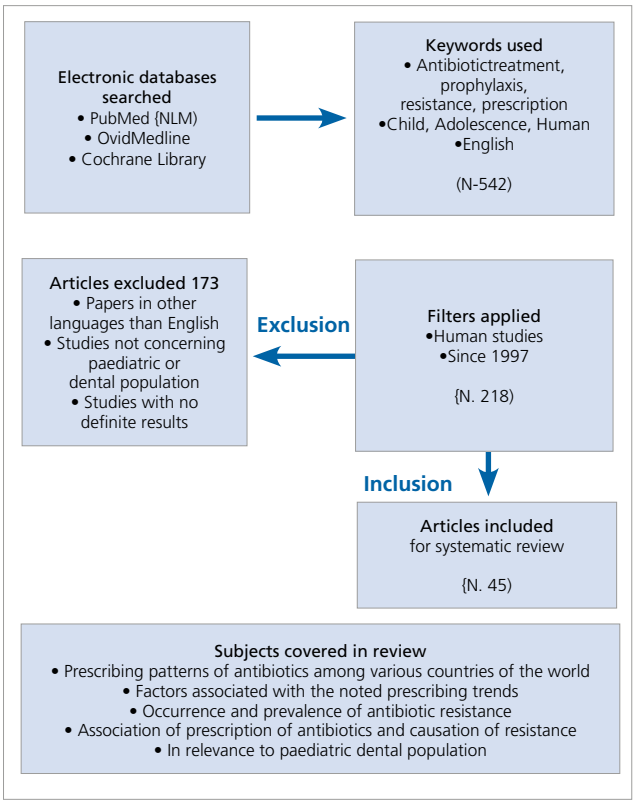

FIG. 1 Schematic overview of search strategy of literature

For practice

Antimicrobial resistance is a global concern and needs prompt addressing. The World Health Organization has announced programmes to ensure effective handling and use of these drugs [Friedrich, 2016]. As a part of prospective practice, it is extremely important to work on holistic approaches like antibiotic stewardship. These programmes involve a continued and collaborative care between the physicians and the other medical staff to assure the correct usage of antibiotics in the form of six directions on correct drug usage for the indicated patient at appropriate dose, correct duration, right route of administration for adequate time, and with effective documentation [Li and Cosgrove, 2017]. An effective cost control by the government through active surveillance can not only curb this resistance but can also help in improving clinical outcomes [Haliti et al., 2015]. Emphasis on topical antibiotic use in the form of double or triple antibiotic paste in the root canals of necrotic primary teeth can offer successful and promising results in dental practice [Albuquerque et al., 2017]. Another important practical solution to overprescription can be in the form of reinforcement of knowledge through clearer and more specific nationwide guidelines which can help in assessing the definite indications of drug therapy but also describe the appropriate duration and dosage regarding the body weight or age of the child [Tong and Rothwell, 2000].

For research

The review suggests a clear-cut lack of evidence to ascertain a relation between the current prescribing trends of antibiotics

in paediatric dentistry and causation of drug resistance. Hence, a need for randomised controlled trials and studies addressing this question of research is felt. Though some prospective studies have been conducted on the use of non-conventional approaches of infection management and control, clinical evidence is lacking and hence, more experimental studies are required in the domain. These alternative approaches include using natural therapy for control of infections like propolis, silica etc. [Shabbir, 2016; Valgas et al., 2007] and photodynamic therapy [Tonon et al., 2015]. The Director General of the WHO had rightly mentioned a virtually "dry pipeline" in terms of development of new antibiotics. Hence, research to assure this refilling can be a significant step to curb antibiotic resistance [Rapkin, 1997]. Another important area of research that can assure promising future outcomes can be in the form of studies which assess fast and easy culture of microorganisms. Although the nanoculture has been suggested as an effective form of microbial culture, the available clinical trials lack for its effective implementation [Neipa et al., 2016].

Conclusions

This systematic review has dealt with one of the most common yet the most neglected practice in dentistry, that is the practice of drug prescription, mainly antibiotics.

1. Antibiotic prescriptions assessed in paediatric dentistry through this review helped in analysing an overprescription of antibiotic use. Although most of the studies were cross-sectional surveys offering a limitation in the form of interviewer bias, the trends suggest an increased prescription and dispensing of antibiotics to the paediatric dental population.
2. Factors like lack of knowledge, uncertain diagnosis, parental, and patient pressure have been considered leading to increased use of antibiotics.
3. Direct evidence has been found on prescribing behaviour with drug resistance, and the increasing prevalence of antibiotic resistance requires a contributory effort by paediatric dentists as well.
4. Clearer nationwide guidelines are required for effective understanding of the indications of antibiotics.
5. Holistic approaches like antibiotic stewardship can be considered to assure prudent antibiotic use.

The antibiotic therapy is a double-edged sword, the misuse of which can be managed by its prudent use. Sir William Osler had rightly quoted that the desire to ingest medicines is a primary feature demarcating animals from men. Hence, prescribing a dose of drug is in broad sense, prescribing or recommending a dose of one's knowledge. Therefore, definite care must be taken while prescribing any antibiotic as "an appropriate action today can assure an effective cure for tomorrow".

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