Systematic Review

Prognosis of Replanted Avulsed Permanent Incisors: A Systematic Review

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Abstract

The objective of this systematic review is to use the principles of evidence-based dentistry to evaluate clinically and radiographically the prognosis of replanted avulsed permanent incisors in the pediatric age group with an immature or mature apex having an extraoral dry time up to 60 min and a follow-up period of 24 months or more. The study inclusion criteria included case reports and case series published in English. Databases used for the search were PubMed, EBSCOhost, Google Scholar, and Cochrane from January 1, 2000 to September 30, 2017. In addition, hand search of dissertations and journals on pediatric dentistry related to the topic of interest was performed in the institutional library. Contact to authors and colleagues working on similar subjects in the field was made through e-mails. Based on the moderate level of evidence available to assess the prognosis of replanted avulsed permanent incisors by clinical and radiographic evaluation, it is fair to conclude that the prognosis of the replanted teeth was best when the extraoral dry time was <15 min and the tooth was stored in osmolality-balanced media such as Hank's balanced salt solution, saline, and milk. The immature teeth showed better prognosis than mature teeth.

Keywords: Dental trauma, replantation, tooth avulsion

NTRODUCTION

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Avulsion is one of the most complicated types of trauma to the teeth, frequently seen in children aged 7-9 years, where a total displacement of the tooth from its socket occurs. It represents 0.5%–3% of the traumatic injuries to the permanent dentition.^[1] Avulsion causes the severing of the periodontal ligament (PDL) and disruption of the vascular-nerve bundle, with a consequent loss of blood supply to the tooth, which can lead to pulp necrosis.

According to the guidelines recommended by the International Association of Dental Traumatology (IADT),^[2] replantation is, in most situations, the treatment of choice for avulsed teeth but cannot always be carried out immediately. Appropriate emergency management and treatment plan are important for good prognosis.

At the time and site of an accident which leads to an avulsion injury, the immediate replantation of the avulsed tooth may not be feasible, owing to the various associated factors such as the person's conscious state, lack of first aid knowledge, informed consent issues, and lack of confidence in strangers gathered at the scene of accident.^[3]

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Dental practitioners also encounter problems relative to the management of the avulsion as it involves consideration a lot of associated factors, such as the place where the trauma took place, whether the child was immediately attended to, the extraoral dry time, the stage of root development of the avulsed tooth, storage medium used, any associated trauma to surrounding soft tissues, and health status of the child.

In this difficult situation, wherein the individual may have suffered multiple injuries other than avulsion, the factors such as type and intensity of injury, stage of root development, and contamination are not in control of any individual. However, the factors such as extraoral dry time and the type of storage media are invariably, in the control of individuals present at the accident site, and play a decisive role in the successful treatment of the avulsed tooth by a clinician.

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87

Replantation may successfully save the tooth, but it is important to realize that some of the replanted teeth have lower chances of long-term survival and may even be lost or extracted at a later stage.

Prognosis of replanted teeth depends on (i) the amount of physical damage to the root surface (cementum and PDL cells), (ii) the extraoral (dry) time,^[1,3,4] (iii) the type of storage medium,^[3-5] and (iv) the amount of root development of the avulsed tooth.^[6]

Choice of treatment is related to the maturity of the root (open or closed apex) and the condition of the PDL cells. An immature (i.e., open apex) tooth has the potential to establish revascularization when there is a minimum of a 1.0 mm apical opening, thereby pointing at a possible favorable outcome.^[7] The periodontal reactions to replantation, as we know, occurs in four different manners, namely, healing with normal PDL, healing with surface resorption, healing with replacement resorption (ankylosis), and healing with inflammatory resorption (infection), of which the former two are the favorable outcomes of the replantation procedure.^[1]

The storage medium and the extraoral dry time are extremely critical for survival of the PDL cells. After a dry time of 60 min or more, all PDL cells are nonviable. In permanent avulsed teeth, this increases the risk for pulp necrosis, root resorption, and ankylosis. For this reason, it is important to assess from the patient's history – the dry time of the tooth, before it was replanted or placed in a storage medium.

