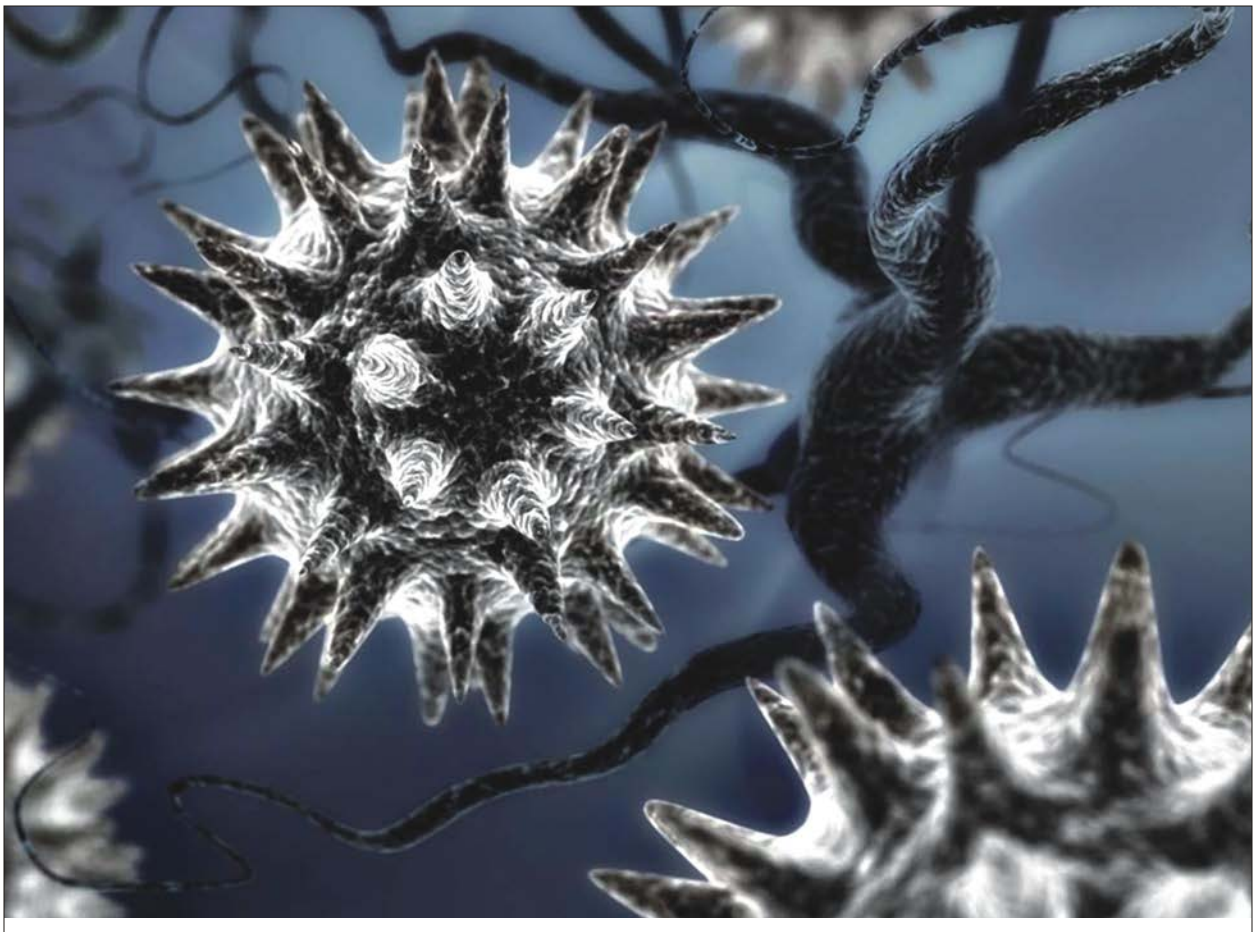

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Serum Antibody Responses after Intradermal Injection of Influenza Vaccine

