Safety of influenza vaccinations administered in nontraditional settings

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Abstract

Nontraditional settings (NTS) are increasingly utilized for adult vaccination but concerns exist about their safety. We conducted this analysis of 542,445 persons vaccinated at an NTS in Minnesota to assess the safety of influenza vaccination in NTS. A total of 112 adverse events (AEs) were reported, 95 immediate and 17 late. Most AEs were mild and resolved within several minutes. 63 persons (0.01%) had a vasovagal reaction to vaccination and 22 (0.004%) reported an injection site problem. Immediate hypersensitivity reactions were very rare with only 10 (0.002%) vaccine recipients having an immediate reaction for which epinephrine was required. Fifteen (0.003%) individuals required evaluation in an emergency room or physician’s office because of an AE. No deaths were reported. We conclude that influenza vaccine administration in mass vaccination clinics is safe and adverse events after influenza vaccination in NTS are extremely low.

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1. Introduction

Influenza causes a significant amount of morbidity and mortality leading to an estimated 35,000–50,000 excess deaths and 94,000–294,000 hospitalizations each year, primarily among individuals \( \geq 65 \) or those with certain chronic medical conditions [1,2]. Annual influenza vaccination is effective in preventing influenza-related hospitalization and death, and the Advisory Committee on Immunization Practices (ACIP) recommends annual vaccination for individuals aged \( \geq 65 \) as well as other groups at high-risk for serious complications, likely to belong to a high-risk group, or likely to transmit the infection to high-risk persons [3]. Despite these recommendations only 65% of adults \( \geq 65 \) and 34% of high-risk individuals 18–64 years old reported receipt of influenza vaccine in 2003, well below the Healthy People 2010 goals of 90% and 60%, respectively [4,5].

Barriers to successful vaccination include a lack of awareness regarding the need for vaccination, concerns about vaccine side effects and inconvenient clinic hours [6–8]. Nontraditional settings (NTS) such as pharmacies and grocery stores have been recognized for their ability to potentially overcome some of these barriers and are increasingly utilized for adult vaccination with 30% of adults reporting receipt of influenza vaccine in an NTS for the 1998–1999 influenza season [9,10]. Despite the importance of NTS in the vaccine delivery system, physicians have expressed concern about the safety of vaccination in immunization programs outside physician offices [11]. To address concerns about safety, we looked at the experience of the NTS provider.

2. Methods

The Minnesota Visiting Nurse Agency (MVNA) is a non-profit organization that provides a full range of public health nursing services. Starting in 1994, the MVNA has conducted...
Table 1
Immediate adverse events associated with influenza vaccination in NTS

<table>
<thead>
<tr>
<th>Immediate AEsa</th>
<th>All vaccinees (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediate AEsa</td>
<td>95(100)</td>
</tr>
<tr>
<td>Vasovagal</td>
<td>63(66)</td>
</tr>
<tr>
<td>Minor, quickly resolved</td>
<td>18(6)</td>
</tr>
<tr>
<td>Syncope, no injury or further treatment</td>
<td>1(1)</td>
</tr>
<tr>
<td>911 Called or evaluation recommended, no further treatment occurred</td>
<td>1(1)</td>
</tr>
<tr>
<td>911 Called, further treatment in ER/MD office/Urgent care</td>
<td>0(0)</td>
</tr>
<tr>
<td>Immediate Hypersensitivity reaction requiring epinephrine reaction requiring epinephrine</td>
<td>1(1)</td>
</tr>
<tr>
<td>Local</td>
<td>11(12)</td>
</tr>
<tr>
<td>Otherb</td>
<td>11(12)</td>
</tr>
</tbody>
</table>

Values in parentheses are percentages.

a Adverse events reported to MVNA within 24 h of vaccination.
b Included: seizure-like activity, wrong vaccine administered, vaccination of person not in high-priority group.

annual influenza vaccination clinics in collaboration with senior citizen centers, grocery stores, pharmacies and local corporations. Between October 1999 and January 2003, the MVNA administered over one-half million influenza vaccinations in NTS.

