

EMDOGAIN

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MEMBER PRESENTATION

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What is Emdogain?

- Enamel Matrix Derivative (EMD) + propylene glycol alginate
- EMD is an extract of enamel matrix that contains amelogenins of various molecular weights.

Where does EMD come from?

- EMD is derived from developing teeth germs of 6 month old piglets.

Is EMD safe?

- EMD is porcine derived = immune response is possible.
- Study completed in 2002 (Nikolopoulos Int J periodontics restorative dent) showed that only a slight, non significant activation of immune system occurred during first year following Emdogain tx.

Is EMD safe cont.

- Multiple studies have been completed using EMD in patients with no negative side effects
 - Except two reported cases of external root resorption no evidence of whether EMD caused the resorption.
- No side effects have been found from multiple exposures to EMD.
- Yes – EMD has been shown to be safe for patients.

Emdogain theory

- Attempt to build new periodontium by replicating the tooth forming apparatus present in tooth development. This is accomplished by:
 - Using enamel matrix derivative to form a matrix
 - Matrix mediates formation of cementum
 - Matrix provides foundation for all necessary tissues in a functional attachment.

Histology review

- Amelogenins - a protein found in developing tooth enamel, belongs to a family of extracellular matrix proteins.
- Mesenchymal cells- cells that can differentiate into different types of cells

Terms review cont.

- Cytokine – cell signaling protein
- Desomdontium – periodontal ligament

Process from Straumann (Days)



- The amelogenins form a matrix layer on the root surface. Contact to cells of the healthy part of the desmo-dontium is established
- Proliferation of mesenchymal cells from the healthy part of the desmodontium.

Process cont. (weeks)

- The cells secrete natural and specific cytokines which promote the required proliferation.
- Attraction and differentiation to cementoblasts, begin of formation of the cement matrix in which the desmodontal fibers will be fixed.



Process cont. (months)

- Anchoring of desmodontal fibers in the root surface.
- Filling of defect with newly formed desmodontal tissue
- New alveolar bone grows on the root surface and in the defect gap.



Process cont. (Year)

- Regeneration of the desmodontium; a new functional attachment has been formed.



Straumann Video

http://www.youtube.com/watch?feature=player_detailpage&v=aePpbyonKuU

Emdogain placement

- Full thickness flap- studies used papilla preservation or modified widman flap.
- Debride root surface
- 24% EDTA gel for 2 minutes –
 - Rinse with sterile saline
- Place Emdogain in defect
- Suture closed

Straumann claims

1. Almost doubles the "highly improved" Clinical Attachment Level (CAL) gain (>4 mm) compared to open flap debridement (OFD) alone²
2. Tripled average percent of defect fill from 23% for surgical procedure alone to 74%³
3. Increases root coverage compared to coronally advanced flap (CAF)

Straumann claims cont.

4. Clinical success maintained over at least 9 years⁷
5. Continued improvement of clinical attachment level gain and recession reduction beyond 12 months was shown in a 5 year study⁸
6. Lower complication rate (dehiscence); 6% vs. almost 100% for guided tissue regeneration (GTR)⁹

Straumann claims cont.

7. Better results compared to GTR

8. Better predictability and outcome than GTR and open flap debridement.

1. Tonetti et al. J Clin Periodontology 2002; 29: 317-325 (RCT)

EMD

- 86 patients
- Cal gain 3.1+/-1.5 mm
- Pocket red 3.9+/-1.7 mm

CONTROL

- 86 patients
- CAL gain of 2.5+/-1.5 mm
- Pocket red 3.3+/-1.7 mm

0.6 mm gain CAL and 0.6 mm pocket reduction with EMD over just flap and debridement

Study also showed that EMD increased the predictability of clinically significant results (CAL gains \geq 4 mm) and decreased the probability of obtaining negligible or no gains in CAL (CAL gains $<$ 2 mm).

2. Froum, J Periodontal. 2001

Comparative study

- 23 patients with multiple defects (53 EMD vs 31 Control)
- PD reduction was 2.7 mm greater with EMD vs. controls.
- average CAL gains were 1.5 mm greater EMD vs. control
- average osseous defect fill 2.4 mm greater EMD vs control
- They concluded “The average percent of defect fill after adjusting for crestal bone loss was more than 3 times greater for EMD versus control-treated sites (74% defect fill with EMD versus 23% defect fill for control sites).”

