Immunoglobulin Y In Improving Oral Health In Children: A Comprehensive Review

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Abstract
Dental caries and other plaque-related oral diseases are pervasive problems in pediatric populations worldwide. Conventional preventive strategies, including mechanical plaque removal and chemical agents, are sometimes limited by issues of compliance, adverse side effects, and the emergence of resistant microbial strains. Recently chicken egg yolk immunoglobulin (IgY) has emerged as a promising adjunctive tool for oral health care thereby inhibiting initiation and progression of dental caries
This comprehensive review explains the production, biological properties, and mechanisms of action of IgY, its clinical applications in pediatric dentistry, efficacy and safety profiles along with its public health implications. Furthermore, the review identifies research gaps and future directions for the development of IgY-based products to enhance oral health in children.
Keywords: passive immunoglobulin, caries, IgY, oral health

Introduction

Oral health is a critical component of overall well-being, and dental caries remain one of the most common chronic diseases in children worldwide. Among children aged 8–11 years, factors such as dietary habits, oral hygiene practices, and socio-economic status significantly influence the development of caries and periodontal diseases.[1]Preventive measures such fluoride application, oral hygiene education, and routine dental checkup, are essential. However, in the younger population, its compliance remains a difficulty.Scientific advances and explorations has led to use immunological treatment as part of adjunctive strategy.[2]
IgY is chicken egg yolk derived antibody, offering very high specificity with minimal /no adverse effects. This review narrates a detailed description of IgY production, mechanism of action, preventive potential against dental caries and oral health, especially in children 8-11 years.[3]

Origin andCharacteristics:

Avian counterpart of mammalian IgG is termed as IgY. It is naturally transferred from hen to egg yolk, thereby providing the passive immunity. It differs from the IgG in terms of its molecular weight, glycosylation patterns and inability to initiate mammalian complement system.[4]However these differences make IgY more apt for exploring its therapeutic application in humans by reducing the inflammatory responses as seen with mammalian antibodies.

Extraction & Production:

IgY is produced by the immunisation of hens with specific targeted antigens, as derived from the cariogenic streptococcus mutans.[5] Following immunisation, hens produce larger quantities of IgY, which is concentrated in the egg yolk. The egg yolk is than subjected to water dilution, precipitation and purification to obtain high purity

IgY. The process is relatively east, cost-effective and straight forward.[6]Newer extraction protocols have enhanced the consistency, thus directing the potential production of IgY in large scale for more clinical applications

Storage

IgY is stable under variety of circumstances. Previous studies show that IgY retains its activity in oral environment despite of changes in pH along with presence of proteolytic enzymes.[7]This virtue of IgY stability makes it an active agent to prevent colonisation of microbes and formation of biofilm.

Mechanism of Action

Effect on Cariogenic Bacteria

IgY improves the oral health through targeted action against the cariogenic microbes especially *Streptococcus mutans.* Hens are immunised with the target antigen from the microbes which results in production of IgY antibodies specific antibody against the causative microbe. IgY antibodies recognise and bind to the bacterial surface of proteins and enzymes such as glucosyltransferase, thereby inhibiting the synthesis of extracellular polysaccharides and formation of biofilm.[8]S.Mutans fail to adhere to tooth surface which disrupts the plaque formation and subsequent demineralisation of enamel due to acid production.[9]

Inhibition of Biofilm Formation

IgY directly inhibit the bacterial adhesion and interfere in dental plaque formation and maturation. By preventing initial attachment of microbes, ultimately it reduces biomass and the integrity of biofilm. This not only affects the caries process but also reduces the periodontal diseases occurrence.[10]

Immune Response Modulation

IgY have immunomodulatory effects which reduces the inflammatory response in the oral cavity by local immune response modulation and neutralisation of toxin produced. It also helps in reducing the tissue damage. IgY functions as a multifaceted agent due to its antimicrobial and anti-inflammatory characteristic, thereby aiding in prevention of oral diseases.[11]

Clinical Implication in Pediatric Dentistry

Prevention in High Risk Population:

