

## Use of systemic antibiotic therapy after the replantation of avulsed permanent teeth: a literature review

Uso de antibioticoterapia sistêmica após o replante de dentes permanentes avulsionados: uma revisão de literatura.

Elizane Ferreira HAMANAKA<sup>1</sup>, Vanessa Ferreira da SILVA<sup>1</sup>, Wilson Roberto POI<sup>2</sup>, Daniela Atili BRANDINI<sup>2</sup>, Sônia Regina PANZARINI<sup>2</sup>

1 – São Paulo State University (Unesp) – School of Dentistry of Araçatuba – Graduate Program in Integrated Clinics – Araçatuba – SP – Brazil.

2 – São Paulo State University (Unesp) – School of Dentistry of Araçatuba - Department of Surgery and Integrated Clinics – Araçatuba – SP – Brazil.

### ABSTRACT

Dental avulsion is the most severe type of dentoalveolar trauma, and the treatment of choice for this type of injury should be the replantation of the exarticulated tooth. After conducting a review of the literature and holding discussions with experienced researchers and clinical specialists from different areas, the International Association of Dental Traumatology (IADT) proposed a protocol for tooth replantation, including a recommendation for systemic antibiotic therapy (SAT) to reduce the risk of root resorption. Several antibiotics have been tested, but tetracycline and amoxicillin are, by far, the most commonly used drugs for avulsion injuries. This paper reviews the literature on the prescription of SAT in cases of immediate and delayed replantation of accidentally avulsed permanent teeth, based on a critical analysis of full-length papers retrieved from the PubMed/Medline, Bireme and SciELO electronic databases. Original research reports and literature reviews published in English-language journals between 1966 and 2016, and directly or indirectly discussing the relation between antibiotic therapy and the replantation of permanent teeth, were searched using “tooth avulsion,” “systemic antibiotic therapy” and “tooth replantation” as key words. The prescription of antibiotics for tooth replantation was found to be a controversial subject, and randomized clinical studies are needed to determine whether antibiotics for tooth replantation are actually indicated. Until the results of these studies become available, the recommendation is to use SAT for the management of permanent teeth replanted after an accidental avulsion. The best prescription option is tetracycline

### RESUMO

Avulsão dentária é o tipo mais grave de traumatismo dentoalveolar, e o tratamento de escolha para esse tipo de lesão deve ser o replante do dente avulsionado. Após realizar uma revisão da literatura e promover discussões com pesquisadores experientes e especialistas clínicos de diferentes áreas, a Associação Internacional de Traumatologia Dentária (IADT) propôs um protocolo para o replante dentário com a recomendação de se usar a antibioticoterapia sistêmica (SAT) para reduzir o risco de ocorrência de reabsorção radicular. Diversos antibióticos foram testados, mas a tetraciclina e amoxicilina são, de longe, as drogas mais comumente usadas para lesões por avulsão. Este trabalho revisa a literatura sobre a prescrição de SAT em casos de replante imediato e tardio de dentes permanentes acidentalmente avulsionados, com base em uma análise crítica de artigos completos recuperados nos bancos de dados eletrônicos PubMed/Medline, Bireme e SciELO. Trabalhos de pesquisa original e revisões de literatura publicados em língua inglesa entre 1966 e 2016 e que contivessem alguma discussão sobre a relação entre antibioticoterapia e replante de dentes permanentes foram buscados por meio da utilização das palavras-chave “avulsão dentária”, “antibioticoterapia sistêmica” e “replante dentário”. Observou-se que a prescrição de antibióticos para dentes replantados é um assunto controverso e que estudos clínicos randomizados são necessários para se estabelecer a real necessidade de se usarem antibióticos para o replante dentário. Até que os resultados desses estudos se tornem disponíveis, a recomendação é de se usar a SAT para o tratamento de dentes permanentes replantados após uma avulsão acidental. A melhor opção de prescrição é a tetraciclina

for 7 days, and the second best prescription option is amoxicillin for 4 to 7 days.