3. Castellanos et al. J Periodontal. 2006

EMD Group (at 12 months)

- 11 patients
- V recessions
from 2.68mm to 0.36mm
- H recessions
from 4.27 mm to 0.77 mm
- keratinized gingiva
from 3.81mm to 4.63 mm

Control (coronally positioned flap) at 12 months

- 11 patients
- V recessions from
2.31 mm to 0.90mm
- H recessions
from 3.68 mm to 1.72 mm
- keratinized gingiva
from 3.31 mm to 3.27 mm

3. Cueva et al. J Periodontal. 2004; 75: 949-956

- 17 patients 58 contralateral sites
EMD vs coronally advanced flaps

EMD had 92.9% root coverage at 6 months

CAF had 66.8 % root coverage at 6 months

Other research for root coverage

Study	CAF + EMD	CTG	CAF only	conclusion
Nemcovsky 70 patients	12 mo 71.7% +/- 16.14% root cov	12 mo = 87.0% +/- 12.22% root cov		CTG superior
Abolfazli -12 pts bilateral sites	24 months - 3.33±0.30 mm of root coverage	24 months - 4.5 ± 0.28 mm root coverage		CTG better long term results
Haghighati - 11 patients 31 teeth	24 weeks 50.24% root coverage	24 weeks 65.82% root coverage		CTG superior, but EMD easier
Del Pizzo 15 pts, bilateral sites	24 months - 90.67% root coverage Total root cov = 73%		24 months – 86.67% root coverage Tot rt cov = 60%	No sig difference

Sources for previous table

Nemcovsky CE, J Periodontol. 2004 Apr;75(4):600-7, A multicenter comparative study of two root coverage procedures: coronally advanced flap with addition of enamel matrix proteins and subpedicle connective tissue graft.

Abolfazli , Med Oral Patol Oral Cir Bucal. 2009 Jun 1;14, Connective tissue graft versus EMD

Haghighati, Journal of Dentistry, Tehran University of Medical Sciences, Tehran, Iran (2007; Vol: 4, No.1, Clinical Comparison of Subepithelial Connective Tissue Grafts and Coronally Advanced Flaps with Emdogain in the Treatment of Gingival Recessions

Del Pizzo, J Clin Periodontol. 2005 Nov;32(11):1181-7. Coronally advanced flap with or without enamel matrix derivative for root coverage: a 2-year study.

4. Sculean et al. Int J Periodontics Restorative Dent. 2007

- 38 patients, 4 different treatment groups
- Evaluated pre surgery at 1 year & at 10 years
 - Results shown at 1 and 10 years respectively (CAL gain)
- EMD alone - 3.4+/-1.0 mm and 2.9+/-1.4 mm
- GTR - 3.2+/-1.4 mm and 2.8+/-1.2 mm
- EMD+GTR - 3.3+/-1.1 mm and 2.9+/-1.2 mm
- OFD - 2.0+/-1.2 mm and 1.8+/-1.1 mm

5. Heden et al. J Periodontol 2006; 77: 295-301

EMD treated site at 1 year

- Initial 114 patients
- CAL gain 4.3mm
- PD reduction 4.9 mm
- **Increase** in recession
0.6mm

EMD treated site at 5 years (additional changes)

- Final 82 patients (102 sites)
- Cal gain 1.1 mm
- PD reduction 0.3mm
- **Decrease** in recession
0.8mm

Cochrane systematic review

Esposito, Eur J Oral Implantol. 2009 Winter;2(4):247-66.

Enamel matrix derivative (Emdogain) for periodontal tissue regeneration in intrabony defects.

- Updated through Feb of 2009.
- Selection criteria
 - Randomized Controlled Trials
 - 3mm deep or greater intra boney defects
 - At least 1 year follow up
 - 13 trials met there criteria

9 trials compared EMD vs OFD or placebo

- EMD treated sites tested superior
 - 1.1mm greater CAL
 - .9mm greater probe depth reduction
 - No differences in aesthetic appearances (judged by patient)
 - No differences in tooth loss
 - No difference in recession
 - High rate of Heterogeneity

5 RCT's compared EMD to GTR

- No significant difference in CAL or probe depth reduction
- 0.42 mm more recession with GTR
- More post operative complications with GTR
 - Mainly flap dehiscence over barriers

Biased studies?

