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ANIMAL STUDY OF APPLICATIONS OF HYALURONIC ACID FOR DENTAL IMPLANT: A SYSTEMATIC REVIEW

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Introduction

Dental implants with osseointegration methodology was introduced in the 1980's to replace a missing tooth have the success rate of up to 95%. Hyaluronic acid (HA) is naturally present in human and animals, has been widely used in medical and pharmaceutical field especially for wound healing, tissue regeneration and skin repair. Due to high water-retaining effect, it is widely used in dermatology and cosmetics, such as in many moisturizing, skin protecting, and anti-aging products. In dentistry, HA is commonly used for oral ulcer and this study is done to see the applications of HA for dental implants, with focus on animal study.

Objective

This study aims to review at the current literatures about application of hyaluronic acid in dental implant treatment with a focus on animal studies.

Methodology

A search in the PubMed, Science Direct and Cochrane databases was conducted in May 2022 using the keywords "hyaluronic acid", "hyaluronan," and "dental implant." according to PRISMA Guideline

Results

The literature search identified 1018 articles, and thirteen animal studies were selected in this study. Two main groups of applications: dental implant surface treatment and used in bone graft/membrane material.

Discussion

HA is a versatile molecule that has vast medical applications. There are already several commercially available HA-based products available in dentistry, such as Gengigel and Aftamed, which is used to treat oral ulcer. However, the application of HA for other types of dental treatments is still relatively new.

HA have been successfully used as an adjuct method in dental implantology by having it as surface treatment material, carrier for other material, as well as in bone graft material and the membrane useful for implant surgery procedures.

Conclusion

Overall, there are encouraging results regarding the use of HA in dental implant therapy from the animal study that can be progressed into human trials.

Author	Animal	Study method	Analysis	Findings
Dental implant				
Stadlinger et al (2012)	Minipig	20 minipig, 120 implants, 6 groups (1) sandblasted, acid-etched Ti, (2) collagen type I, (3) collagen type I + low amount (CS 1), (4) collagen type I +high amount (CS 2), (5) collagen type I + high-sulfated HA (Hya 1), (6) collagen type I + low-sulfated HA (Hya 2). Sample taken 4 and 8 weeks.	histologic and histomorphometric	Significant increase BID in Coll and Hya 2 between 4 to 8 weeks. Significant increase BVD 4 to 8 weeks in Coll and Hya 2. There is a positive effect of a specific collagen–glycosaminoglycan combination on early bone formation
Jiang et al (2013)	Rabbit	30 rabbits, 15 each group implanted with Ti implant treated with Multilayers of cationic lipid/rhBMP-2 plasmid DNA complex (LDc) and anionic hyaluronic acid (HA) or control Ti implant. Sample analysis in 2, 4, 8 weeks.	histomorphometric	The BMP-2 gene coated sandblasted dual acid-etched titanium implants slightly accelerated early bone formation around implants.
Lee et al (2014)	Rabbit	17 rabbits, Ti implant treated with rhbmp2+HA powder gel carrier, HA powder gel and implant only	microCT and histologic	Better osseointegration. HA powder gel as a carrier for rhbmp2
Schulz et al (2014)	Pig	6 pigs, 36 implants inserted with coll/sHA1D6s and coll/sHA1 and control	histologic and histomorphometric	aECM coatings containing low sHA increase peri-implant bone formation around dental implants in maxillary bone compared to controls in the early healing period
Korn et al (2014)	Minipig	Thirty-six screw-type, total of 6 minipigs. Three surface states were tested: (1) uncoated control (2) coll/CS (3) coll/sHya.	histologic and histomorphometric	highest bone volume density in coll/sHya, followed by coll/CS and control
Pan et al (2016)	Beagles	4 beagles with 24 implants, implanted with dental implants coated with dried or wet rhBMP-2-HA hydrogel, simple dip or control	histomorphometric	simple dip coating has highest bone area.
Boot et al (2017)	Rabbit	18 titanium rods, uncoated, coated with hydrogel and hydrogel+vancomycin	microCT and histologic	no effect on the volume or timing of bone apposition near the implant, and did not induce an inflammatory reaction.
Yazan et al (2019)	Rabbit	10 rabbits, each groups. HA gels in cavity after implant insertion	histomorphometric	No significant different, but more bone formation
Bone graft/ Membrane				
de Brito et al (2012)	Rat	32 rats with bone defect, treated in four groups, 1. 1%HA, 2. 1% HA and ACS, 3. blood clot, 4. ACS.	histology and histometric	1% HA gel associated with a collagen scaffold can improve new bone formation in critical-size defects.
Subramaniam et al (2016)	Rat	48 rats with periodontal bone defect undergone bone augmentation. hydroxyapatite, calcium sulfate hemihydrate, and HA laden collagenase (HAP/CS/HA-Col) as a bone substitute for alveolar bone regeneration. 3 groups, HAP/CS/HA-Col, HAP/CS/HA, porous HAP	microCT and histologic	improved bone formation in HA with collagenase
Eliezer et al (2019)	Diabetic rat	16 diabetic rat and 16 control, implanted with CM immersed with HA	histomorphometric	HA maintained the membrane thickness and residual collagen in the diabetic group
Kang et al. (2020)	Rabbit	Femur defect grouped into collagen, HA-Gelatin/TCP, and HA-Gelatin/TCP/BCP groups.	Micro-CT, histology, immunohistochemistry.	HA-Gelatin/TCP/BCP group showed excellent hemostatic property, promote bone regeneration
Yilmaz et al. (2021)	Sheep	6 sheep, 60 iliac defects experimented into control and test. Test group of autologous bone+HA and HA only.	Histology and histomorphometric	Control group with autologous bone+ membrane has the highest bone formation, followed by autologous bone+ Hyalonect

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