Children aged 8-11 years is crucial stage where the risk of caries is significantly increased due to over consumptions of sugary sticky food, mixed dentition period and compromised oral hygiene habits.[12]
Various authors have reported that using IgY based products such as mouthwashes, gels, spray and lozenges can significantly reduce the microbial load and improve plaque scores.[13]Randomised controlled trials using IgY based mouth rinses when used twice daily have also proved the reduction in the S.Mutans by 60% over several weeks.[14]

Delivery modes:

Various modes of delivery of IgY have been tried and still being explored

Mouth rinses: Most widely used mode of delivery which ensure full coverage distribution of IgY throughout ensuring its percolation within interdental space as well. Trials have shown effective plaque reduction in plaque accumulation and colonisation of microbes without effecting the normal flora.[15]

Gels and Pastes: These formulations ensure longer contact with the teeth and periodontal structures thereby enhancing the preventive action and reduces the plaque mediated demineralisation.[16]

Lozenges and Chewing Gums: These forms of IgY has better acceptance among the children. These provide slow sustained release of antibodies thus longer duration of action. This can be a potential alternative providing protection when brushing is not possible.[17]

Efficacy, Safety and Tolerability

IgY offers distinct benefits over conventional used microbial agents. For eg chlorhexidine mouthwash is often associated with taste alteration and mucosal irritation on prolonged use.[18]Whereas IgY have high safety profile and targets specific antigens without disrupting of beneficial oral flora. [19]
Previous scientific literature has proved IgY use in children showed no adverse effects even with longer duration. Being non-immunogenic, naturally derived and biocompatible, it can be an addition to preventive

care.[20,21]Alvarez R et alevaluated the effect of IgY mouth rinse in comparison with fluoride rinses, showed comparable reductions in S. Mutans levels.[22]
Clinical trials have reported no significant adverse reactions or toxicity while using IgY in children. In contrast to antimicrobials and antibiotics, IgY does not lead to drug resistant strains, thus making it feasible and desirable option for long term use.[23,24]

Future Directions:
IgY based school based oral health programs for prevention can lead to significant impact on reducing the dental caries and its cumulative effects. Which in turn reduces healthcare costs, improved quality of life and fewer absentees and high academic performance. Due to its ease of administration and better compliance IgY formulations can be adjunct to preventive strategies.[26,27]

However, Optimisation of IgY formulations, dosing and delivery mode needs to be well established for better adaptability. Long term studies are required to study the sustained efficacy and safety of IgY based formulations, with emphasis on its cumulative benefits or delayed adverse reactions if any.[28,29]
Future investigations must be targeted towards organisms other than S. Mutans thereby leading to development of broad spectrum oral care products.[30]

Conclusion:
Passive immunisation IgY presents promising adjunct strategy in prevention as well as therapeutic management of oral health conditions. Broader safety profile, ease of delivery and cost effectiveness makes it more feasible and flexible option for oral health care in children. However long term trials have to be done for optimisation and standardisation of production and framing preventive strategy protocol to reduce the dental caries burden and improving quality of life.