- Authors separated studies into high and low risk of bias based on:
 - Allocation concealment
 - Blinding of assessor
 - Reasons for drop outs.
- If any of these criteria were violated than it was placed in a high risk of bias category.
 - i.e. Tonetti study used by Straumann was high risk because assessor knew which cases were EMD.

Results from only low bias studies

- EMD vs. OFD or placebo (propylene glycol alginate)

CAL was only 0.62 mm improved over control

Results Table

Study	EMD	GTR	Control
Heijil 1997 – 34 sites	CAL = 2.2 mm		CAL = 1.7 mm
Okuda 2000 – 16 patients	CAL = 1.72 +/- 1.07 mm PD = 3.00+/-0.97mm		CAL = 0.83 +/- 0.86 mm PD=2.22 +/- 0.81mm
Silvestri 2004 – 98 patients	CAL = 4.1+/-1.8 (41%) PD = 5.3+/-1.9	CAL =4.3+/-1.9 (48%) PD = 5.6+/-1.5	
Tonetti 2002 – 172 patients	Cal = 3.1+/-1.5 mm PD = 3.9+/-1.7 mm		CAL = of 2.5+/-1.5 mm PD = 3.3+/-1.7 mm
Sanz 2004 – 75 patients	CAL = 3.1 +/- 1.8 mm PD = 3.8 +/- 1.5 6% complication rate	CAL= 2.5 +/- 1.9 PD = 3.3 +/- 1.5 mm 100% complication rate	
Rosing 2005 – 16 patients	CAL = 2.01 mm PD = 4.27 mm No sig dif		CAL = 2.16 mm PD = 4.39 mm No sig dif
Crea 2008 – 39 patients	CAL = 2.9 +/- 1.4 mm PD = of 3.5 +/- 1.4 mm Results decreased at 3Y	CAL = 2.5 +/- 1.2 mm PD = 3.5 +/- 1.2 mm Results decreased at 3Y	

GTR results

- Systemic review in 2000 found average GTR results to be:
 - CAL gains 3.7 +/- 1.7 mm
 - 1.1 mm better than OFD alone

Discussion

- High rate of heterogeneity
 - Many differences between studies included in meta - analysis
 - Different skill levels of operators
 - Different antibiotic usage
 - Different flap techniques
 - Wide range of results
 - Different types of barriers used

Discussion cont.

- Contradictory evidence for long term studies
- Heden vs. Sculean studies
 - Heden concluded more CAL gain, continued probed depth reduction on loss of recession with time
 - Sculean concluded that there was a slight backslide with time (about 10%)
 - Bottom line – EMD results are maintained over time

Discussion cont.

- CAL and PD is improved over OFD
 - 1mm improvement (double may be a stretch)
 - The study Straumann uses only shows an average difference in about .6mm or about 20%
 - Less success when high risk of bias studies removed only .62mm difference.
 - Clinically significant?
 - No evidence that EMD leads to less tooth loss.

Discussion cont

- EMD performs statistically similar to GTR
 - EMD appears to be less technique sensitive
 - Less complications and predictable results
 - However, Majority of studies that showed comparable results also had less than average results for GTR.

Discussion cont.

- It could be argued that GTR has a higher success rate when completed without dehiscence – but it is harder to achieve a complication free surgery with a barrier than with EMD.
- Studies show EMD is most successful in deep narrow defects.
 - Suspected that in order for Gel to work it needs to be in contact with root surface .

Discussion continued

- Variable results for root coverage of CAF or CAF + EMD
 - increased results from using EMD for root coverage may not be clinically significant enough to justify use.
 - More research or meta-analysis needed
- CTG appears to be superior to EMD + CAF

Additional information

- 2 studies showed no significant difference between GTR alone and GTR + EMD
- Heijl – 66% bone defect fill
- Okuda – 20% bone density gain vs -3.94% for control
- Crea – Bone fill GTR 57.0% +/- 21%
Bone fill EMD 50.5% +/- 19%

Cost

3 X .3mL syringes with 24% EDTA (prefgel) \$495
single tooth on a single patient

3 X .7mL syringes with prefgel \$725
3 teeth on a single patient

Conclusion

- Is Emdogain the “cure all” to periodontal surgery?
 - No – results are not always clinically significant
 - Is potentially .6 mm of CAL gain worth \$165
- Is Emdogain worth trying?
 - Yes – clinical research supports that Emdogain can improve results

Questions?