



Title	Immunogenicity of intradermal trivalent influenza vaccine with topical imiquimod: a doubleblind randomised controlled trial
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IMMUNOGENICITY OF INTRADERMAL TRIVALENT INFLUENZA VACCINE WITH TOPICAL IMIQUIMOD: A DOUBLEBLIND RANDOMISED CONTROLLED TRIAL

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BACKGROUND: Imiquimod, a synthetic toll-like receptor 7-agonist enhanced immunogenicity of influenza vaccine in a mouse model. We hypothesised that topical imiquimod before intradermal trivalent influenza vaccination (TIV) will produce similar effect in human.

METHODS: We performed a prospective 1-year follow-up double-blind randomised controlled trial on adults with co-morbidities. Subjects were randomised to one of the three vaccinations: topical 5% 250 mg imiquimod ointment followed by intradermal TIV (IntanzaR15, Sanofi-Pasteur, France), or topical aqueous-cream followed by intradermal TIV, or topical aqueous-cream followed by intramuscular TIV (VaxigripR, Sanofi-Pasteur, France). Patients and investigators were blinded to the type of topical treatment applied. Haemagglutination inhibition (HI) and microneutralisation antibody titres were measured. Primary outcome was day-7 seroconversion rate.

RESULTS: A total of 91 recruited subjects completed the study. The median age was 73 years. On day 7, 27/30 (90%) patients who received imiquimod and intradermal TIV achieved seroconversion against the H1N1 strain by HI, compared to 4/30 (13.3%) who received aqueous-cream and intramuscular TIV ($P<0.001$) and 12/31 (38.7%) who received aqueous-cream and intradermal TIV ($P<0.001$). The seroconversion, seroprotection, and geometric mean titre fold increase were met in all three strains in the imiquimod and intradermal TIV group 2 weeks earlier, and the better seroconversion rate was sustained from day 7 to year 1 ($P\leq 0.001$). The better immunogenicity was associated with less hospitalisation for influenza or pneumonia ($P<0.05$). All adverse reactions were self-limited.

CONCLUSIONS: Pretreatment with topical imiquimod significantly expedited, augmented, and prolonged the immunogenicity of influenza vaccination. This strategy for influenza immunisation should be considered in the elderly population.

Note: The study was published in the *Clinical Infectious Diseases*: Hung IF, Zhang AJ, To KK, et al. Immunogenicity of intradermal trivalent influenza vaccine with topical imiquimod: a double blind randomized controlled trial. *Clin Infect Dis* 2014;59:1246-55.