## KEYWORDS

Anti-bacterial agents; Tooth avulsion; Tooth replantation.

durante 7 dias e a segunda melhor opção é a amoxicilina durante 4 a 7 dias.

## PALAVRAS-CHAVE

Agentes antibacterianos; Avulsão dentária; Reimplante dentário.

## CRITICAL REVIEW

Avulsion of permanent teeth is the most severe type of tooth injury. It is characterized by complete dislodgement of the tooth from its socket, causing severe damage to the supporting tissues and to the vascular and nerve structures [1]. It is responsible for 1% to 16% of all tooth injuries [1-3], and the treatment of choice should be the replantation of the exarticulated tooth [4]. The prognosis of a replanted tooth depends on the viability of the periodontal ligament cells, on the integrity of the root cementum and on minimal bacterial contamination [5], conditions directly related to the amount of extra-alveolar time, storage medium and root surface alterations [3,5].

Prescription of systemic antibiotic therapy (SAT) when attempting tooth replantation is based on the results of experimental studies and is recommended for preventing or minimizing bacterial proliferation, a critical etiologic factor in root resorption processes [6-8]. According to the guidelines of the International Association of Dental Traumatology for the management of avulsed permanent teeth, the antibiotic regimen of choice in case of tooth replantation is the administration of tetracycline for 7 days or amoxicillin for 7 days, as a second option [4].

The aim of this paper was to review the literature on the prescription of SAT for cases of immediate or delayed tooth replantation of permanent teeth following accidental avulsion.

Original research studies and literature reviews published in English-language journals between 1966 and 2016, and directly or indirectly

discussing the relation between antibiotic therapy and the replantation of permanent teeth were searched in the PubMed/Medline, Bireme and SciELO electronic databases using “tooth avulsion,” “systemic antibiotic therapy” and “tooth replantation” as key words.

Damage caused by tooth avulsion injuries is unavoidable. A better prognosis is expected if the damage is small and not sustained by infection; in this case, the replanted tooth may remain for a longer period of time in its socket. However, if avulsion involves loss of periodontal ligament vitality and root surface contamination, the outcome will be severe inflammation that may evolve to inflammatory or replacement resorption and ankylosis [5,9-11].

The most widely used systemic antibiotics after tooth replantation are tetracyclines and amoxicillin. Tetracyclines are part of the macrolide antibiotic family. They display bacteriostatic activity by inhibiting bacterial protein synthesis, and diffuse well inside the cell, thus making them excellent antibiotics against intra-cellular bacteria. Short- and long-acting tetracyclines (doxycycline, minocycline) have the same spectrum of antimicrobial activity, mechanism of action, side effects and cross-resistance, and are frequently used in clinical practice. These antibiotics should not be administered to pregnant women because they cause bone and dental deformities in the fetus [12]. Their use is not advised for children younger than 8 years, because they cause tooth darkening and may be associated with the occurrence of enamel hypoplasia. Permanent tooth darkening does not occur in adults [12].

Another option for SAT is phenoxymethylpenicillin (Pen V) or amoxicillin, a semi-synthetic penicillin belonging to the  $\beta$ -lactam family, which has broad spectrum antimicrobial activity and irreversibly inhibits the transpeptidase enzyme, thus acting on the bacterial cell walls [13]. Amoxicillin has comparatively greater bioavailability after oral administration, with an absorption rate of 74% to 92% [14].

SAT has been recommended after replantation of accidentally avulsed permanent teeth [4], but its beneficial effects on pulp and/or periodontal healing are a controversial issue [15]. Studies on tooth replantation in animals suggest that prescription of SAT immediately after replantation improves periodontal ligament healing, thereby reducing the extent of inflammatory root resorption [5,6,9,10]. In a study on tooth replantation in monkeys that received SAT, Hammarstrom et al. [5] also observed a reduction in initial local inflammation and alveolar bone resorption. Nevertheless, SAT has not been able to entirely prevent the occurrence of inflammatory root resorption or the development of ankylosis and replacement resorption [6]. The main factor involved in initiating inflammatory root resorption is the contamination of the pulp owing to pulp necrosis, which can be effectively controlled by endodontic treatment [16], whereas replacement resorption and ankylosis are consequences of the loss of periodontal ligament vitality [11].

