

EVALUATION OF SIDE EFFECTS OF INFLUENZA VACCINE ON THE ORAL HEALTH AND CORRELATION WITH FLU

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Abstract

Background: Vaccines have come a long way. They have been an important aspect of controlling and eradicating various life-threatening diseases. Vaccination is being widely used for Influenza which is one of the most common conditions affecting a large population and affects day to day activity. A vaccine being a double-edged sword, it presents various side effects as a whole and on oral cavity like ulcers, bleeding gums, white spots, sores in the oral cavity, lips, along with halitosis, etc.

Objective: This prospective study was aimed to assess and understand the bad impact on by influenza vaccine on the oral cavity as well as to establish if any correlation exists between the flu vaccine and adverse oral symptoms.

Methods: A total of 268 subjects studying at Government Medical College, were randomly screened for the study. Out of which only 32 received the vaccine for influenza in the past 6 months. All the subjects were given a multiple-choice questionnaire consisting of 12 short response questions related to general and oral side effects post-vaccination. The data collected was evaluated and assessed.

Results: Study subjects that took the influenza vaccine within a period of the past 6 months, only ten patients suffered by side effects in which 6 suffered from flu-like symptoms and only 4 suffered orally-related symptoms simultaneously. Three manifestations that were found related to the oral cavity were white patches in the oral cavity, swelling of the lips, and atypical oral ulcers, soreness, swelling, redness, and pain in the upper arm. Other symptoms encountered in responders were fever, weakness, headache, and dizziness. The results of the present study indicated that 30% (n=3) of participants reported moderate pain (level 2). The remaining 70% reported levels 1, 3, and 5 pain with 30% reported level 1, 20% level 3 pain, and 20% level 5 pain respectively of Likert's Pain Scale. Only 2 subjects (20%) required medical treatment for experienced symptoms. The severely unbearable pain of level 5 was reported by 2 subjects.

Conclusions: No substantial relationship is observed between receiving the flu vaccine and oral symptoms. The most common symptom reported by survey participants were soreness, redness, and swelling in the upper arm with associated pain. All these systems are part of body immune defence to foreign vaccine particles and are cured naturally with immunity.

Keywords: Flu, Immune Reaction, Influenza, Oral Cavity, Vaccination.

Introduction

A vaccine provides acquired active immunity against disease and is a biologic preparation. Vaccines contain an agent identical to the organism causing the disease made from killed/weakened microbial toxin forms, surface proteins. The mechanism of action for vaccines is to make the body believe that the infectious agent has invaded it and by stimulating immune system which acts and kills microorganism by producing antibodies and T-lymphocytes.¹ Edward Jenner known as "founder of vaccinology," in the late 1700s created the first vaccine of the world for smallpox. The term vaccination or vaccine is derived from "Variolae Vaccinae," meaning smallpox of the cow in Latin.² At present 25 diseases can be prevented to large extent using vaccination including Diphtheria, Adenovirus, Haemophilus influenza type b (Hib), Anthrax,

Hepatitis B, Hepatitis A, Seasonal Influenza (flu), Human Papillomavirus (HPV), Mumps, Measles and varicella. Among these 25 diseases, two diseases (Smallpox and Polio) are entirely eradicated using preventable vaccines and many of these diseases like pertussis (whooping cough) and measles are on the verge of complete eradication. Centers for Disease Control and Prevention (CDC) recommended a schedule for childhood vaccine. According to the CDC schedule, a person by the age of 18 years receives 69 doses of 16 vaccines.³ The vaccination for influenza give annually has proved to be an effective strategy against seasonal influenza and its complications. The side effects of the influenza vaccine range from mild symptoms resembling flu-like runny nose, fever and throat soreness to severe complications leading to death.^{4,5} Although vaccines provide great benefits with their ability to prevent various life-threatening diseases still, various minor and rarely major