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Abstract: The present study was Conducted determine the antibody response of an intradermal injection of trivalent inactivated influenza vaccine, with 40% of the usual dose and then to compare with the immunogenicity and safety of usual influenza vaccine, In this randomized control trial, we evaluated the antibody response of intradermal vaccine among 97 cases who were selected randomly from health care workers and then results compared with results in 94 cases of health care workers who were received intramuscular influenza vaccine with usual dose. One hundred ninety one cases with age range of 22-50 years, have been vaccinated by one experienced person then blood samples were evaluated for titers of hemagglutination- inhibition (HAI) antibody before and after injection of vaccine. Also, local and systemic adverse events assessed. Present study showed that there was no significant difference in seroconversion and seroprotection rates after vaccination, between two groups ($p>0.05$). Local reactions (induration and redness) were significantly more common, among recipients of intradermal injections than among recipients of intramuscular injection, but such reactions were mild and transient. We conclude that reduced dose of influenza vaccine given by the intradermal route in healthy adults was safe and immunogenic, similarly to intramuscular injection with usual dose and dose sparing with intradermal injection could be to increase the number of available doses of vaccine.

Key words: Influenza vaccine, intradermal, intramuscular, seroconversion, seroprotection

Introduction

The most effective measure available for the control of influenza is the annual administration of inactivated influenza vaccine (Treanor, 2005). Inactivated influenza vaccine has been shown to be effective in the prevention of influenza A and relatively high efficacy is observed in healthy young people, who were vaccinated intramuscularly with dose of 15 μg of antigens (Belshe *et al*., 2004). In all controlled studies that conducted among young adults, there was a suitable level of protection (70 to 90%), when there was a good antigenic match between the vaccine and the epidemic virus. (Jackson *et al*., 1999). Intradermal admiminstration of antigens is expected to facilitate their exposure to antigens-presenting cells, such as macrophages and dendritic cells, which are present at higher level in skin than in muscle (Janeway *et al*., 1999). Therefore, intradermal vaccination may induce similar serum antibody responses with a smaller quantity of antigen. The intradermal route has been evaluated for rabies and hepatitis B, influenza virus vaccine, (Sabchareon *et al*., 1998; Redfield *et al*., 1985; Belshe *et al*., 2004) previously and the results were different but all studies showed that this route could be immunogenic (Belshe *et al*., 2004; Kenney *et al*., 2004; Brown *et al*., 1977). Intradermal injection of a fraction of the dose of commercial influenza vaccine would be a highy desirable

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dose-sparing strategy if it was found to be as immunogenic as a full-dose intramuscular injection. There is no any study about the antibody response of influenza vaccine in Iran. Therefore, we decided to conducted this study.

Materials and Methods

In this randomized control study, in Zahedan a city in Southeast of Iran, 97 cases of health care workers who, were selected by using rondom number table from Zahedan health centers vaccinated with an intradermal dose 0.2 mL (40% of the standard dose) by an experienced person. Also, we selected randomly 94 cases of health care workers who vaccinated intramuscularly, with an Iranian - icensed influenza vaccine at the standard dose 15 μg in December 2004 (This vaccine was licensed three strain of virus; A/Fujian/411/2002 (H_3N_2), A/New Caledonia/20/99 (H_1N_1), B/shanghai/361/2002). After vaccination, subjects were asked about the painfulness, redness, swelling, induration, at the injection site and fever, headache, myalgia and coryza during three initial days after injection. All 191 subjects were free of obvious health problems before enrollment, as established by a review of their medical history and a clinical examination. Subjects were excluded if they had been taking immune suppressant or other immune modifying drugs within two months before vaccination or were pregnant or lactating. Data on age, sex was obtained using a questionnaire. Blood samples were colleted before and after immunization (on 21-28 days) and then sera that obtained from the subjects were examined by the standard HAI assay. Seroconvertion defined as the four- fold increase in titer of antibody or titers of at least 1:40 after vaccination. Seroprotection defined as a titer of 1:40 or more. Analysis of results were performed with the using of SPSS software version 11.5.