Studies comparing the effects of tetracycline and amoxicillin have found that tetracycline is superior in reducing the inflammatory resorption associated with tooth replantation in dogs [9,10], owing to its anti-resorption properties in addition to its antibacterial properties [4,9,10].

The International Association of Dental Traumatology (IADT) [4] issued a protocol for tooth replantation in which SAT was recommended to help delay the resorption

process. According to this protocol, the best option is to administer tetracycline for 7 days, and the second best option is to administer amoxicillin for 7 days. However, amoxicillin can be administered for 7 days as an alternative to tetracycline [4,17], for patients older than 12.

Unlike laboratory animal studies, the studies investigating the effects of SAT on the events following replantation of human permanent teeth have reported no significant relationship favoring periodontal ligament healing or a reduction in root resorption [11,18-21].

Andreasen et al. [11] evaluated the factors related to periodontal healing after replantation of 400 avulsed permanent incisors using a research protocol in which most patients received 500,000 IU of penicillin orally for 4 days. The authors reported no significant difference between the groups with or without SAT, in terms of periodontal healing, but the extent of root resorption was not evaluated. Another study assessing the association between SAT and tooth replantation observed less resorption in the teeth of patients who were administered antibiotics immediately after replantation, but none of the teeth escaped root resorption entirely [6].

In an evaluation of human teeth replanted within up to 15 minutes after avulsion, Anderson and Bodin [21] did not find any association between root resorption and SAT. However, the results of this study were derived from an evaluation of 21 teeth, 19 of which were from patients that received antibiotics, and only 2 of which were from patients who were not submitted to SAT, with extraoral periods of 1 and 5 minutes, respectively.

Crona-Larsson et al. [20] analyzed the effect of luxation and avulsion injuries on permanent teeth and found no evidence of any beneficial effect to the healing process of 6 patients with dental avulsion who started SAT at the emergency room. However, they did not

specify the type, dose or duration of the SAT that was administered.

Sae-Lim and Yuen [18] followed the periodontal status of 34 teeth replanted after accidental avulsion for 1 year, and concluded that SAT did not enhance the periodontal healing process. The authors reported that the antibiotic regimen prescribed followed a local protocol—traditionally penicillin or erythromycin—but they did not specify dose or duration. Andreasen and Hjørtting-Hansen [19] performed a clinical and radiographic examination of 110 human teeth replanted after accidental loss, and reported that no favorable results were observed from the administration of SAT.

A systematic review of SAT in tooth replantation [15,22] found no conclusive evidence supporting an association between SAT and improved periodontal healing. Nevertheless, the authors emphasized the need to be cautious in applying this finding to patient care, because the analyses were based on the results of only three studies. They also expressed concern regarding the lack of randomization in these studies, and concluded that, until the results of future research become available, it is recommendable to follow the current protocol of prescribing an antibiotic regimen for cases of tooth replantation [4].

Gomes et al. [23] evaluated the influence of SAT (amoxicillin and tetracycline) on delayed tooth replantation in rats, according to the different phases (7, 15, 30 days) of the repair process. After replantation, one group of animals received no antibiotics, a second group was medicated systemically with amoxicillin, and a third, with tetracycline. Regardless of the evaluation period, the acute inflammatory infiltrate was less intense and the root resorption was less extensive in depth in the group treated with amoxicillin. Therefore, the authors concluded that SAT had a positive influence on the repair process after delayed tooth replantation, and that amoxicillin represented an excellent antibiotic option.