side effects following vaccines are reported. The most common side effects following vaccination are inflammation, headache, or fever. Side effects following vaccination are also reported in various parts of the oral cavity including lips, gums, oral mucosa, teeth, and tongue.⁶ Also, many systemic conditions are presented in the mouth. Side effects of vaccines can be easily detected in the oral cavity due to its easy accessibility for examination. The severity of oral manifestations reflects the severity of the disease and can be used in implementing effective treatment plans.⁷ Various oral side effects following vaccination for Polio, Diphtheria, Pertussis, Tetanus are reported in the literature including ulcers, bleeding gums, bad breath, sores, white spots on the oral mucosa and lips.⁴ Oral Pemphigus has also been reported following anthrax vaccine administration.⁸ Other symptoms reported following the HPV vaccine in the oral cavity included erythema multiforme, squamous cell carcinoma, and warts. These symptoms might occur immediately or may be delayed.^{9,10}

Materials and Methods

The prospective study was undertaken at Department Of Dentistry, Bharat Ratna Late Shri Atal Bihari Vajpayee Memorial Government Medical College, Rajnandgaon, Chhattisgarh. Subjects included were undergraduate students of same institute. Exclusion criteria for the study were students with underlying systemic disease, patients under any medication presently or within a span of past 6 months, asthmatic patients, and patients with a history of recurrent oral ulcerations. A total of 268 patients were randomly screened for the study. All the patients were 18 years of age or above. Then patients with the history of flu within the past 6 months were included in the study were asked about the history of flu vaccine, those who took vaccine at least before 3 weeks were included. Only 32 patients fulfilled the criteria for flu vaccine lending the sample size to 32. Informed consent was taken from all the subjects as they voluntarily included in the study and ethical clearance was obtained from the institutional ethical committee.

All the subjects were given a multiple-choice questionnaire to determine if any correlation exists between influenza vaccine and oral side effects and to understand sequelae following flu vaccine administration. The questionnaire also served as a means of collecting information. Multiple choices Questionnaire contained 12 questions to be answered by responders.

The questionnaire determined the experience of subjects after receiving the vaccine for flu and if any side effects are experienced, flu-like or oral side effects along with duration and severity of symptoms, the persistence of symptoms, and if medical attention was taken for any symptom encountered. The questionnaire was completed to prevent bias. The results were compiled and were tabulated. The data collected were tabulated and various side effects in

general and on the oral cavity were assessed and evaluated by the principal investigator.

Results

The study subjects comprised students from the age group of 18 to 29 years of age with 76% female participants (n= 204) and 24% male participants (n=64). Only 220 of the 268 (82.08%) reported with flu vaccine in previous live, but only 32 participants received it. (Figure 1)

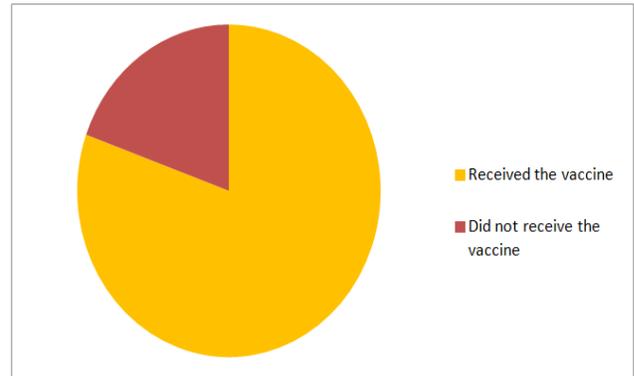
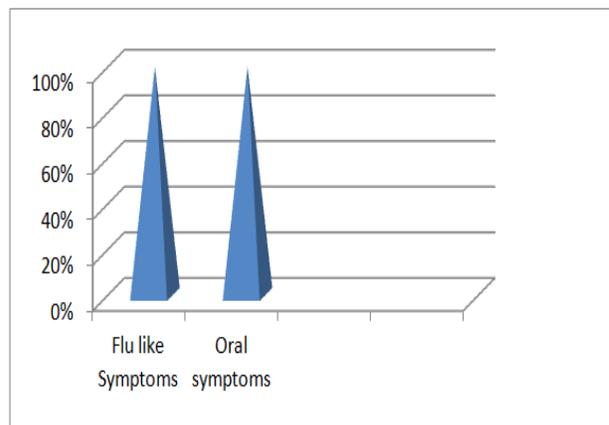