According to Andreasen and Hjorting-Hansen, teeth that were replanted within 30 min had better success rates than those with longer extraoral dry period.^[8,9]

Although plenty of research has been done on replantation of avulsed permanent incisors, not many articles are available to help us determine the prognosis of the replanted avulsed teeth to provide evidence in deciding on an ideal treatment protocol which can lead to good prognosis.

Furthermore, the retrospective studies in the literature fail to provide any standardization regarding the treatment protocol and outcome.

Hence, a systematic review comprising multiple case reports can be considered as helpful evidence for deciding the chairside treatment protocol and outcome in both emergency and delayed cases.

The present systematic review aims to determine the prognosis of replanted avulsed mature and immature permanent incisors having an extraoral dry time of >60 min.

DATA SOURCES

This systematic review was performed in accordance with the PRISMA guidelines. A computerized systematic search was performed on three electronic databases: PubMed, EBSCOhost, and Google Scholar. The various keywords used to search articles in the PubMed and EBSCOhost databases were as follows:

- 1. "Tooth avulsion AND replantation"
- 2. "Tooth avulsion AND replantation AND dental trauma"
- 3. "Tooth avulsion AND permanent teeth AND replantation AND extra-oral dry time"
- 4. "Tooth avulsion AND permanent teeth AND dental trauma AND replantation"
- 5. 'Tooth avulsion AND permanent teeth AND replantation AND transport media''
- 6. "Knocked out teeth AND replantation"
- 7. "Knocked out teeth AND dental trauma"
- 8. "Knocked out teeth AND reinsertion"
- 9. "Tooth avulsion AND permanent incisors AND reimplantation"
- 10. "Tooth avulsion AND permanent front teeth AND reimplantation"
- 11. "Dental trauma AND permanent front teeth AND reimplantation"
- 12. "Avulsion AND replantation AND permanent incisors"
- 13. "Dental trauma AND reimplantation."

Hand searches were undertaken to find additional relevant published material that might have been missed in electronic searches. The articles published from January 1, 2000, to September 30, 2017, were included in the study.

In the first step of the screening process, titles and abstracts were used to identify full articles concerning the prognosis of avulsed mature and immature permanent teeth in pediatric population.

In the second step of the screening process, the duplicates from the respective searches were removed and one single article was selected. In the third step, these articles were subjected to the inclusion and exclusion criteria of the review.

The inclusion criteria

- 1. Articles in English or those having detailed summary in English
- 2. Studies published between January 1, 2000, and September 30, 2017
- 3. Case reports, case studies, and longitudinal studies stating the prognosis of replanted avulsed permanent incisors
- 4. Studies reporting follow-up 24 months or more.
- 5. Studies reporting clinical and radiographic success rates
- 6. Studies which have followed up the avulsed teeth with extraoral time <60 min
- 7. Studies which have the IADT recommendations for replantation of avulsed teeth
- 8. Studies reporting replantation of avulsed permanent teeth.

The exclusion criteria

- 1. Reviews, comments, abstracts, letters to editors, and editorials
- 2. Studies published before January 1, 2000
- 3. Articles published in languages other than English
- 4. Studies for primary teeth
- 5. Animal studies.

All the studies identified by applying the inclusion and exclusion criteria underwent assessment for data extraction by a single reviewer.

The data were extracted using specifically designed data extraction forms. For each included study, the qualitative and quantitative information was extracted, including year of publication, experimental and control treatments, numbers and age of patients, treatment and follow-up durations, author's conclusions, and all the information needed for methodological quality evaluation.

PIOS

P – Participant: Children up to 18 years of age with avulsed permanent incisors

I - Intervention: Replantation of avulsed permanent incisors

O – Outcome measure: Prognosis of replanted permanent incisors

S - Study design: Case report and case series.

Resources Selection

The data search was carried out by initially identifying 1485 articles from electronic database based on the title relevant to the systematic review. Majority of the articles were retrieved from the PubMed database.

After removal of 30 duplicates, 1326 articles remained which were screened through abstracts. Of these, 129 full-text articles were analyzed for eligibility, of which 11 were selected for qualitative synthesis of the systematic review. This comprised 8.53% of the total articles obtained pertaining to the data search (11 out of 129).

The selected articles in the systematic review are included in Table 1 followed by the articles excluded enlisted in Table 2.

