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Letter to the Editor

Is anti-resorptive regenerative therapy working in case of replantation of avulsed teeth?

In three recent publications by Pohl et al. (2005) it was proposed to make significant changes in the presently used treatment strategy for tooth avulsions (1–3). It was argued that such changes might optimize periodontal ligament healing and tooth survival after replantation (1–3). These conclusions came out of a study based on 28 replanted human teeth with a follow-up period ranging from 5 months to 8 years. The authors are to be complemented for a very detailed study with precise documentation of treatment details and healing outcomes. However, these articles suffer from methodological shortcomings that make it doubtful whether the conclusions are reliable. In the following, a critical analysis will therefore be made on various issues of this study.

Design of the study

The most significant shortcoming of this study is the lack of a control group of conventionally managed avulsed teeth (i.e. immediately replanted teeth without extra-oral root filling). Instead, all 28 teeth were treated according to a combination of five methods proposed to prevent or reduce root resorption activity.

1 Extra-alveolar resection of a significant part of the apex (to remove the most resorption-prone part of the tooth).
2 Extra-alveolar root filling in the form of a titanium post cemented in the enlarged root canal to prevent inflammatory resorption.
3 Placement of the tooth for a minimum of 30 min in a tissue culture medium (to condition the periodontal ligament).
4 Topical application of Emdogain® (a periodontal ligament regenerative medium that has been demonstrated to work in regenerative procedures in the marginal periodontium).
5 Systematic administration of antibiotics (tetracycline).

Various combinations of these five methods were used, a fact that makes it very difficult, if not impossible, to analyze any separate effect of the procedures. There was no attempt to ramdomize the use of these five methods. Furthermore, no control group was established where replants were performed using conventional methods.

Criteria for healing

Standard healing criteria were used (i.e. functional healing, replacement resorption and inflammatory resorption). All together, only nine teeth were found to exhibit functional healing. Unfortunately, teeth with just 5–6 months of observation were included in the analysis, an observation period that is too short to eliminate the possibility of late periodontal ligament (PDL) healing complications especially ankylosis. In a previously published study of about 400 replanted teeth, about one-third of all replanted teeth showed clinical and/or radiographic signs of root resorption later than 6 months (4). Similar results have also been reported in a prospective study of 50 replanted teeth (5). To be on the safe side in diagnosing functional healing (i.e. no root resorption) a minimum of 1 year should have been used.

General healing outcome

Functional healing was registered for nine of 28 replanted teeth (approximately 25%) and this was considered optimal. However this healing rate does not differ significantly from previous studies from other authors using conventional replantation methods and cited in the study (1, 4–6; Table 1).

The 5 year survival of the replanted teeth was about 58% for mature and 23% for immature roots after 5 years (3) and this is actually much lower than a previous study using conventional methods where 5 year survival for immature root development was 75% for mature and 65% for immature root development (7).

Table 1. Rates of healing after replantation

Reference	No. of teeth	Favorable healing [*n* (%)]	*P*-value (chi-square + Yates correction)		
Pohl et al. (1–3)	28	8 (25)	0.46		
Andreasen & Hjörting-Hansen (6)	110	22 (25)		0.70	
Andreasen et al. (4)	400	94 (24)			0.67
Boyd et al. (5)	50	18 (36)			

Effect of 'conditioning' the PDL on the root surface

This concept originally arose because of a finding in a clinical study on replanted teeth published by Cvek et al. (8), who found that 30 min storage in saline before replantation tended to improve PDL healing after replantation, however, this difference was not significant. A later clinical study in humans, using paired controls, did not support this finding (4). Likewise, animal experiments with 30 min drying with or without conditioning for extra 30 min in saline did not influence healing (9). Furthermore, placing teeth in a tissue culture medium for 5–14 days after a drying period of 60 min did not improve PDL healing (10). Likewise conditioning the root surface with Emdogain® also failed in a recent clinical study (13). Therefore, the concept of pre-replantation conditioning should be considered speculative and of little benefit. Another consideration is that conditioning will prolong the extra-oral time and thereby increase the likelihood of ankylosis [such an effect has actually been demonstrated in monkeys (11) and in humans (4, 12)].

In the present study, conditioning for a minimum of 30 min with a mixture of tissue culture media and sometimes followed by application of Emdogain® renders it impossible to separate the effects of these two media. Furthermore, the rationale for the application of Emdogain® (presumably used in an effort to regenerate PDL) in conjunction with a retrograde titanium root canal post (that may integrate with the adjacent alveolar bone) placement is unclear and seemingly contradictory. The effect of conditioning was performed in a separate analysis of groups of teeth, which had different length of dry and wet extra-oral periods. In this analysis, cases with more than 20 min dry period and <60 min dry storage and 35 min non-physiologic wet storage anti-resorptive regenerative therapy (ART) was tested for its effect and the following distribution appeared.

	Healing (FH)	Resorption (RR) + (IRR)
−ART	0	8
+ART	3	5

It is indicated that a chi square test (uncorrected) with a calculated *P*-value of 0.06 (one sided). However, in a 2 × 2 table with one cell having an expected value <5, a chi square test is not reliable. Instead, a two-tailed Fischer's exact test should have been employed as both improvement and deterioration of PDL healing could be expected. Such a test applied to the figures actually shows a *P*-value of 0.20 (double sided).

Of similar concern is that one of the three cases in the ART group had only 6 months observation; in fact if that tooth shows a later ankylosis, the table changes to the following:

	Healing	Resorption
−ART	0	8
+ART	2	6

This implies a *P*-value of 0.46 (Fisher's exact test, double sided).

In the groups with more than 60 min drying (hopeless group) no teeth avoided root resorption so that ART did not change the healing in this group. In the non-compromised group (i.e. teeth with less that 20 min drying), optimal healing was found in all cases and only half of these had ART treatment (five cases). Thus healing took place irrespective of ART and the frequency of healing found in this group is very much like that found in other studies for teeth with very short extra-oral periods (4).

In summary, the proposed ART could not be demonstrated to favor healing in the *not compromised group*. In the *compromised group* an effect could not be proven and in the *hopeless group* there was no effect whatsoever.

Effect of non-physiologic media

In the article it is claimed that milk is most likely a non-physiologic media as most cases developed root resorption. An analysis of the figures hardly supports this statement. Six teeth were stored in milk and among those, two had an extra-oral storage time of 90 min, which will without any doubt doom them to resorption irrespective of storage media. Four teeth were found in the compromised group and one of these healed at a ratio that is not too different from the remaining teeth in this group, where only two of 12 showed healing.

Effect of the titanium post

From the present data there is no doubt that the use of a titanium post calibrated to the enlarged root canal served as an effective root filling as very few cases of inflammatory resorption were found. What is of concern is whether the use of titanium as a supplement for a root tip would invite to ankylosis either by injury inflicted upon the root surface during insertion or by osseous integration phenomenon or titanium. The whole principle of titanium implants is naturally osseous integration and so the question arises whether ankylosis could actually start by osseous integration of the titanium post.

Summary

In conclusion, the findings in this study have in our opinion not brought safe evidence that this radical approach can change the general dubious outcome of replantation of avulsed tooth as long as neither the resorption pattern or tooth survival were optimized in comparison with other studies using a conventional approach. However, the authors should be complimented for their attempt to improve healing in avulsion cases and it is hoped that different treatment approaches are tested in a more systematic way in the future.

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