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Emdogain® does not prevent progressive root resorption after replantation of avulsed teeth: a clinical study

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Abstract – Emdogain® has been shown in clinical and experimental studies to promote regeneration of all periodontal tissues: cementum with anchoring fibres, a functional, periodontal ligament and alveolar bone in connection with treatment of marginal periodontitis.The intention of this study was to analyse whether this regenerative capacity upon the periodontal ligament also worked in a trauma situation where a significant number of PDL cells have been eliminated because of unphysiologic storage or actual damage during avulsion or replantation. Furthermore if ankylosis sites already established because of earlier replantation after avulsion could be surgical removed and application of Emdogain® could revert the ankylosis stage to a normal PDL situation. The first treatment situation was tested in seven patients with a total of 16 avulsed teeth with varying time of extra oral storage. The teeth were extra-orally endodontically treated and the root and socket covered with Emdogain® before replantation. All teeth demonstrated subsequent ankylosis, primarily diagnosed by a percussion test. The second treatment situation where an ankylosis was already established constituted of seven patients with a total of 11 teeth because of previous replantation after avulsion. These teeth were all extracted, the ankylosis sites removed and the root and socket treated with Emdogain®. After 6 months all teeth showed recurrence of ankylosis. It is concluded that Emdogain® was not able to prevent or cure ankylosis.

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Key words: Emdogain®; root resorption; tooth ankylosis; tooth avulsion; tooth replantation

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Replantation of teeth has a doubtful long-term prognosis because of the resorption and more than half of the teeth are eventually lost because of ankylosis or inflammatory resorption (1, 2). The most frequent cause of root resorption is the loss of vitality of the periodontal ligaments (PDL) a phenomenon, which is very dependent on length of extra-oral time and type of storage wet or dry (3). Subsequent to replantation, infection related resorption is very frequent. In this case the initial resorption has penetrated cementum and exposed dentinal tubules and toxins from bacteria present in the dentinal tubules and/or the infected root canal are transmitted via the exposed tubules to the PDL. The result is continuation of the osteoclastic process on the root and an associated inflammation in the PDL leading to resorption of the lamina dura and adjacent bone. This process will usually continue until the root canal is exposed (2). If proper endodontic treatment is carried out whereby bacteria are eliminated from the root canal and the dentinal tubules the resorptive process will be

arrested and the resorption cavity filled with cementum or bone according to the type of vital tissue found next to the resorption site, being either PDL or bone marrow derived tissue (2, 3).

In case of moderately sized injuries (1–4 mm^2) an initial ankylosis is formed. However, this can later be replaced with new cementum and PDL if the tooth is allowed to functional mobility by the use of a semi-rigid splint or no splinting at all (4, 5). In case of larger injuries (>4 mm^2) an ongoing ankylosis will develop. This means that the tooth becomes a part of the surrounding bone and thereby also a part of the remodelling system (5).

In children this process is very active, and in a short span of years (2) it leads to gradual infra-occlusion and arrested development of the alveolar process, and in the end the loss of the tooth. Adults have the advantage that the replacement resorption is significantly slower and the tooth is often in function for 5–20 years (2).

In 1971 it was shown that inflammatory root resorption could be successfully treated by varying endodontic techniques primarily based on calcium hydroxide (6). However, the treatment of ankylosis has in spite of numerous experimental approaches not been successful. Topical fluoride treatment has been used on teeth of adults with an extended extraoral period in order to protract the resorption process. In cases with extensive extraalveolar dry storage the use of fluoride treatment may double the tooth survival time (7). The reason for this is supposed to be incorporation of the fluoride in the cementum surface whereby osteoclastic activity is slowed down.

A concept of preventing ankylosis has recently been forwarded that applicating of a medium to the root surface which favours regeneration of injured parts of the PDL may prevent ankylosis (8). In 1992 such a product was marketed named Emdogain® (BIORA AB, Malmö, Sweden). This is an enamel product, which has been developed with the purpose of regeneration of the lost parts of the periodontium as it occurs in marginal periodontitis. When this product is applied to the root surface the amelogenin-rich protein matrix precipitates out of the solution and assembles into an insoluble layer on the root surface that promotes the attachment of mesenchymal cells. These cells produce new matrix components and growth factors that participate in the recreation of a new periodontal attachment. At the same time Emdogain® inhibits epithelial cells growth that could interfere with the regenerative process (8).

