

Alum as an Adjuvant in Tetanus Toxoid Vaccine

Nazar-ul-Islam^{1*}, Hajra Haneef²

¹N.I.H. Islamabad

²Ex-student of QAU

Abstract— Aluminium hydroxide, Aluminium phosphate and calcium phosphate are used as adjuvant in (TT) vaccine. In this review mechanism, potency, benefits and limitations of alum adjuvant have been discussed.

Keyword— Aluminium hydroxide (Alum/AlOH), Aluminium phosphate (AlPO₄), Calcium phosphate (CAP/CaPO₄), Tetanus Toxoid (T.T), Vaccine.

I. INTRODUCTION

By using adjuvants, quality of vaccines can be enhanced that can selectively excite immunoregulatory responses [3]. Chemical nature of adjuvants is unpredictable [21]. Hundred of materials have been tried as adjuvant and used in realistic vaccination for more than 60 years [17,22]. In human vaccinations aluminum and calcium phosphate, oil emulsions, nanoparticles and molecular assemblies have some use [5,12]. AlPO₄ and AlOH used as an adjuvant in many vaccines licensed by the US Food and Drug Administration [16]. Alum is most commonly used chemical as adjuvant (such as tetanus toxoids) in human and veterinary vaccines also [6,15].

II. MECHANISM

Adjuvants should be selected for routine use as it may have adverse mean of action and alum mechanism is not fully understood [4, 15]. However mode of action of alum adjuvant can enhance both T helper cell 1 as well as T Helper cell 2 cellular response by NLRP3 pathway.6. Alum activates caspase-1 and induce secretion of mature Interleukin-1 β and Interleukin-18 [8].

III. POTENCY

Potency of adjuvants reliant upon the physio-chemical uniqueness and electrostatic forces between adjuvant and foreign agent [1]. One study in murine model showed CAP is more potent than alum and nano particulate adjuvant of CAP would possible to use [3]. While another research showed CAP adjuvanticity is lower or equal to alum [2]. If number of organisms (e.g; pertusis) present in vaccine is less would result in reduced potency [10].

IV. BENEFITS

Authors conclude that alum is competent to provoke a good antibody (Th2) response [6, 14]. Single dose immunization with potent alum adsorbed toxoids is possible and booster immunization with alum toxoids elicit the IgE [9,19]. In vivo purified TT and AlPO₄ adjuvant bring out vascular permeability-increasing and poisonous effects to macrophages [13,18]. CAP is natural constituent of body and enhances an insignificant IgE responses [3].

V. LIMITATIONS

Limitations of alum adjuvants consist of local response, augmentation of IgE antibody reaction, incompetence for some antigens and failure to boost cell-mediated immune (especially cytotoxic T-cell) responses [14,16]. Aluminium salts in vaccines do not cause severe or long lasting undesirable effects [7]. Investigation on adjuvants indicates that alum can be replace with other adjuvant formulations like MF59 emulsion and poly lactide co-glycolide (PLG) [20]. One study on young children showed that vaccination with alum caused significantly more local reactions than plain vaccines [7]. There is haemolytic effect by Ca-gel [18].

REFERENCES

- [1] Gupta,R.K. Aluminium compound as vaccine adjuvants. Advanced drug delivery reviews 1998;32: 155-172.
- [2] Aggerbeck, H. Heron I. Adjuvanticity of AlOH and CaPO₄ in diphtheria-tetanus vaccines—I. Vaccine 1999; 13: 1360-1365.
- [3] He,Q.Mitchell,A.R.Johnson,S.L.Bartak,C.W.Morcol.T . Bell.S.J.D. CaPO₄ Nanoparticle Adjuvant. Clinical and Vaccine Immunology 2000; 7:899-903.
- [4] Vogel F.R. Improving Vaccine Performance with Adjuvants. Clinical Infectious Diseases 2000; 30: 266-270.
- [5] Powell,B.S.Alexander K.Andrianov, Peter C. Fusco. Polyionic vaccine adjuvants: another look at aluminum salts and polyelectrolytes. Clinical and Experiment Vaccine Research 2015; 1:23-45.