STUDY SELECTION

Selection of studies was done initially by reading the title and abstract of the articles obtained from each database. Only those

Table 1: Resource	selection -	articles	included in	the
systematic review				

Study	Year of publication
Kinoshita et al.	2002
Davidovich et al.	2006
Werder et al.	2007
Arrow	2008
Wang et al.	2010
Walter et al.	2011
Ratson and Peretz	2012
Al-Kahtani	2013
Tezel et al.	2013
Biagi et al.	2013
Munavalli et al.	2017

articles that were relevant to the review were collected and put for further evaluation. Articles reporting information based on dental trauma other than avulsion, avulsion and replantation for primary teeth, and animal studies were excluded. Case reports, case series, and longitudinal studies fulfilling the inclusion criteria were assessed further for the review.

Full-text articles of the selected abstracts were then evaluated independently. The selection process involved two independent investigators, and a consensus decision was made with a third evaluator to shortlist the articles that met all the inclusion criteria for the systematic review.

Reference lists of the selected articles were also searched for additional data that may have been missed. There were no restrictions placed on the maximum follow-up period or sample size for the studies selected.

The study selection was done using the PRISMA 2009 guidelines as mentioned in Table 3.

Study Characteristics

The data were collected and analyzed from each article on discussion by the same investigators who selected them, and a standard pilot data extraction sheet was prepared in consultation with the evaluator as an expert. The searches identified 1485 studies. After removal of duplicates and screening the abstracts, 129 full-text articles were selected. Of these 129 articles, only 11 articles fulfilled the inclusion criteria. A summary of all the included trials is shown in Table 4.

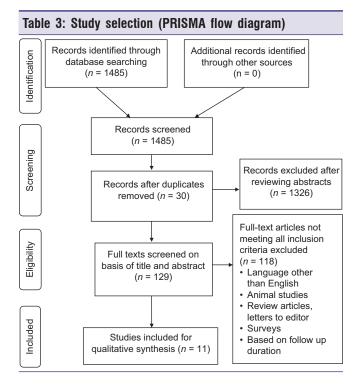
DISCUSSION

In spite of many studies investigating the prognosis of replanted avulsed permanent incisors, only 11 studies were considered appropriate for inclusion in this systematic review. It was possible to formulate a quantitative conclusion because only the case reports following IADT guidelines^[2] were included for assessment.

The advantage of assessing only case reports was that they could provide evidence for deciding the chairside treatment protocol and outcome in both emergency and delayed cases. The disadvantage with the assessment of retrospective studies was that they fail to provide any standardization regarding the treatment protocol and outcome.

There are different criteria to evaluate the prognosis of replanted avulsed permanent teeth. These include the amount of physical damage to the root surface (cementum and PDL cells) the extra oral dry time, type of storage medium and the amount of root development of the avulsed tooth. A variety of other factors such as age of the individual, type of splinting, mastication, treatment of the socket, endodontic treatment, antibiotics and time of replantation, macroscopic contamination, storage media, and storage period can also influence the clinical success of replantation. The most important is survival followed by healing of the PDL cells.

References	Reason for exclusion
Sonoda et al. (2008), Martins et al. (2004)	Age of the patient is not as per the inclusion criteria
Misra et al. (2008), Goldbeck et al. (2006), Chung et al. (2010), Chappuis et al. (2005)	Delayed extraoral dry time
Maniglia Ferreira (2017)	Describes intentional replantation
Barret et al. (2005), Berrezouga et al. (2011), Emerich et al. (2010)	Delayed extraoral dry time
Zachrisson et al. (2008)	Describes the transplantation of premolars
Rai et al. (2007)	Describes the self-replantation of avulsed incisor
Polat <i>et al.</i> (2008)	Describes the aesthetic treatment of the replanted avulse permanent incisors and not the procedure of replantation
Hecova et al. (2010)	Retrospective study with delayed extraoral dry time
Tzigounakis et al. (2008)	Review article
Soares et al. (2012)	Follow-up period is only for 1 year



The long-term retention of replanted avulsed permanent incisors is directly affected by the health of the PDL cells.

There are reports of replanted teeth remaining in function for over 30 years. On an average, they are functional at least for 5 years, and most are ultimately lost because of progressive root resorption or other associated problems such as ankylosis.^[10] The replanted teeth were followed for different evaluation periods up to 10 years in our systematic review, the mean radiographic examination being 2–5 years.

