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The safety, immunogenicity, and acceptability of inactivated influenza vaccine delivered by microneedle patch (TIV-MNP 2015): a randomised, partly blinded, placebo-controlled, phase 1 trial

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Summary

Background

Microneedle patches provide an alternative to conventional needle-and-syringe immunisation, and potentially offer improved immunogenicity, simplicity, cost-effectiveness, acceptability, and safety. We describe safety, immunogenicity, and acceptability of the first-in-man study on single, dissolvable microneedle patch vaccination against influenza.

Methods

The TIV-MNP 2015 study was a randomised, partly blinded, placebo-controlled, phase 1, clinical trial at Emory University that enrolled non-pregnant, immunocompetent adults from Atlanta, GA, USA, who were aged 18–49 years, naive to the 2014–15 influenza vaccine, and did not have any significant dermatological disorders. Participants were randomly assigned (1:1:1:1) to four groups and received a single dose of inactivated influenza vaccine (fluvirin: 18 μg of haemagglutinin per H1N1 vaccine strain, 17 μg of haemagglutinin per H3N2 vaccine strain, and 15 μg of haemagglutinin per B vaccine strain) (1) by microneedle patch or (2) by intramuscular injection, or received (3) placebo by microneedle patch, all administered by an unmasked health-care worker; or received a single dose of (4) inactivated influenza vaccine by microneedle patch self-administered by study participants. A research pharmacist prepared the randomisation code using a computer-generated randomisation schedule with a block size of 4. Because of the nature of the study, participants were not masked to the type of vaccination method (ie, microneedle patch *vs* intramuscular injection). Primary safety outcome measures are the incidence of study product-related serious adverse events within 180 days, grade 3 solicited or unsolicited adverse events within 28 days, and solicited injection site and systemic reactogenicity on the day of study product administration through 7 days after administration, and secondary safety outcomes are new-onset chronic illnesses within 180 days and unsolicited adverse events within 28 days, all analysed by intention to treat. Secondary immunogenicity outcomes are antibody titres at day 28 and percentages of seroconversion and seroprotection, all determined by haemagglutination inhibition antibody assay. The trial is completed and registered with ClinicalTrials.gov, number NCT02438423.

Findings

Between June 23, 2015, and Sept 25, 2015, 100 participants were enrolled and randomly assigned to a group. There were no treatment-related serious adverse events, no treatment-related unsolicited grade 3 or higher adverse events, and no new-onset chronic illnesses. Among vaccinated groups (vaccine via health-care worker administered microneedle patch or intramuscular injection, or self-administered microneedle patch), overall incidence of solicited adverse events (n=89 *vs* n=73 *vs* n=73) and unsolicited adverse events (n=18 *vs* n=12 *vs* n=14) were similar. Reactogenicity was mild, transient, and most commonly reported as tenderness (15 [60%] of 25 participants [95% CI 39–79]) and pain (11 [44%] of 25 [24–65]) after intramuscular injection; and as tenderness (33 [66%] of 50 [51–79]), erythema (20 [40%] of 50 [26–55]), and pruritus (41 [82%] of 50 [69–91]) after vaccination by microneedle patch application. The geometric mean titres were similar at day 28 between the microneedle patch administered by a health-care worker versus the intramuscular route for the H1N1 strain (1197 [95% CI 855–1675] *vs* 997 [703–1415]; p=0·5), the H3N2 strain (287 [192–430] *vs* 223 [160–312]; p=0·4), and the B strain (126 [86–184] *vs* 94 [73–122]; p=0·06). Similar geometric mean titres were reported in participants who self-administered the microneedle patch (all p>0·05). The seroconversion percentages were significantly higher at day 28 after microneedle patch vaccination compared with placebo (all p<0·0001) and were similar to intramuscular injection (all p>0·01).

Interpretation

Use of dissolvable microneedle patches for influenza vaccination was well tolerated and generated robust antibody responses.

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National Institutes of Health.

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