During the years covered by this study persons had to be ≥9 to receive vaccination at an MVNA clinic. Vaccination timing guidelines recommended by the Minnesota Department of Health were followed and adherence to these guidelines has been demonstrated in a prior study[12]. In all clinics conducted by the MVNA, after reviewing each person’s self-reported medical history and lack of any contraindications to vaccination (allergic reaction to prior influenza vaccination; allergy to eggs, thimerosal or latex; history of Guillain Barre Syndrome; acutely ill; first trimester of pregnancy or planning to become pregnant in the following month), trained nurses administer influenza vaccine according to a standing order protocol approved by the physician medical director. Trivalent, inactivated influenza vaccine was used for all vaccinations during the study time period. After vaccination, individuals are asked to remain in the immediate area for 15 min of observation. Nurses evaluate any adverse events noted during this period and record a description of the adverse event on a standardized form, including symptoms and vital signs, and any needed emergency care is administered. Later events occurring after an individual has left the vaccination site are collected through use of a telephone call or return visits to an MVNA vaccine clinic. To assess the safety of influenza vaccination in NTS we reviewed all adverse events recorded by the MVNA over four consecutive influenza vaccination seasons. This study was reviewed and approved by the Institutional Review Board, human studies subcommittee, of the Minneapolis Veterans Affairs Medical Center.

3. Results

Over four consecutive influenza vaccination seasons from October 1999 through January 2003, 542,445 individuals received influenza vaccination at an NTS conducted by the MVNA. Sixty-eight percent of all vaccinations were given at retail sites such as grocery stores and pharmacies, 27% at local corporations, and 5% at other sites including schools, churches and senior citizen centers. Vaccination clinics were held at 1675 different locations. Forty-eight percent of persons paid cash for the service at the time of vaccination. Twenty-five percent of vaccine recipients were Medicare beneficiaries and had their vaccination paid by Medicare. Other recipients who were Medicare eligible had vaccination paid for by Health Maintenance Organizations (HMOs) or other insurance providers.

A total of 95 immediate and 17 late adverse events (AEs) were reported by the MVNA over this time period. Rates of AEs per 100,000 vaccinated individuals were low. Immediate AEs occurred at a rate of 18/100,000 and late AEs in 3/100,000 vaccinated individuals. Rates of AEs were similar throughout the 4 years of the study.

A description of the immediate AEs is shown in Table 1 and Fig. 1: 63(66%) involved vasovagal reactions in vaccine recipients. The majority (57%) of the vasovagal reactions were minor and resolved after several minutes of observation or with minor interventions such as administration of food or lying supine for several minutes. Ten individuals fainted with no resulting injury and no therapy needed. In 11 (17%) individuals with vasovagal reactions, nurses felt the reaction was severe enough to require further evaluation. In these individuals 911 was either called and paramedics responded or a recommendation was made to call 911 but the vaccine recipient refused. None of these 11 individuals required further treatment however and all left the NTS site.

Fig. 1. Type of immediate adverse events following influenza vaccination (n = 95).
Surveys have shown that 20–60% of adult influenza vaccine recipients reported adverse event following influenza immunization. Of the most common reasons reported by individuals beneficiaries found that concerns over side effects was one route to improving vaccination rates. A survey of Medicare yet concerns about vaccine side effects remain a major obstacle in such a large number of individuals.

Rates of hypersensitivity reactions requiring epinephrine were rare. Overall, 10 of the 542,445 (0.002%) vaccine recipients had an immediate reaction for which epinephrine was administered. All individuals improved after the epinephrine, two required a second dose. One individual recovered completely and was able to leave the NTS, and the remaining 9 people were transported to local emergency departments for further evaluation and observation. No deaths were reported.

Other immediate reactions following vaccination were rare. Eleven individuals (0.002%) reported a local problem such as pain or redness at the vaccination site. A number of other adverse events were also reported including seizure-like activity in four individuals. In addition, one person fainted while waiting in line prior to vaccination.

Few late reactions were reported (data not shown). A total of 17 people (0.003% of all vaccinated individuals) either called the MVNA to report problems encountered after vaccination or returned to one of the MVNA clinics. Eleven (65%) of these reactions involved local soreness or other problems at the injection site and 5 (29%) were people complaining of influenza-like symptoms shortly after vaccination. Only four people indicated that they had sought care from a primary physician for the late AE.