The periodontal reactions to replantation, as we know, occur in four different manners, namely, healing with normal PDL, healing with surface resorption, healing with replacement resorption (ankylosis), and healing with inflammatory resorption (infection), of which the former two are the favorable outcomes of the replantation procedure.^[1] Andreasen *et al.*^[1] studied PDL healing following replanted permanent incisors and concluded that the most significant factors in PDL healing were stage of root development, length of extra-alveolar dry storage, immediate replantation, and length of wet storage, and they have recommended immediate replantation wherever possible.

Andersson et al.^[2] followed up 21 avulsed permanent incisors replanted within 15 min radiographically for 5 years. Fifteen teeth out of the 21 teeth showed initial or no signs of any resorption. The teeth which showed no resorption were replanted immediately or within 10 min. In contrast, six teeth which were replanted 15 min after avulsion showed signs of resorption. According to this study, all teeth were most likely replanted with viable PDL cells, which has been demonstrated to prevent the cementum from resorption and thereby resulting in favorable prognosis. It has been suggested that initial cemental resorption opens up communication between the periodontal membrane (PDM) and the pulp, through the dentinal tubules, which can lead to infection of the pulp, which in turn elicits and maintains inflammatory root resorption on the root surface.^[11-13] Such initial resorption of the cementum has been demonstrated in teeth replanted with necrotic PDM.^[14-16]

Thus, we can state that the prognosis of an avulsed tooth is proportional to its extraoral time, which is a direct correlation of the status of the PDL cells.

If immediate replantation in cases of a severely injured or conscious patient is not possible or in cases where the tooth is severely contaminated, vitality of PDL cells on the root surface must be maintained for a period by storing the tooth properly during the extra-alveolar time. Experimental studies have shown that storing the tooth in milk, saliva, Hank's balanced salt solution (HBSS), and coconut water^[17-21] or wrapping the tooth in plastic foil^[22,23] prevents the PDL cells from injury and prevents later root resorption.

The choice of treatment is related to the maturity of the root (open or closed apex) and the condition of the PDL cells. An immature (i.e., open apex) tooth has the potential to establish revascularization when there is a minimum of a 1.0-mm apical

lable	4: Study	characteris	TICS								
Study id	Author's name	Location	Year of publication	Study design	Sample size	Age group	Setting	Population	Intervention	outcome	authors remark
1	Walter <i>et al</i> .	Basel, Switzerland	2007	case report	1	18 years	clinical	a caucasian male with 3 avulsed permanent teeth , e/o dry time of 6 minutes , stored in saline for 1 hr	teeth were reimplanted & fixed with flexible splint, root canal treatment was performed 9 days post trauma	healing was clinically uneventful, probing depth 2-3 mm, clinical attachment 2-3 mm and mobility was 0 & 2 central incisors showed signs of replacement resorption/ankylosis	the article showed clinical as well as radiologically successful replantation treatment after a follow up of 3 years
2	Werder et al	Bern, Switzerland	2011	case report	42	14-18 years	clinical	37 individuals with 42 avulsed permanent central incisors , e/o dry time upto 60 mins	teeth were reimplanted & fixed with non-rigid splint, root canal treatment was performed 2 days post trauma	The survival rate of the teeth in this survey was 83.3% (35/42 teeth) with a median follow-up period of 2.8 years (range 1 year to 5 years) after replantation. Seven teeth were lost during the follow-up period. Periodontal healing could be observed in 20 teeth. It was found more often in teeth with a closed apex (17/33 teeth) than in teeth with an open apex (3/9 teeth)	the article showed clinical as well as radiologically successful replantation treatment after a follow up of average of 2.8 years
3	Kinoshita et al	Nigata , Japan	2002	case report	32	5-14 years	clinical	10 children with 10 avulsed permanent incisors, 5 teeth showed e/o dry time less than 60 mins	teeth were reimplanted & fixed with wire composite resin	The outcomes of replanted incisors were fairly good both clinically and radiographically, except for one case in which the tooth had to be extracted	the article showed clinical as well as radiologically successful replantation treatment after a follow up of average of 5 years
4	Kahtani <i>et al</i>	Riyadh, Saudi arabia	2013	case report	1	10 years	clinical	10 year old male, with 2 avulsed permanent incisors with e/o dry time of 45 mins	teeth were reimplanted & repositioned & stabilized using orthodontic wire and composite splint, MTA apexification was done after 1 month	the outcome of the teeth was clinically and radiographically favourable	the teeth were clinically sound and did not show any symptoms of resorption or ankylosis after a follow up period of 12 months
5	Arrow P	Perth , Australia	2008	case report	1	9 years	clinical	9 year old male with avulsed permanent lateral incisor with immature tooth apex, E/o dry time 5-10 mins, stored in milk,	tooth replanted by teacher immediately after placing it milk, repositioned and splinted using a flexible splint in the dental clinic	A review nine months after the initial trauma, in April 2006, found an asymptomatic lateral incisor which exhibited normal colour, mobility, percussive sounds and soft tissue architecture. Calcific changes were seen in the pulp canal. 2 year follow up showed complete canal calcification	The article presented the continued obliteration of the pulp canal space by calcific material, similar in appearance to bone with the root surrounded by normal periodontal tissues as a response to replantation