Results

A total of 191 health care workers participated in this study (146 female, 68 male, mean age 24 years, range 22-50 years). Ninety four cases (85 female, 36 male) were enrolled in Group 1 and had been vaccinated with usual dose of influenza vaccine, intramuscularly and Group 2 included ninety seven cases (65 female, 32 male) who were vaccinated by reduced dose of influenza vaccine, intradermally. Body mass index (BMI) accounting in group1 (mean: 23.91±3.15) and Group 2 (mean: 23.05±3.49). Demographic characteristics were no significant differences between the groups ($p \geq 0.06$). All side effects recorded during 3 initial days after vaccination. All related adverse events reported during this trial were mild and transient local reactions were slightly more frequent among recipients of an intradermal injection than among recipients of intramuscular injection ($p<0.02$) (Table1).

Table 1: Incidence of adverse events of influenza vaccination

Symptoms	Group 1 (N = 94) %	Group 2 (N = 97) %	Total (N = 191) %
Systemic:			
Headeche	9.6	6.2	7.9
Fever	2.1	4.1	3.1
Myalgia	3.2	4.1	3.7
Coryza	3.2	4.1	3.7
Local:			
Pain	1.1	2.1	1.4
Redness	0	8.2	4.2
Induration	0	6.2	3.1
Pruritus	0	1	0.5

There was no significant difference in side effect between two groups ($p>0.1$)., Induration and redness were more frequent in group ∏ ($p<0.02$).

Table 2: Strain-specific Hemagglutination

Variable	A/fujian / (H_3N_2)	A/New caledonia (H_1N_1)	B/shanghai
Seroconversion Titer (%)			
Group 1	63.8	71.3	63.8
Group2	59.8	71.1	55.7
Total	61.3	71.2	59.7
Seroprotection prevaccination (%)			
Group 1	92.6	89.4	90.4
Group 2	88.7	86.6	87.6
Total	90.6	88	89
Seroprotection postvaccination (%)			
Group 1	98.9	100	96.8
Group 2	97.9	97.9	96.9
Total	98.4	99	96.9

There was no significant difference in seroconvertion between two groups ($p \geq 0.4$) and seroprotection ($p \geq 0.5$)

A titer of antibody 1:40 or more (seroprotection) was seen in more than 96% of health care workers in response to each of the three strains in the vaccine in two groups and there was no significant difference in titer of antibody after vaccination (Seroconvertion) on 21-28 days between two groups ($p \geq 0.5$ and $p \geq 0.4$, respectively) (Table 2).

Discussion

Vaccination against influenza virus is a important public health measure to help protect against the annual morbidity and mortality associated with influenza (Kenney *et al*., 2004). The quantity of antigen in the current intramuscular influenza vaccine provides moderate protection (efficacy of 40 to 90%, depending on the recipients age) against influenza strains that are well matched antigens (Haper *et al*., 2004). The dense population of first-line immune cells (dendritic cells) suggests that the skin is an ideal target for the delivery of vaccine antigen (Steinman *et al*., 2002). Studies involving intradermal injection of hepatitis B virus and rabies vaccine suggest the potential for improved immunogenicity (Redfield *et al*., 1985; Bryan *et al*., 1992; Briggs *et al*., 2000) but such studies are complicated by the fact that only small volumes of fluid can be injected and thus direct dose-for-dose comparisons are more difficult to conduct.

Treanor *et al*. (2002) found that 50% of the usual dose influenza vaccine was nearly as immunogenic as full-dose influenza vaccine in healthy young persons.

Other study showed that the intradermal administration of one fifth of the standard dose of A/Swine/NJ/76 infiuenza vaccine produced antibody titers similar to those elicited by the standard intramuscular dose in healthy adults and resulted in fewer systemic reaction (Brown *et al*., 1977). Kenney et al study defined that, intradermal administration of one fifth the standard intramuscular dose of an influenza vaccine elicited immunogenicity and result was smiliar that elicited by intramuscular injection (Kenney, 2004). However intradermal vaccination of healthy young persons with reduced dose inactivated influenza vaccine could be considered in order to stretch vaccine supplies (Weller *et al*., 1948; La Montagen *et al*., 2004).

