

A study of the side effects of Pandemrix® influenza (H1N1) vaccine after whole-crew vaccination on board a Norwegian naval vessel

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ABSTRACT

Background. The frigate His Norwegian Majesty's ship (HNoMS) Fridtjof Nansen was participating in operations in the Gulf of Aden in support of the EU mission tasked with protecting vessels from the threat of piracy. The crew was therefore prioritized and given the first batch of Influenza A (H1N1) vaccine (Pandemrix®).

Objectives. To investigate the type, frequency, and intensity of side effects after whole-crew vaccination with Pandemrix vaccine in healthy subjects in a controlled environment.

Material and methods. A hundred and thirty-three members of the crew were vaccinated, and then they participated in the study. The side effects of the vaccination were evaluated through a survey.

Results. Seventy-five per cent of the vaccinated sailors reported adverse reactions to the vaccine, with 9% not being able to perform their daily duties for one day. Muscle pain, headaches, malaise, and fatigue were the most frequent symptoms reported.

Conclusions. The vaccination program using Pandemrix H1N1 vaccine resulted in a high rate of side effects, which were generally mild and resolved within a few days. No serious lasting side effects of the vaccination were reported or registered. The adverse effects of the vaccination did not affect the operational capacity of the vessel.

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Key words: H1N1-vaccination, whole-crew vaccination, side effects

INTRODUCTION

Immunization is still the method of choice in preventive medicine in order to combat epidemic diseases [1]. As a result of the World Health Organization declaring a "public health emergency of international concern" on 25 April 2009, after the outbreak in Mexico of pandemic influenza A (H1N1) virus, the Norwegian health authorities initiated a po-

pulation-wide vaccination strategy using the Pandemrix® H1N1 vaccine. This was in line with several other countries which implemented their plans for responding to pandemic influenza. The vaccination of the Norwegian population started in September 2009 and vulnerable groups were prioritized. The groups targeted initially were pregnant women, indigenous populations, and persons with gross obesi-

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ty or serious underlying medical conditions. Together with caregivers of small children and subjects between the ages of six months and 24 years, these groups had been identified worldwide as the most vulnerable to poor outcomes [2, 3].

The transmission of contagious diseases like influenza is of concern to the shipping industry since it could affect the safe operation of vessels. In addition to safety hazards, a non-operative crew would have financial consequences as well as the practical consequence of having to re-crew the ship. Recently, a vessel from a major shipping company had to be re-crewed due to food poisoning, which was very taxing for the manning organization and had a considerable financial cost. It could also be argued that contamination of a ship's crew could be more extensive due to increased contact between personnel on board as a result of confined working and living conditions. Thus, empirical studies on whole-crew vaccination are called for.

Studies have shown that adverse responses to influenza vaccine vary. For instance, a study of Turkish health workers reported that as many as 36% of the vaccinated sample showed at least one side effect [5]. There was no relationship between adverse responses and age and gender. However, health workers vaccinated for the first time reported higher levels of side effects than groups who had been vaccinated before. Reasons for opposition to vaccination were the idea that influenza could not be considered a serious illness (29.5%), the vaccine's low level of credibility (no immunization; 26%), lack of reward for participating in the vaccination study (25%), fear of side effects (10.7%), a preference for other preventive actions (17.9%), and fear of injections/needles (6.9%).

Since vaccination is the primary prevention strategy in combating pandemic diseases, more studies on side effects are called for because of the general public debate about vaccination and the variation in attitudes to vaccination found in vaccination studies. The present study was designed to investigate the frequency and type of adverse responses to H1N1 vaccine during whole-crew vaccination. In spite of reports of serious side effects of "swine-flu" vaccine (H5N1), such as Guillain-Barré syndrome [6], these effects are not common. The most frequently reported adverse responses to the H1N1 vaccine are mild reactions at the injection site and systemic reactions [6–10]. In addition, researchers have evaluated the occurrence of selected adverse events, including

neurologic, immune system, or other serious reactions. According to these studies, none of the enrolled participants experienced these selected events [ref. in 8, 9]. One study reported tenderness, pain, redness, and hardening of skin, swelling, and bruising [8] as common local side effects. The reactions were reported to be generally mild or moderate and resolved after 72 hours. The most common systemic side effects were muscle aches. In addition, whole-body side effects occurred in response to H1N1 vaccination. Headaches, malaise (feeling out-of-sorts), muscle pain, chills, nausea, vomiting, and fever are examples [8]. In a study of immunogenicity after vaccination of two different doses of H1N1 vaccine, Greenberg et al. [9] reported 56.3% local adverse effects after receiving the vaccine. The most frequent local side effects were injection site tenderness and pain. Of the subjects, 53.8% reported systemic adverse effects. The most frequently reported symptoms were headaches, malaise, and myalgia. The symptoms were mild for both the local and systemic symptoms (86.3%). Greenberg et al. [9] also reported unsolicited adverse effects in 45% of the subjects, 9.2% of which were evaluated as being related to vaccination. The majority of symptoms (64.7%) were reported as mild. Unsolicited symptoms encompassed headaches, oropharyngeal pain and back pain. Clark et al. [10] reported higher levels of local side effects (e.g. pain at injection site: 70%) within a period of seven days of vaccination and 42% showing the systemic adverse response of muscle aches.