91

Table	Table 4: contnd											
Study id	Author's name	Location	Year of publication	-	-	Age group	-	Population	Intervention	outcome	authors remark	
6	Ratson	Tel aviv	2012	case report	1	7.5 years	clinical	7.5 year old male with avulsed permanent right incisor, e/o dry time of 30 mins ,	tooth replanted and repositioned using orthodontic wire splint for 2 weeks	The apex of the right central incisor remained wide open, a thin radiolucent line covering the inner part of the dentinal walls was evident	an arrested formation of the root with bone-like tissue within the root canal.	
7	Wang	Taipei, Taiwan	2010	case report	1	7 years	clinical	7 year old male with immature avulsed permanent left incisor with uncomplicated crown fracture, E/0 dry time of 50 mins , stored in tap water	replanted immediately in the dental clinic using semi rigid fixation, pt was kept on antibiotic prophylaxis.	3 weeks post op , tooth was asymptomatic both clinically and radiographically. 2 months post op, pt reported with fractured restoration and sinus assocaiated with 21. RCT was done and CaoH dresssing was placed. At 5 month follow up , tooth showed hard tissue barrier formation both clinically and radiographically with continued root development.	at 1 year follow up the tooth showed complete root length development and normal PDL radiographically. Normal response to palpation and percussion. The probing depth and mobility grade were within normal range. No metallic sound or infraocclusion was detected	
8	Tezel	Izmir, Turkey	2013	case report	1	13 years	clinical	13 year old female with avulsed mature permanent right central incisor, stored in saline with e/o dry time of 0 mins	was washed with saline solution to remove the blood clot and the avulsed maxillary right central incisor was replanted back into the alveoler socket with the help of finger pressure . The tooth then splinted to the adjacent teeth with composite resin and the gingival lacerations were also repaired with sutures . 10 days post op splinting was removed & CaoH	Radiographic and clinical examinations were performed during 27 months followup period. During the 15 months followup period, the tooth remained in a stable functional position and did not reveal clinical ankylosis or replacement resorption. The replanted incisor developed mild infraocclusion (of about 1 mm) and replacement root resorption 21 months after the replantation. Twentyseven months after the replantation, the tooth still remained in a stable functional position. Infraocclusion was about 0.5 mm		

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Study id	Author's name	Location	Year of publication		Sample size	Age group	•	Population	Intervention	outcome	authors remark
9	Munavalli	Sangli, India	2017	case report	1	12 years	clinical	12 year old female with an avulsed mature permanent right central incisor, placed in its own socket	The half of the tooth was placed in the socket. The tooth was removed out of its socket and it was cleaned under running water to remove superficial debris on tooth surface and then it was placed into HBSS solution which was easily available in department. Then, fresh bleeding was prompted in the alveolar socket and the tooth was placed into the alveolar socket. A radiograph was taken to check the proper placement of the avulsed tooth and after confirmation of proper placement; tooth splinting was done with the composite splint. Any sharp edges were smoothened and adjacent tissues were irrigated using betadine solution	of splinting was planned. At the end of 3rd week, splint was removed and radiograph was taken. Radiograph after 3 weeks showed normal periapical tissues and vitality testing also showed the	good clinical and radiographic success after 2

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opening, thereby pointing at a possible favorable outcome after replantation. Cvek *et al.*^[24] have reported a higher revascularization rate after soaking the tooth in doxycycline. The topical application of doxycycline was found to decrease the frequency of microorganisms in the pulpal lumen, thereby decreasing the frequencies of ankylosis and inflammatory root resorption and resulting in a favorable prognosis post replantation.