In present study, similarly, all the 95% confidence intervals for the difference between the intramuscular and intradermal route in the rates of seroconversion and seropretection indicating that differences between the groups in these binary outcomes were not significant in study.

It is possible that results similar to our would not be seen in other populations, such as elderly persons, young children, or those with underlying medical conditions. We recommend that the use of dose-sparing intradermal injection of influenza vaccine in healthy young groups as a solution to future shortages of influenza vaccine.

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References

Belshe, R.B., F.K. Newman and J. Cannon *et al*., 2004. Serum antibody responses after intradermal vaccination against influenza the new Eng. J. Med., 351: 22.

Briggs, D.J., A. Banzhoff and U. Nicolay *et al*., 2000. Antibody response of patients after post exposure rabies vaccination with small intradermal dose of purified chick embryo cell vaccine or purified vero cell rabies vaccine. Bull. World Health Organ, 78: 693-698.

Brown, H., J.A. Kasel and D.M. Freeman *et al.* 1977. The immunizing effect of influenza A/New Jersey/(HsW1N1) virus vaccine administered intradermally and intramusculary to adults. J. Infect. Dis., 136: S466 – S471.

Bryan, J.P., M.H. Sjogren and P.L. Perine *et al*., 1992. Low dose intradermal and intramuscular vaccination against hepatitis B. Clin. Infect. Dis., 14: 697–707.

Harper, S.A., K. Fukula and T.M. Uyeki *et al*., 2004. Prevention and Control of Influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recomm Rep.53(RR-6):1-40.[Erratum, MMWR Recomm Rep 2004;53:743]

Jackson, L.A., S.J. Homles and P.M. Mandelman *et al*., 1999. Safty of a trivalent live a attenuated intranasal vaccine, FluMist, administered in addition to parnteral trivalent inactivated influenza vaccine to seniors with chronic medical conditions. Vaccine, 17:1905 – 1909.

Janewaym, C. J., P. Travers, M. Walport and J.D. Capra, 1999. The Immune System in Health and Disease. 4th Edn. New York: Gerland Publishing.

Kenney, R.T., S.A. Frech and L.R. Muenz *et al*., 2004. Dose sparing with Intradermal injection of Influenza vaccine. The New England J. Med., 351: 22.

La Montagne, J.R. and A.S. Fauci, 2004. Intradermal influenza vaccination-can less be more? The New England J. Med., 351: 2330-2332.

Redfield, R.R., B.L. Innis and R.M. Scott *et al*., 1985. Clinical evaluation of low-dose intradermally administered hepatitis B virus vaccine: a cost reduction strategy.JAMA.254:3203-3206.

Sabchareon, A., P. Chantavanich and S. Pasuralertsakul *et al*., 1998. Persistence of antibodies in children after intradermal or intramuscular administration of preexposure primary and booster immunizations with purified vero cell rabies vaccine. Pediatr Infect Dis J., 17: 1001-7.

Steinman, R.M. and M. Pope, 2002. Exploiting dendritic cells to improve vaccine efficacy. J. Clin. Invest., 109: 1519-1526.

Treanor, J.J., 2005. Influenza virus. In: Principles and Practice of Infectious Disease, (6th Eds ., G.I. mandell, J.E. Bennett, R. Raphael Dolin),Philadelphia, Churchill living stone, pp: 2060-2085.

Treanor, J., W. Keitel and R. Belshe *et al*., 2002. Evaluation of a single dose of half strength inactivated influenza vaccine in healthy adults. Vaccine, 20: 99-105.

Weller, T.H., F.S. Cheevers and J.F. Enders, 1948. Immunologic reaction following the intradermal inoculation of influenza A and B vaccine. Proc. Soc. Exp. Biol. Med., 67: 96-101