As a replanted tooth usually has areas of lost or destroyed PDL, Emdogain® has been considered a treatment choice to optimize PDL healing and avoid ankylosis. An experimental study in dogs where extracted teeth were replanted with varying drying time showed that the presence of ankylosis was significantly less frequent in the group treated with Emdogain® especially after 12 weeks compared with the control group. However ankylosis still existed although to a lesser degree in the experimental group (9).

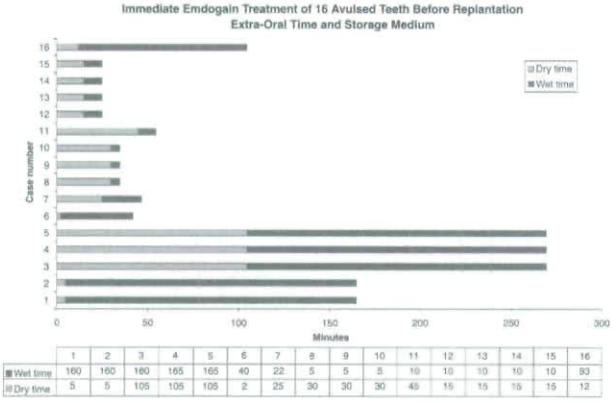
A clinical study was carried out by Filippi et al. in 2001 whereby replanted ankylozed teeth in children were extracted an intentionally reimplanted with the root covered with Emdogain® after being endodontically treated and having 20–50% of the apex resected (10). The removed part of the root was substituted by a titanium post. After a mean follow-up period of 6.3 months all teeth were in full function and with mobility within normal range. In a subsequent follow-up study of 16 previously ankylosed teeth with an average observation of 15 months, 11 teeth showed no sign of ankylosis (11). In a recent case report, an avulsed maxillary lateral incisor which had been found stored dry for an hour and then placed in Hank's Balanced Salt Solution for 30 min was stripped of all remaining periodontal ligament cells by pumice and a rubber cup in a slow speed handpiece. Emdogain® was applied to the root and replanted into a clot-free socket. After a follow-up period of 3 months no early signs of rejection, root resorption or ankylosis could be detected (12). The short observation period cannot exclude that ankylosis will occur at a later time.

The purpose of the present study was to analyse the effect of Emdogain® upon the two following treatment situations:

1 Will an avulsed tooth benefit from root surface and alveolar socket treatment with Emdogain® in relation to periodontal ligament healing.
2 Will an already established ankylosis in a replanted tooth benefit from extraction of the tooth and removal of the ankylosis sites and subsequent treatment of the root surface and the socket with Emdogain® before replantation.

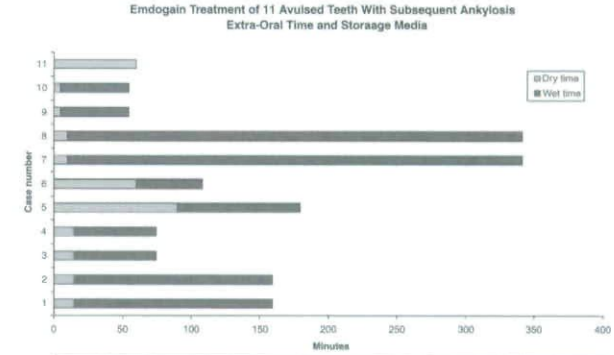
Material and methods

The present study was performed at the Trauma Centre of the University Hospital of Copenhagen, Denmark. One group of patients had Emdogain® treatment for the avulsed teeth within 24 h. This group consisted of seven patients with a total of 16 avulsed teeth. The mean age was 12.4 years (range 8.5–17.6 years). The extraoral storage varied from 25 to 270 min and most of the avulsed teeth had undergone dry storage as well as wet storage from 40 to 270 min and most of the avulsed teeth had undergone dry as well as wet storage (Fig. 1). The replantation was performed under local



	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Wet time	160	160	160	165	165	40	22	5	5	5	10	10	10	10	10	90
Dry time	5	5	105	105	105	2	25	30	30	30	45	15	15	15	15	12

Fig. 1. Extra-oral time and storage media of 16 avulsed and later replanted teeth.



	1	2	3	4	5	6	7	8	9	10	11
Wet time	145	145	60	60	90	49	332	332	50	50	0
Dry time	15	15	15	15	90	60	10	10	5	5	60

Fig. 2. Extracted teeth and storage media of 11 replanted and subsequently ankylosed teeth.

anaesthesia. The Emdogain® treatment was either performed at the time of initial replantation at the Trauma Centre, or the following day in the Department of Maxillo-Facial Surgery at the University Hospital after initial replantation at the Trauma Centre.