The mature teeth in children and adolescents exhibit more extensive inflammatory root resorption after replantation compared to adults. The mentioned increase in resorption rate is related to the bone remodeling which is more extensive in children during the growing period. The root resorption and ankylosis may give rise to infra-occlusion during the growing process.

Arrow^[25] has described the formation of calcific material within pulp space of a replanted avulsed immature tooth along with normal PDL with an extraoral dry time of 5–10 min after a 2-year follow-up. The robustness of Hertwig's epithelial root sheath to withstand trauma and retain its ability to function appears to be a major factor responsible for this. It is possible that pulp remnants were left in the socket and along with the remaining Hertwig's root sheath continued to function to mineralize both the dentine and cementum, contributing to the favorable prognosis. This case reported the initiation of calcification as early as 11 weeks after trauma.

This illustrates calcification as a possible healing outcome of severe trauma to a tooth with an immature root and highlights the need to institute regular follow-ups and continued monitoring of immature teeth that have sustained severe trauma, such as luxations and avulsions for obtaining a better prognosis.^[26,27]

The reparative powers of periapical tissues have been reported in a number of articles describing the replantation of avulsed tooth with an immature apex.

In the report by Greer *et al.*,^[28] it was reported that there were pulp remnants in the tooth socket and the root that developed

Study d	Author's name	Location	Year of publication	Study design	Sample size	Age group	Setting	Population	Intervention	outcome	authors remark
0	Davidovich	Jerusalem, Israel	2006	case report	1	6.5 years	clinical	6.5 years old male with avulsed maxillary primary incisors and permanent left maxillary central incisor, e/o dry time of 10 mins and stored in saline	Under local anesthesia the permanent tooth bud was replanted in the dental clinic. A resin splint was placed between the replanted tooth and the primary canine. After 6 weeks of stabilization of the traumatized teeth, splint was removed & the child was provided with a mouth guard to reduce the risk of additional trauma to the anterior teeth	Four weeks later tenderness to percussion was no longer present. The response to cold test appeared 2.5 months after the trauma, lasted for 15 months and then disappeared. Radiographs taken during the follow-up period revealed that the root was gradually developing, followed by irregular formation of dentin. The PDL appeared normal. At 6 months after the trauma, calcifications and partial obliteration appeared in the root canal of the tooth. Advanced obliteration was also noted after 12-month follow-up At 24-month follow-up, the root was fully developed, with normal PDL and advanced obliteration	the replanted tooth showed good clinical and radiographi success after 2 years

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was similar to the contralateral incisor with calcified dentine and cementum. In this case report, the tooth socket was not observed after the avulsion, but it is possible that pulp remnants were left in the socket and along with the remaining Hertwig's root sheath continued to function to mineralize both the dentine and cementum.

In one case of a luxated tooth without any active intervention as reported by Welbury and Walton,^[29] there was an apparent development of a root apex totally separate from the body of the tooth. In this study, the child was seen again 7 years after trauma and the radiograph showed arrested root development and an opaque mass apical to the tooth. The tooth and the opaque mass were extracted because of associated pathological changes. When the opaque mass was examined microscopically, it showed similar structure to that of a root apex.

This case yet again highlights the capacity of the immature tooth structures to withstand considerable trauma and apparently retain their functionality. Kondo *et al.*^[30] have also described favorable prognosis after replanting a tooth with open apex within 10 min of avulsion. The tooth was subjected to endodontic therapy and showed apical barrier formation radiographically with normal color, response to palpation, and percussion. This favorable prognosis could yet again be contributed to vitality of PDL cells as a result of shorter extraoral dry time and implementation of endodontic therapy 3 weeks after trauma which aided in limiting the initiation inflammatory resorptive process.

The risk of infection-related root resorption should be weighed up against the chances of revascularization in teeth with open apices. Such resorption is very rapid in teeth of children. If revascularization does not occur, root canal treatment may be recommended.