- [6] He,P.Zou,Y.Hu,Z.Advances in aluminum hydroxide-based adjuvant research and its mechanism. Human Vaccines & Immunotherapeutics 2015; 11:477-488.
- [7] Jefferson,T.Rudin,M. Pietrantonj,C.D. Adverse events after immunisation with aluminium-containing DTP vaccines: systematic review of the evidence.The Lancet Infectious Diseases 2004; 4: 84-90.
- [8] Li,H.Nookala,S.Re,F. Aluminum Hydroxide Adjuvants Activate Caspase-1 and Induce IL-1 β and IL-18 Release¹. The Journal of Immunology 2007; 178: 5271-5276.
- [9] VERONESI,R.CORREA, A. ALTERIO,D.Single dose immunization against tetanus. Promising results in human trials.Revista do Instituto de Medicina Tropical de Sao Paulo 1970; 12: 46-54.
- [10] BURLAND,W.L.SUTCLIFFE,W.M.VOYCE,M.A.HILTON,M.L.MUGGLETON,P.W.Reactions to combined diphtheria, tetanus and pertussis vaccine: a comparison between plain vaccine and vaccine adsorbed on ALOH. Medical Officer 1968; 2:17-19.
- [11] Grangette,C. Alouf,H.M. Goudercourt,D. Geoffroy,M.C. Turneer,M. Mercenier,A.Mucosal Immune Responses and Protection against Tetanus Toxin after Intranasal Immunization with Recombinant *Lactobacillus plantarum*.Infection and Immunity 2001; 69:1547-1553.
- [12] Siber,G.R.Gupta,R.K. Adjuvants for human vaccines—current status, problems and future prospects. Vaccine 1995; 13: 1263-1276.
- [13] Siber,G.R.Gupta,R.K. Comparison of Adjuvant Activities of AlPO₄, CaPO₄ and Stearyl Tyrosine for Tetanus Toxoid.Biologicals 1994-2002; 22:53-63.
- [14] Petrovsky,N. Aguilar.J.C. Vaccine adjuvants: Current state and future trends. Immunology and Cell Biology 2004; 82: 488-496.
- [15] HogenEsch,H. Mechanisms of stimulation of the immune response by aluminum adjuvants.Vaccine 2002; 20:34-39.
- [16] Baylor,N.W. Egan,W. Richman,P. Aluminum salts in vaccines—US perspective. Vaccine 2002; 20:18-23.
- [17] Lindblad,E.B. Aluminium compounds for use in vaccines. Immunolgy and Cell Biology 2004; 82: 497-505.
- [18] Goto,N. Kato,H. Maeyama,J.I. Eto,K. Yoshihara,S.Studies on the toxicities of Alum and CAP as immunological adjuvants for vaccines 2002; 11: 914-918 .
- [19] Tchavdar L. Vassilev. AlPO₄ but Not CaPO₄ Stimulates the Specific IgE Response in Guinea Pigs to Tetanus Toxoid. Allergy 2007; 33:155-159.
- [20] Singh,M.Ugozzoli,M.Kazzaz,J.Chesko,J.Soenawan,E. Mannucci,D.Titta.F.Contorni,M.Volpini,G.Guidice,G. D. A preliminary evaluation of alternative adjuvants to alum using a range of established and new generation vaccine antigens.Vaccine 2006; 24:1680-1686.
- [21] Gupta,R.K. Relyveld,E.H. Lindblad,E.B. Bizzini,B. Efraim,S.B. Adjuvants — a balance between toxicity and adjuvanticity. _Vaccine_ 2002; 11: 293-306.
- [22] Cox,J.C. Coulter,A.R. Adjuvants—a classification and review of their modes of action. Vaccine 1997; 15: 248-256.