The treatment of the teeth consisted of extraction if already replanted followed by an extra oral retrograde root canal treatment using gutta-percha points and IRM® as sealer after mechanical preparation and rinsing of the root canal with physiological saline. The root tip was smoothed with a scalpel blade. During the entire treatment the root surface was kept moist with saline. Then Emdogain® was applied directly to the root surface and into the saline rinsed alveolar socket. The tooth was then replanted, stabilized and splinted for 7 days using a semi-rigid splint (Protemp®, 3 MEspe, Seefeld, Germany). A radiograph was taken immediately upon replantation using a standardized technique (3). Penicillin was administered for 4 days.

The other group of patients had Emdogain® treatment of replanted teeth with ankylosis already diagnosed by a high percussion tone (Fig. 2). This group consisted of seven patients with a total of 11 teeth. The mean age was 12.7 years (range 8.1–15.1 years). The treatment consisted of extraction and subsequent removal of the ankylosis sites on the root surface with a scalpel and using binoculars with a magnification of 5×. If the tooth was not already endodontically treated an extraoral retrograde root canal treatment was performed using gutta-percha points and IRM® (Dentsply, DeTrey, Germany) as sealer after mechanical preparation and rinsing of the root canal with saline. The root tip was smoothed with a scalpel blade. During the entire treatment the root surface was kept moist with saline. Emdogain® was applied directly to the root surface and into the saline rinsed alveolar socket. The tooth was then replanted, stabilized and splinted for 7 days using a semi-rigid splint (Protemp®).

At the onset of general anaesthetics three patients were administered penicillin.

When the splint was removed after 1 week in both groups. The patients then entered a follow-up program at 3 weeks and 2, 6 and 12 months after replantation. At each control a clinical examination was carried out with special emphasis on the result of a percussion test i.e. normal percussion tone or metallic, ankylotic. Furthermore a radiograph was taken using a standardized procedure with a film holder (1–3).

Results

In the group of 16 immediately replanted teeth treated with Emdogain® before repositioning ankylosis occurred in 50% after 2 months and 59% after 4 months. After 12 months ankylosis had occurred in all teeth (Figs 3 and 4).

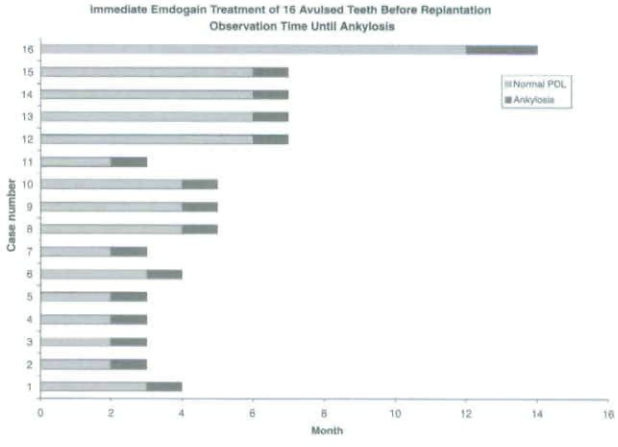


Fig. 3. Observation time until ankylosis of 16 avulsed teeth treated with Emdogain® before replantation.

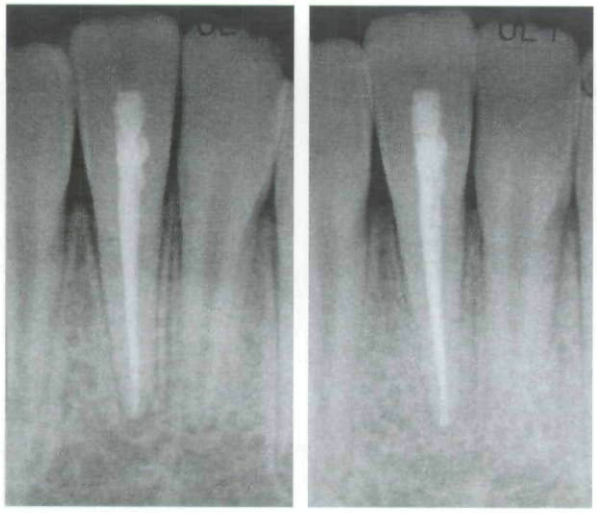


Fig. 4. Immediate treatment with Emdogain® of an avulsed and later replanted central mandibular incisor. Ankylosis was detected after 2 months.