Favorable healing of an immediately replanted tooth with mature apex was reported by Tezel *et al.*^[31] and Munavalli *et al.*^[10] The teeth showed functional stability, normal vitality, and radiographic findings.

Table 4: contnd												
Study id	Author's name	Location	Year of publication		Sample size	Age group	Setting	Population	Intervention	outcome	authors remark	
11	Biagi et al	Milano, Italy	2013	case report	1	16.2 years	clinical	16.2 year-old female with concussion of tooth 12; extrusive luxation of tooth 11; avulsion of tooth 21 and subluxation with complicated crown fracture of tooth 22, Tooth 21 was dry stored for 15 minutes, then in milk for 60 minutes.	The tooth 11 was gently pushed back into its socket; the root of tooth 21 was rinsed with saline, such as its alveolus to remove the contaminated coagulum, prior to its replantation in its socket with a gentle pressure; the tooth 22 was treated with pulp capping with calcium hydroxide & dentin bonding agent to create a seal against bacterial invasion into dentinal tubules. A functional splinting with an orthodontic 0.016-inch stainless steel wire and composite resin was positioned from tooth 13 to tooth 23 for a period up to 2 weeks. After 3 weeks, and not after 2 weeks as planned, teeth 11, 21 and 22 where endodontically treatedand the splint was removed.	The patient was scheduled for follow-up and was monitored weekly in the first month after the trauma, then after 3 months, 6 months, 1 year and 2 years. An initial phase of replacement root resorption of tooth 21 was suspected at the 6 months radiographic control and became evident 6 months later (1 year follow-up). The last radiographic examination during the 2 years recall revealed a dramatic increase of replacement root resorption of tooth 21	Replacement root resorption of tooth 21 was suspected after 6 months, was confirmed after 1 year and appeared severe after 2 years recall. All the other teeth were in good condition and a poor oral hygiene was observed.	

Another study by Walter *et al.*^[32] reported arrested resorptive process and a favorable prognosis at 3-year follow-up after endodontic therapy in replanted avulsed teeth having an extraoral dry time of 6 min. A slowly progressing replacement resorption occurred on the two central incisors, 11 and 21. Tooth 12 showed periodontal healing to a large extent. The three avulsed teeth were treated according to the same protocol; however, the differences in healing may be because of a different degree of PDL damage^[33] (Andreasen and Kristerson, 1981) or the biological variances, such as size of the root surface of the tooth types involved^[34] (Otis *et al.*, 2004). The arrested resorptive process could have been seen as a result of the short extraoral dry time, use of a storage medium such as saline followed by administration of tetratcycline which induces antiresorptive and antibacterial effect, and last but not the least endodontic therapy.

On the other hand, Davidovich *et al.*^[35] reported replantation of nonerupted tooth with open apex having an extraoral dry time of 10 min. After 2 years, the tooth showed favorable prognosis as the root was found to be fully developed associated with advanced obliteration in pulp space with normal PDL.

Bone-like structure filling the entire pulp space was reported by Ratson and Peretz^[36] in a replanted avulsed immature tooth with an extraoral dry time of 30–60 min.

According to the statement of Huang *et al.*,^[37] even if infection is present in the canal cavity and reaches the periradicular tissues, stem cells from the apical papilla may survive and contribute to tissue regeneration. Therefore, appropriate management of an infected canal may provide a favorable environment for tissue regeneration.

The report by Wang *et al.*^[38] describes the continued root formation followed by the formation of a hard-tissue barrier at the end of 1 year following replantation and conventional root canal therapy of a traumatically avulsed open-apex tooth with suppurative apical periodontitis, thus validating the statement of Huang *et al.*^[37]

Some possible mechanisms may explain this phenomenon. First, it is possible that Hertwig's sheath survived and retaining its ability to continue its role of root organization when the inflammatory process was eliminated. Second, the mesenchymal stem cells may reside in the apical papilla of permanent immature teeth. These stem cells appear to be the source of odontoblasts and can develop root dentin.

The cases reported by Chueh *et al.*,^[39] Ding *et al.*,^[40] Thibodeau *et al.*,^[41] and Iwaya *et al.*^[42] have also shown regeneration of an open apex in teeth with pulpal necrosis and infection.