Figure 1: Students that Received the Flu vaccine

Out of the 32 subjects who received the vaccination for flu in the period of the past 6 months, only 31.25% (n=10) reported side-effect irrespective of its kind. Reported side effects were categorized into the following two classes; one being oral side effects seen in the mouth and other being flu-like symptoms. (Graph 1)



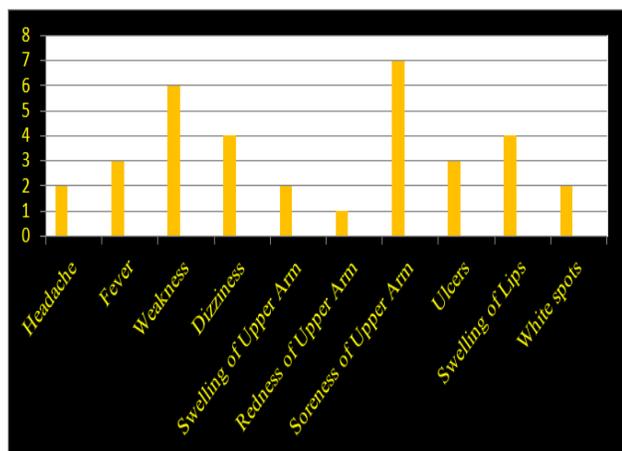
Graph 1: Symptoms observed

In multiple-choice questionnaires, oral symptoms and common flu symptoms were listed which could result after receiving the vaccine for the influenza virus. Participants were asked to choose if they experienced any of the listed symptoms in 3 weeks after administration of the vaccine. Three manifestations were found related to the oral cavity as reported by study subjects, which were white patches in the oral cavity, swelling of the lips, and atypical oral ulcers. Flu-like side effects were reported such as redness, swelling, or soreness of upper arm related to pain, and other encountered

symptoms were fever, weakness, headache, and dizziness (Table 1) Graph 2.

Table 1: Symptoms reported following the flu vaccine

| SYMPTOM | ORAL/FLU LIKE | N | % |
|-----------------------|---------------|---|--------|
| Headache | Flu-Like | 2 | 5.88% |
| Fever | Flu-Like | 3 | 8.82% |
| Weakness | Flu-Like | 6 | 17.64% |
| Dizziness | Flu-Like | 4 | 11.76% |
| Swelling of Upper Arm | Flu-Like | 2 | 5.88% |
| Redness of Upper Arm | Flu-Like | 1 | 2.94% |
| Soreness of Upper Arm | Flu-Like | 7 | 20.58% |
| Ulcers | Oral | 3 | 8.82% |
| Swelling of Lips | Oral | 4 | 11.76% |
| White spots | Oral | 2 | 5.88% |



Graph 2: Symptoms reported following the flu vaccine

The duration of the symptoms lasted from one to over a week. The severity of the symptoms was also noted. Pain scale ranging from mild to unbearable was noted using Likert's pain scale. In this pain scale scores are allotted based on pain severity ranging from 1 which represents mild pain or light pain to a score of 5, where score 5 represents several and unbearable pain. Level 3 pain was average. The results of the present study indicated that 30% (n=3) of participants reported pain of level 2 (moderate). Whereas the remaining 70% patients reported level 1, 3, and 5. Pain with 30% reported level 1, 20% level 3 and 20% level 5 pain respectively. Only 2 responders (20%) of the subjects who reported side effects took medical attention for the symptoms encountered and 2 reported a severely unbearable pain of level 5 (Table 2).