The contradiction involving the prescription of SAT for tooth replantation is based on there being no clinical or laboratory studies that can be compared. The clinical studies that demonstrated no favorable results for the administration of antibiotics [11,18-21] were not aimed at evaluating the effect of SAT on the outcome of tooth replantation, but rather identified an association incidentally between outcomes and the prescription of antibiotics in some cases of emergency treatment.

As stated by Shah and Ashley [24], the uncertainty about how necessary it actually is to prescribe SAT for all cases of tooth replantation is justified by the number of variables involved in the tooth replantation repair process. The site of the accident, the storage medium where the avulsed tooth is kept and the extra-alveolar amount of time elapsed after injury are factors that contribute importantly to the overall level of contamination. On the other hand, systemic conditions, such as diabetes, rheumatic fever or heart diseases, per se, require SAT prescription as a prophylactic measure. The extent of the injury and debilitation of the patient should also be considered. These data should be obtained through a careful review of the patient's history and through clinical examination. Moreover, each case should be assessed individually to determine the actual need for prescribing an antibiotic regimen.

Provided the tooth replantation protocol is followed scrupulously regarding treatment of the alveolar socket, root surface and root canal, as well as the splinting procedure and post-replantation follow-up, the expected sequelae are more likely to be dependent on the viability of the periodontal ligament cells at the time of replantation. So far, the literature has failed to clearly demonstrate that SAT can offer a significant contribution to the healing process [15]. Furthermore, considering that resistance to antibiotics is an increasing and challenging problem, this issue requires profound reflection and continuing research to establish the action

of antibiotics in the repair process taking place after tooth replantation.

In conclusion, until future laboratory studies and randomized clinical trials can conclusively assess the effect of SAT on the healing process of permanent teeth replanted after avulsion, the protocol recommending the prescription of antibiotics to patients undergoing tooth replantation still stands [4]. The best prescription option remains that of tetracycline for 7 days, and the second best option is amoxicillin for 4 to 7 days.