Biagi *et al.*^[43] reported an unfavorable outcome of replacement resorption after a 2-year follow-up in a tooth with an extraoral dry time of 15 min followed by its placement for next 60 min in milk. In this clinical case, the development of the root was already complete, so the revascularization potential of the pulp was extremely limited. Hence, in this case, the replacement root resorption may have been caused by inadequate tooth storage: The tooth must not have been kept in milk immediately; however, only after a period in dry storage, the prognosis would probably be the same of any other dried and replanted tooth as dead cells cannot be revitalized by milk.

Contrary to this, Al-Kahtani^[44] reported arrested external root resorption after a 2-year follow-up in tooth with no extraoral dry time but placed in milk for 45 min. This favorable prognosis would have been as a result of the ability of milk to maintain the viability of PDL cells. The recent studies performed by Souza *et al.*^[45] and Moreira-Neto *et al.*^[46] have stated that milk has a better capacity to maintain PDL cell viability as compared to coconut water of which the latter study showed an 80% viable PDL cells after 4 h storage in milk.

A study by Werder *et al.*^[47] concluded that favorable periodontal healing was observed in teeth which had an extraoral dry time of <15 min. External root resorption was the most frequent complication of teeth having extraoral dry time of 15–60 min. Replacement resorption was seen in teeth which had an extraoral dry time >60 min.

In a study by Kinoshita *et al.*,^[48] four out of five teeth replanted within 30 min exhibited some degree of root resorption and thereby showing fair prognosis. One tooth showed unfavorable prognosis due to extensive inflammatory resorption.

Thus, yet again, the study stresses on the importance of a minimum extraoral dry time for better prognosis. The PDL cells of the teeth which were stored in the storage medium were in compromised state due to the extraoral dry time of 30 min or more. However, the wet storage helped in maintaining the viability, thereby decreasing the amount of

resorption that could have otherwise been possibly seen. The tooth which showed extensive inflammatory resorption had extraoral dry time of >1 h and the PDL cells were completely nonviable. No wet storage could bring back the viability of these cells owing to which the unfavorable outcome was observed.

Amount of damage to tooth and supporting structures, emergency treatment, and follow-up period play a role in the prognosis of avulsed tooth. Great importance is attached to frequent follow-up visits in case of severe trauma to teeth, such an avulsion of immature teeth. Many complications, including pulp necrosis, replacement, or inflammatory resorption, may occur and may be anticipated.^[6,49-54]

CONCLUSION

Based on the moderate level of evidence available to assess the prognosis of replanted avulsed permanent incisors by clinical and radiographic evaluation, it is fair to conclude that the prognosis of the replanted teeth was the best when the extraoral dry time was <15 min due to viability of the PDL cells.

Teeth which were stored in osmolality-balanced media such as HBSS, saline, and milk showed better prognosis as they helped to maintain the viability of the of the compromised PDL cells. Furthermore, the replanted teeth with immature root development showed continued root development with normal PDL membrane or complete pulpal space obliteration indicative of a better prognosis over the replanted mature teeth which more often showed resorptive changes postoperatively.

Limitations

Complete matching of the samples would not have been possible at the start of the included studies due to different clinical scenarios of children reporting with avulsed permanent incisors and patient response toward the treatment.

Short periods of evaluation and follow-up should not be indicated to assess the prognosis of replanted teeth, and hence, studies having a follow-up period <24 months were excluded.

As the clinical scenarios are different for every case of avulsion, it is not possible to follow a particular treatment protocol that can help in determining the outcome of the replanted tooth.

The prognosis of the replanted teeth also depends upon factors such as the extraoral dry time, storage medium used, and stage of root development. These factors cannot be standardized, can be subjective, and not under the clinician's control.

In addition, data searched for this systematic review were limited to less number of electronic databases and articles published in English language only.

Future implications

More number of case reports and case series on replanted avulsed permanent incisors having an extraoral dry time of <60 min and having at least 24-month follow-up period stored in a suitable, economical, and widely available storage

medium and using stem cells,^[55] platelet-rich fiber, and osteogenic proteins in humans for the regeneration of PDL needs to be carried out so as to understand and improve the prognosis of the replanted tooth.

This data will be helpful for the clinicians in better handling of these emergency procedures in their clinical practice.

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Conflicts of interest

There are no conflicts of interest.

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