Table 2: Symptoms duration and severity

| Number of Orally-related symptoms | Number of Flu-like Symptoms | Duration of symptoms | Severity of Symptoms | Medical Attention Needed |
|-----------------------------------|-----------------------------|----------------------|----------------------|--------------------------|
| 1 | 4 | 3 days | 1- mild | No |
| 1 | 2 | 5 days | 3- severe | No |
| 0 | 1 | 3 days | 2- moderate | No |
| 0 | 1 | 3 days | 5- unbearable | Yes |
| 0 | 3 | Over a week | 2- moderate | No |
| 1 | 1 | 1 day | 3- severe | No |
| 0 | 2 | 1 day | 1- mild | No |
| 0 | 1 | 3 days | 2- moderate | No |
| 1 | 4 | Over a week | 5- unbearable | Yes |
| 0 | 1 | 3 days | 1- mild | No |

Discussion

There is very scarce evidence in the literature to date documenting the ill effect of the influenza vaccine on the oral cavity. Present study was undertaken to correlate the two. However, symptoms encountered following vaccination just as flu-like are common ad takes place due to the normal immune response of the body to the influenza virus which is identified as a foreign material. Also I most instances, side effects encountered following vaccination are much milder than the symptoms caused by influenza.¹

Of the ten positive responders that reported to have suffered from side effects after receiving the vaccine, only one was male with the symptom rate score of 1. This can be attributed to lower pain tolerance in females as compared to males. As the symptoms experienced by study subjects including pain have to be self-reported by responders, subjective nature and less pain tolerance in females could have led to selecting a higher level by female responders.¹¹ Oral cavity related manifestations were also reported by females only.

Various other side effects following the influenza vaccine were previously reported in the literature. One such research was done in the year 2006 by DiMiceli *et al.*¹² where they searched in literature for reports regarding the history of yeast allergy present before vaccination in the VAERS database from 1990 to 2004. They found a total of 107 reports mentioning yeast allergy history. Of these reports, two also reported anaphylaxis following the influenza vaccine. One case was described where a 64-year-old woman reported with itchy watery eyes and oral oedema after 15–45 minutes following vaccination for influenza. Another case was of a 29-year-old woman who reported difficulty in breathing, tachycardia, and numbness within 20 minutes of administering influenza vaccine.¹²

Another case report of 2007 by Lasley¹³ described a male child of 2.5 years who received his first dose of influenza vaccine and shortly after vaccination, he presented with scattered hives on the whole body. One month later, the patient received the booster dose and within 10 minutes again reported with hives, coughing, and wheezing.

Albuterol and diphenhydramine were given as treatment. The associated history of perioral hives after gummy candy fruit snacks consumption was given by the patient's mother. Antiboine gelatin IgE was seen following serum testing. This study was in agreement with the statement that reaction following vaccination is a result of normal immune system reaction.¹⁴

However such symptoms usually resolved on its own and rarely requires medical attention as shown in the present trial, only two cases took medical attention and noticed severe symptoms. One such case was reported by Cyrus et al; he reported recurrent oral papilloma cases due to HPV-32 which resolved entirely following quadrivalent HPV vaccination and also reports of complete resolution of disseminated and recalcitrant warts post-vaccination was discussed. The possible mechanism behind this can be attributed to cytotoxic T cells and the production of protective immunoglobulins. The authors also suggested the critical role and need for randomized clinical trials for judging the effectiveness of quadrivalent HPV vaccination in treating cutaneous verruca Vulgaris and oral squamous papillomas.⁹

Oral symptoms have also been found after administering various other vaccines such as hepatitis B. A review supporting this was carried out by Tarakji et al in 2014.¹⁴ Even though, hepatitis B vaccine is considered as highly safe (like influenza vaccine), various adverse reactions following vaccination are reported. A PubMed literature search was carried out from 2980 to 2014 for the Hepatitis B vaccine and its complications by the National Library of Medicine PubMed interface. A total number of 1147 articles were obtained and among those that mentioned Hepatitis B or its complications occurring either orally or elsewhere in the body were separated for research. 15 review articles, 58 case reports, or case series, 1 retrospective study, and 4 cross-sectional studies have such mention. The authors concluded that complications following the Hepatitis B vaccine include chronic fatigue syndrome, multiple sclerosis, sudden infant death syndrome, vasculitis optic neuritis, systemic lupus erythematosus, idiopathic thrombocytopenic purpura, anaphylaxis, neuromuscular disorders, and lichen planus. Out of the complications encountered, few are either manifested orally or carry the potential to be manifested orally. Most of the reported complications are self-arresting and self-limiting, few can be serious conditions, which often need immediate medical care and sometimes hospitalization with intensive care and attention. The findings of this review were in agreement with the present trial.¹³

Conclusion

Flu is the most common presentation seen during weather changes and affects a large population worldwide. The vaccine for influenza or flu majorly contains inactivated forms of the causative virus and includes the most prevalent strains. The side effects encountered are a part of immune

reaction to foreign vaccine particles with fewer side effects. The most-reported symptom by study subjects was redness, soreness, and swelling of the upper arm associated with pain. This can be attributed to a healthy reaction of the body's immune system which is elicited as an inflammatory response at the site of injection. This reaction is caused by serum administered in the vaccine and the needle prick.