4. Discussion

Between October 1999 and January 2003, over one-half million influenza vaccinations were safely given in NTS by the MVNA, a major mass vaccinator in Minnesota. Over all only 112 (0.02%) individuals reported an immediate or late adverse event following vaccination. The majority of these events were mild and required no evaluation beyond the NTS. Other studies evaluating adverse events after influenza vaccination have involved several hundred to almost 17,000 participants [13–16]. We are not aware of any other studies that have examined adverse events following influenza vaccination in such a large number of individuals.

Serious adverse events from influenza vaccination are rare, yet concerns about vaccine side effects remain a major obstacle to improving vaccination rates. A survey of Medicare beneficiaries found that concerns over side effects was one of the most common reasons reported by individuals ≥65 who had failed to receive influenza vaccine [8]. Other patient surveys have also shown that as many as half of all adults believe that influenza vaccine can make them ill and these individuals are more likely to go unvaccinated [17–19].

Local reactions at the vaccine site are the most commonly reported adverse event following influenza immunization. Surveys have shown that 20–60% of adult influenza vaccine recipients report local symptoms such as pain or redness at the injection site in the week following vaccination, the majority being mild [10–12]. We found a low rate of local reactions in our study with only 22 (0.004%) of vaccine recipients reporting an immediate or late reaction at the injection site. We relied on passive reporting of adverse events however and it is likely that most individuals did not report mild-moderate symptoms and the true rate of local reactions was thus likely underestimated.

We found the most common reaction immediately following immunization to be vasovagal events characterized by lightheadedness, dizziness, hyperventilation or syncope. Syncope is a known though uncommon event following immunization. From 1990 to 2001, 2269 reports of syncope were reported to the Vaccine Adverse Event Reporting System (VAERS), a passive surveillance system administered jointly by the Centers for Disease Control and Prevention and the Food and Drug Administration [20]. A report of syncopeal events following immunization found that 63% occurred within 5 min of vaccination and 98% within 30 min [21]. Ten percent of individuals with syncope required hospitalization, consistent with our finding that 10% of individuals with a syncopeal or near syncopeal event following vaccine administration in an MVNA NTS clinic required further medical evaluation. Tonic-clonic movements are frequently associated with vasovagal syncope and may explain the seizure-like activity observed in 4 patients in our study [13].

The most feared complication following vaccination is a life-threatening, immediate hypersensitivity (anaphylactoid) reaction occurring within minutes of vaccine administration. Only 452 anaphylactoid reactions were reported to VAERS from 1991 to 2001 and over 1.9 billion doses of vaccine were administered over this same time period for a rate of 1 anaphylactoid reaction for every 4 million vaccine recipients [22]. One study of influenza vaccine found that only 2 of 16,500 (.012%) vaccine recipients had an acute reaction resembling anaphylaxis, similar to the .002% observed in our study [13].

Our findings of vaccine safety in NTS are particularly important as NTS are increasingly recognized for their potential to overcome important barriers to vaccination. Self-reported patient barriers to vaccination include inability to get to a vaccine location and forgetting about need for vaccination during a scheduled appointment [8]. A study on pneumococcal vaccination in NTS found that individuals overwhelmingly found vaccinations in these settings to be well tolerated and convenient and ≥99% would recommend a NTS to others [23]. Another study found that convenience and proximity were the most important factors associated with the choice of vaccination site [24]. Reducing the distance from the vaccine setting to the population to be vaccinated, offering more convenient clinic hours and reducing administrative barriers to vaccination have all been recommended as ways to improve vaccine coverage levels as part of a multi-component program [25]. Vaccination in NTS has also been shown to have favorable cost-utility ratios compared to those of other recommended vaccines [26].
This study has several limitations, including our reliance on self-report of adverse events following vaccination. It is likely that some individuals failed to report adverse reactions, particularly delayed reactions. However, all reactions immediately following vaccination were recorded by nurses directly at the vaccination site and our rate of serious immediate reactions is consistent with prior studies. Other studies have also demonstrated low rates of side effects from influenza vaccination. Also, the experience with NTS in Minnesota may not reflect what is happening with NTS in the rest of the country.

5. Conclusions

Influenza immunization rates remain well below national goals and NTS may play an important role in improving vaccination rates. This study has shown that influenza administration in mass vaccination clinics is safe and adverse events after influenza vaccination in NTS are extremely low. This study should address potential provider and patient concerns about vaccination in NTS.

References