Most studies on adverse effects of vaccination have used the general population as subjects. These samples could be biased by the lack of control of the subjects participating in the studies. This includes pre-morbidity and co-morbidity, exposure (types and level), as well as other contextual factors such as temperature and nutrition.

One way to study the prevalence of side effects in more controlled environments is by utilizing naval personnel on sea duty. Naval personnel are selected both somatically and psychologically. One can thereby reduce the influence of co-morbidity that could affect the reporting of adverse effects of vaccination. Another advantage of using naval personnel at sea is the control this gives over contextual variables. Since sea-going personnel operate in an isolated environment, they are exposed to the same sources of contamination and nutrition, etc. This results in increased control of third variables that can influence the reporting of adverse effects of vaccination.

The Frigate HNoMS Fridtjof Nansen participated in an international anti-piracy operation in the Gulf of Aden as part of Operation Atalanta. As a standard procedure, personnel in international operations were prioritized in the vaccination procedure in order to maintain military operational capability.

The aim of the present study was to investigate the type, frequency, and intensity of side effects after vaccination with Pandemrix® (H1N1) vaccine in healthy subjects in a controlled environment. This was motivated by a need for knowledge about vaccination programs involving the whole crew of a vessel and the operational effects of such a vaccination program.

MATERIAL AND METHODS

SUBJECTS

The frigate was manned by a crew of 149 sailors. Seven sailors did not wish to participate in the vaccination program and an additional five subjects had previously shown influenza-like symptoms (either verified or suspected H1N1). Four subjects were not vaccinated due to lack of vaccine. Thus, 133 (89%) of the crew were vaccinated and participated in the study. Intensity data for six sailors were lost due to technical problems. The crew was screened medically and psychologically in accordance with the Armed Forces' procedure before embarking on international operations.

QUESTIONNAIRE

A 13-item (incl. an item reporting no side effects) self-report questionnaire was developed in which the intensity (light, moderate, or severe) of ordinary side effects of influenza vaccine was registered. The items included headaches, malaise, muscle pain, swelling of the injection site, pain in joints, fatigue, sleep loss, skin abnormalities, and fever. In addition, the questionnaire included one item asking whether the symptoms resulted in sailors not being able to perform their scheduled duties as well as the length of absence from duty. The questionnaire also included an open-ended item in which other unspecified symptoms could be reported. The subjects could report multiple symptoms when filling in the questionnaire.

PROCEDURE

The vaccination program was carried out in week 45 of 2009 after the crew returned from Norway from a two-week leave/maintenance period. The vac-

ination program was conducted over a four-day period in order to prevent any reduction in the operational capability of the crew as a result of side effects. The vaccine was administered intramuscularly in the deltoid muscle of the non-dominant hand. The questionnaire was administered to all personnel at the same time and collected three days after the administration of the last vaccine. The vessel was sailing during the whole vaccination and observation period, and was thus isolated from outside influence.

RESULTS

The response rate to the questionnaire was 100%. Of the subjects, 33 (25%) did not report any adverse reactions to the vaccine, while 100 (75%) reported various side effects. Twelve (9%) subjects reported the symptoms to be so severe that they were not able to perform their normal duties. Eleven of these subjects were absent from watch duty for one day, and one was absent for two days. Although 12 subjects were unable to perform their normal duties, the side effects causing this absence were not considered to be severe by the medical staff on board the vessel. Possible long-term effects were monitored by the surgeons, anaesthesiologists and nurses who made up the on-board medical team. No long-term effects were observed by the medical team throughout the operation.

Table 1 shows subjective evaluation (frequencies and percentages) of intensity of the side effects during the first three days after vaccination.