## REFERENCES

- Andreasen JO, Andreasen FM, Andersson L. Textbook and color atlas of traumatic injuries to the teeth. 4th ed. Oxford: Blackwell; 2007.
- Petersson EE, Andersson L, Sorensen S. Traumatic oral vs non-oral injuries. *Swed Dent J*. 1997;21(1-2):55-68.
- Panzarini SR, Gulinelli JL, Poi WR, Sonoda CK, Pedrini D, Brandini DA. Treatment of root surface in delayed tooth replantation: a review of literature. *Dent Traumatol*. 2008 Jun;24(3):277-82. doi: 10.1111/j.1600-9657.2008.00555.x.
- Andersson L, Andreasen JO, Day P, Heithersay G, Trope M, DiAngelis AJ, et al. Association of Dental Traumatology guidelines for the management of traumatic dental injuries: 2. Avulsion of permanent teeth. *Dent Traumatol*. 2012 Apr;28(2):88-96. doi: 10.1111/j.1600-9657.2012.01125.x.
- Hammarström L, Blomlöf L, Lindskog S. Dynamics of dentoalveolar ankylosis and associated root resorption. *Endod Dent Traumatol*. 1989 Aug;5(4):163-75.
- Hammarström L, Blomlöf L, Feiglin B, Andersson L, Lindskog S. Replantation of teeth and antibiotic treatment. *Endod Dent Traumatol*. 1986 Apr;2(2):51-7.
- Cvek M, Cleaton-Jones P, Austin J, Lownie J, Kling M, Fatti P. Pulp revascularization in reimplanted immature monkey incisors – predictability and the effect of antibiotic systemic prophylaxis. *Endod Dent Traumatol*. 1990 Aug;6(4):157-69.
- Consolaro A. The four mechanisms of dental resorption initiation. *Dental Press J Orthod*. 2013 May-Jun;18(3):7-9.
- Sae-Lim V, Wang CY, Trope M. Effect of systemic tetracycline and amoxicillin on inflammatory root resorption of replanted dogs' teeth. *Endod Dent Traumatol*. 1998 Oct;14(5):216-20.
- Sae-Lim V, Wang CY, Choi OW, Trope M. The effect of systemic tetracycline on resorption of dried replanted dogs' teeth. *Endod Dent Traumatol*. 1998 Jun;14(3):127-32.
- Andreasen JO, Borum MK, Jacobsen HL, Andreasen FM. Replantation of 400 avulsed permanent incisors. 4. Factors related to periodontal healing. *Endod Dent Traumatol*. 1995 Apr;11(2):76-89.
- Yagiela JA, Dowd FJ, Johnson B, Mariotti A, Neidle EA. *Pharmacology and Therapeutics for Dentistry*. 6th ed. St. Louis: Mosby; 2010.
- Döhren HV. Antibiotics: Actions, origins, resistance, by C. Walsh. *Protein Sci*. 2004 Nov; 13(11):3059–3060.
- Chow Y, Wu J, Li R. Influence of 6-aminopenicillanic acid on amoxicillin synthesis and p-hydroxyphenylglycine methyl ester hydrolysis. *Biocatal Biotransform*. 2005 Mar;23(5):347-51.
- Andreasen JO, Jensen SS, Sae-Lim V. The role of antibiotics in preventing healing complications after traumatic dental injuries: a literature review. *Endod Top*. 2006 Jul;14(1):80–92.
- Andreasen JO, Borum MK, Jacobsen HL, Andreasen FM. Replantation of 400 avulsed permanent incisors. 2. Factors related to pulpal healing. *Endod Dent Traumatol*. 1995 Apr;11(2):59-68.
- Dajani AS, Taubert KA, Wilson W, Bolger AF, Bayer A, Ferrieri P, et al. Prevention of bacterial endocarditis: recommendations by the American Heart Association. *Clin Infect Dis*. 1997 Dec;25(6):1448-58.
- Sae-Lim V, Yuen KW. An evaluation of after-office-hour dental trauma in Singapore. *Endod Dent Traumatol*. 1997 Aug;13(4):164-70.
- Andreasen JO, Hjorting-Hansen E. Replantation of teeth. I. Radiographic and clinical study of 110 human teeth replanted after accidental loss. *Acta Odontol Scand*. 1966 Nov;24(3):263-86.
- Crona-Larsson G, Bjarnason S, Norén JG. Effect of luxation injuries on permanent teeth. *Endod Dent Traumatol*. 1991 Oct;7(5):199-206.
- Andersson L, Bodin I. Avulsed human teeth replanted within 15 minutes – a long-term clinical follow-up study. *Endod Dent Traumatol*. 1990 Feb;6(1):37-42.
- Hinckfuss SE, Messer LB. An evidence-based assessment of the clinical guidelines for replanted avulsed teeth. Part II: prescription of systemic antibiotics. *Dent Traumatol*. 2009 Apr;25(2):158-64. doi: 10.1111/j.1600-9657.2008.00736.x.
- Gomes WD, Silva CA, Melo ME, Silva VF, Almeida MM, Pedrini D, et al. Delayed tooth replantation in rats: effect of systemic antibiotic therapy with amoxicillin and tetracycline. *Dent Traumatol*. 2015 Dec;31(6):448-56. doi: 10.1111/edt.12207.
- Shah P, Ashley P. Routine systemic antibiotic prescription in the management of permanent avulsed teeth – should we stop? *Dent Traumatol*. 2010 Jun;26(3):301. doi: 10.1111/j.1600-9657.2010.00875\_1.x.

### Sônia Regina Panzarini (Corresponding address)

Departamento de Cirurgia e Clínica Integrada, Disciplina de Clínica Integrada, Faculdade de Odontologia do Campus de Araçatuba, UNESP  
Rua José Bonifácio 1193, CEP: 1601-050. Araçatuba, SP, Brasil  
E-mail: panzarini@foa.unesp.br

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