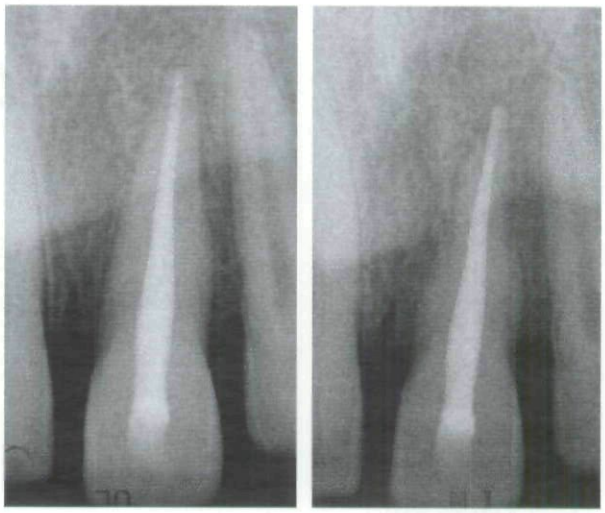


Fig. 6. Emdogain® treatment of a central incisor with known ankylosis. The tooth was extracted and treated with Emdogain®. Ankylosis was detected after 2 months.

In the group of 11 teeth with ankylosis diagnosed prior to extraction and replantation after Emdogain® treatment, ankylosis had occurred in 36% after 1 month by 2 months 72% were ankylosed and by 4 months all teeth were ankylosed (Figs 5 and 6). As it appears from Fig. 2 there was no relation to time of new ankylosis in regard to the length of the extraoral period and the type of storage medium.

Discussion

It is known that cementoblasts or cementoblast-near cells have an ankylosis protecting nature (5). The theory behind the use of Emdogain® is that it promotes the regeneration of cement, PDL fibres and bone (8). This effect has been demonstrated in experimental and clinical studies where Emdogain® has been applied in marginal periodontitis cases to an injured or necrotic root surface (13). In the present study Emdogain® was applied in a severely compromised situation where a minimum of cemental periodontal cells could be expected to be alive because of drying or mechanical injury. The negative result of Emdogain® in this situation seems to indicate that there must be a critical number of PDL cells alive before any protection can be established against the development of ankylosis. The present negative effect of Emdogain® upon healing of teeth with a compromised PDL is supported by a recent experimental study in dogs (15).

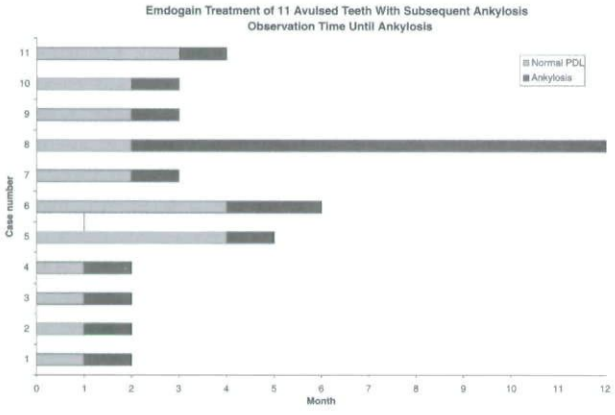


Fig. 5. Observation time until new ankylosis after Emdogain® treatment of 11 already replanted and subsequently ankylosed teeth.

In the present study a percussion test was used to determine whether the tooth was subject to ankylosis. A high metallic tone implies that the injured tooth is directly connected with the bone. This finding is also confirmed if a finger is placed on the oral surface of the tooth to be tested. It is possible to feel the tapping of the instrument on a tooth with a normal PDL. In the case of ankylosis percussion cannot be felt through the tooth tested. The reliability of a percussion test has been verified by an experimental study (14). The method of using radiographs in determining whether there is an ongoing ankylosis process is not sensitive enough in the earlier phases of ankylosis and may explain some earlier positive effects of Emdogain® upon healing after replantation (10–12).

As seen in the present study the application of Emdogain® in order to prevent or cure ankylosis was not successful in any case of the avulsed and replanted teeth. It is therefore very questionable

whether Emdogain® has any particular role in treatment of avulsion injuries.

This study, however, leaves the question whether Emdogain® delays the progress of replacement resorption (ankylosis). Such a study is now in progress.

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