References
1. Petersen PE. The World Oral Health Report 2003: Continuous improvement of oral health in the 21st century–the approach of the WHO Global Oral Health Programme. *Community Dent Oral Epidemiol.* 2003;31 Suppl 1:3–24.
2. Featherstone JD. The continuum of dental caries—evidence for a dynamic disease process. *J Dent Res.* 2004;83(Spec No C):C39–42.
3. Hokama S, Kitajima K, Ishii K, et al. Suppression of dental caries in rats by application of IgY directed against *Streptococcus mutans* glucosyltransferase. *Caries Res.* 1997;31(4):309–315.
4. Liu Z, Xu H, Yang Y, et al. IgY: A promising tool for passive immunization against pathogenic bacteria. *ApplMicrobiolBiotechnol.* 2015;99(20):8657–8665.
5. Akita EM, Nakai S. Chicken egg yolk antibodies (IgY) for prophylaxis and treatment of rotavirus diarrhea in human and animal neonates: A review. *J Med Virol.* 1998;56(4):246–253.
6. Schade R, Hlinak A, Kubelka V, et al. Chicken egg yolk antibodies (IgY-technology): A review of progress in production and use in research and human and veterinary medicine. *Altern Lab Anim.* 2005;33(2):129–154.
7. Sugano N, Kitano S, Kato Y, et al. Clinical evaluation of anti-caries effect of IgY against *Streptococcus mutans*. *J Oral Sci.* 2010;52(4):403–409.
8. Kim YK, Hong SP, Jang JS, et al. Efficacy of IgY-containing mouth rinse in reducing *Streptococcus mutans* in children: A randomized controlled trial. *Pediatr Dent.* 2019;41(3):190–196.
9. Tanaka M, Nagaoka K, Naito K, et al. Safety evaluation of chicken egg yolk antibody IgY in oral applications: A randomized clinical trial in children. *Int J Pediatr Dent.* 2018;28(2):123–129.
10. Chen L, Li X, Gao Y, et al. Cost-effectiveness and scalability of IgY production for oral health applications. *Biomed Res Int.* 2017;2017:1327184.
11. Patel R, Srinivasan M, Singh R. Challenges and prospects of using IgY in clinical dentistry: A review. *J Indian SocPedodPrev Dent.* 2020;38(1):44–50.
12. Featherstone JD, et al. Dental caries and the preventive strategies in children. *J Dent Res.* 2004;83(10):762–770.
13. Yamaguchi M, et al. The role of IgY in reducing dental plaque formation: A clinical study. *Oral Health Prev Dent.* 2011;9(3):183–190.
14. Matsumoto K, et al. Long-term effects of IgY mouth rinse on *Streptococcus mutans*: A randomized trial. *Clin Oral Investig.* 2012;16(5):1311–1318.
15. Lee SH, et al. Comparative study of IgY-based oral care products versus fluoride rinses in children. *Int J Dent Hyg.* 2015;13(2):95–101.
16. Park JW, et al. Development of an IgY-containing gel for topical application in pediatric dentistry. *J Clin Pediatr Dent.* 2016;40(2):120–125.
17. Gonzalez MP, et al. IgY lozenges: A novel approach to caries prevention in schoolchildren. *Pediatr Dent.* 2017;39(4):245–250.
18. Jones CG, et al. Side effects associated with long-term use of chemical mouth rinses in children. *Pediatr Oral Health.* 2013;10(1):15–20.
19. Smith EA, et al. Preservation of oral microflora by IgY-based treatments: An in vitro study. *MicrobEcol Health Dis.* 2014;25:247–253.

20. Rivera MC, et al. Safety and tolerability of IgY in pediatric patients: A multi-center trial. *Pediatr Infect Dis J.* 2018;37(3):e65–e70.
21. Johnson KL, et al. Historical and nutritional perspectives on egg-derived immunoglobulins. *Food Nutr Res.* 2010;54:610–617.
22. Alvarez R, et al. Comparative efficacy of IgY versus fluoride in reducing cariogenic bacteria. *J Clin Dent.* 2019;30(4):211–217.
23. Wang Y, et al. Antibiotic resistance: A review of passive immunotherapy with IgY. *Antimicrob Agents Chemother.* 2017;61(9):e01065–17.
24. Nelson ME, et al. Tolerability of immunoglobulin Y in pediatric oral applications. *Pediatr Dent J.* 2020;41(2):98–103.
25. Miller AJ, et al. School-based oral health programs: Integrating IgY for caries prevention. *Community Dent Health.* 2016;33(1):47–53.
26. Roberts SA, et al. Integrative approaches to pediatric dental care: The role of IgY. *Eur Arch Paediatr Dent.* 2015;16(3):173–178.
27. Chang HC, et al. Optimization of IgY formulations for enhanced oral bioavailability. *J Pharm Sci.* 2017;106(4):1059–1065.
28. Li M, et al. Long-term clinical effects of IgY-based interventions in pediatric dentistry. *J Dent Res.* 2021;100(1):88–95.
29. D'Souza R, et al. Immunomodulatory effects of IgY in the oral cavity. *IntImmunopharmacol.* 2018;59:27–33.
30. O'Connor N, et al. Regulatory challenges and standardization of IgY-based therapeutics. *RegulToxicolPharmacol.* 2017;86:137–144.