Limitations: Although the study had several limitations such as selection bias as all the responders were students and the uniform population was selected which was exposed to a similar environment which might affect the results. The sample size of the study was relatively small with an even smaller sample size received the flu vaccine for flu symptoms. There might be an inaccuracy with the questionnaire given to responders as only a few oral symptoms were listed. Participants might have encountered different oral symptoms than the ones asked in the questionnaire. Hence more number of studies with larger sample sizes and more extended monitoring periods are required to reach a definitive conclusion.

References

1. CDC. "Understanding How Vaccines Work." Vaccines 2018
2. S.A. Plotkin, History of Vaccine Development, in: S.A. Plotkin (Ed.), Springer New York, New York, NY, 2011
3. Hamborsky, Jennifer, et al. Epidemiology and Prevention of Vaccine-Preventable Diseases. USA. Department, of Health and Human Services, Centres for Disease Control and Prevention, 2015.
4. Kimoto, T.; Kim, H.; Sakai, S.; Takahashi, E.; Kido, H. Oral vaccination with influenza hemoagglutinin combined with human pulmonary surfactant-mimicking synthetic adjuvant SF-10 induces efficient local and systemic immunity compared with nasal and subcutaneous vaccination and provides protective immunity in mice. Vaccine 2019, 37, 612–22.
5. Centers for Disease Control and Prevention. Update: vaccine side effects, adverse reactions, contraindications, and precautions: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Morb Mortal Wkly Rep 1996;45:1-35.
6. Bascones-Martínez A, García-García V, Meurman JH, Requena-Caballero L. Immune-mediated diseases: what can be found in the oral cavity? Int J Dermatol. 2015;54:258–70
7. Warnakulasuriya S, and W M Tilakaratne. Oral Medicine and Pathology : A Guide to Diagnosis and Management. 1st ed., New Delhi; Philadelphia: Jaypee Brothers Medical Publishers, 2014.
8. Muellenhoff, M., Cukrowski, T., Morgan, M., and Dorton, D. Oral Pemphigus vulgaris after anthrax

- vaccine administration: association or coincidence? *J. Am. Acad. Dermatol* 2004;50, 136–9.
9. Mohamed M, Belhadjali H, Hammedi F, Ben Meriem C, Zili J. Pityriasis rubra pilaris occurring after vaccination with diphtheria-pertussis-tetanus and oral poliovirus vaccines. *Indian J Dermatol Venereol Leprol* 2015;81:618-20
 10. Cyrus N, Blechman AB, Leboeuf M, et al. Effect of quadrivalent human papillomavirus vaccination on oral squamous cell papillomas. *JAMA Dermatol.* 2015;151:1359-63.
 11. Field MJ. Oral health objectives and dental education. In: Field MJ, ed. *Dental education at the crossroads: challenges and change*. Washington, DC: National Academy Press, 1995:59-87.
 12. DiMiceli L, Pool V, Kelso JM, Shadomy SV, Iskander J. Vaccination of yeast sensitive individuals: Review of safety data in the US Vaccine Adverse Event Reporting System (VAERS). *Vaccine.* 2006;24:703–7.
 13. Lasley MV. Anaphylaxis after booster influenza vaccine due to gelatin allergy. *Pediatric Asthma, Allergy and Immunology.* 2007;20:201–5.
 14. Tarakji B., Ashok N., Alakeel R. et al. Hepatitis B vaccination and associated oral manifestations: A non-systematic review of literature and case reports. *Ann. Med. Health Sci. Res.* 2014;4:829-36.