DISCUSSION

No severe side effects were reported as a result of the vaccination program using Pandemrix® vaccine, and the side effects reported did not influence the operation of the ship. This is in line with other reports on the side effects of "swine flu" vaccine. [8] However, a higher than expected rate of side effects was found. A total of 75% of those vaccinated reported adverse responses after vaccination. This is higher than other reports [4]. In an Australian study, approximately 44% of participants reported mild side effects within seven days of receiving the first dose of flu vaccine. Researchers tested an inactivated H1N1 vaccine developed by CSL Ltd. on a group of 240 volunteers [ref in 8]. However, the present study shows a lower rate of side effects compared to the 86% of subjects who reported adverse reactions after one or two doses of the Novartis H1N1 vaccine.

Table 1. Frequencies (n) and percentages (%) for subjective evaluations of reported side effects during the first three days after vaccination. The table is broken down by intensity level

Side effect	Mild		Moderate		Severe		Total	
	n	%	n	%	n	%	n	%
Muscle pain	30	24	44	35	14	11	88	70
Headaches	17	13	24	19	9	7	50	39
Fatigue	19	15	22	17	9	7	50	39
Malaise	18	14	22	17	9	7	49	38
Pain in joints	15	12	10	8	8	6	33	26
Swelling of the injection site	9	7	3	2	0	0	12	9
Fever	11	9	5	4	6	5	22	18
Sleep-loss	9	7	3	2	6	5	18	14
Skin abnormalities	3	2	0	0	1	1	4	3
Nightmare*							1	0.7

*Reported as other symptoms

The most frequent symptom of the Novartis vaccine was the local side effect of injection site pain; the reactions were generally mild or moderate and resolved after 72 hours [ref. in 8]. Contrary to Greenberg et al. [9] and Clark [10], the present study also showed higher frequencies of systemic side effects compared to local effects. The type of vaccine used in the present study could have caused our high numbers of side effects. An alternative interpretation could be the high response rate in the present study, which could have resulted in higher levels of recorded symptoms. The response rate in this study is also considerably higher than that observed following the nationwide vaccination program in which 2.2 million (45%) members of the Norwegian population participated [11]. This compliance rate could be due to military personnel's perception of the operational consequences of a widespread influenza outbreak on board. Another interpretation could be the sailors' positive attitude to recommendations from authorities.

Eleven per cent of the crew did not report for duty due to adverse effects of the vaccine. This did not affect the ship's organization or operation. The barrier to taking "sick-leave" while on a mission and leaving your work to your fellow sailors is very high. Some of those who were absent from duty for a day reported that, if they had been on land, the sick leave would have lasted four to five days. However, this proportion of a crew on sick leave after whole-crew

vaccination could have a greater effect on a civilian vessel due to lower manning levels on board commercial vessels.

The most frequently reported symptom in the present study was muscle pain. This is a common minor side effect. Eleven per cent of the sailors reported severe muscle pain caused by the vaccination. The present study also found high frequencies of the systemic side effects of headaches, fatigue, and malaise. Forty-one per cent of the subjects reported one or more of these three symptoms; 24% of them reported the symptoms to be mild, 17 to 19% reported moderate symptoms, and 7% reported severe symptoms. Systemic effects were also reported by CSL and recipients of Novartis vaccine referred to in a 2009 review by Doyle [8]. Approximately 36% of volunteers who were given the swine flu vaccine manufactured by CSL experienced mild systemic side effects. Eight per cent of vaccine recipients reported moderate systemic side effects, and less than 1% experienced a severe adverse reaction to immunization. Severe intensity was reported for side effects such as malaise, muscle pain, and nausea. The present study revealed higher frequencies of moderate and severe symptom intensity (moderate = 17–19%; severe = 7%). Muscle aches were the most common systemic side effect reported by participants receiving the H1N1 vaccine produced by Novartis, and no severe systemic side effects were reported. Thus, our study is in line with previously reported data on systemic adverse res-

ponses to H1N1 vaccines. However, due to the small sample size, the prevalence and type of symptoms should be interpreted with some caution.

Self-reported data have methodological limitations. The data are based on subjective evaluation of symptoms, which could result in a bias in reporting, or they could be the result of other transmittable sources of the reported effects. However, during the observation period, the medical team was present on 24-hours standby. Thus, medical evaluations were possible, and no outbreak of contagious diseases was present during the observation period that could explain the reported level of symptoms.

CONCLUSIONS

The vaccination program using the Pandemrix® H1N1 vaccine resulted in a high rate of side effects, which were generally mild and resolved within a few days. Nine per cent of the vaccinated subjects showed a severity of symptoms that led to the subjects being absent from their regular duties. This did not affect the operation of the vessel. A system of whole-crew vaccination over a four-day period is one possible way of reducing the operational consequences of possible side effects when administering the vaccine. The decision to vaccinate the whole crew was based on recommendations from the Joint Medical Staff, based on the pandemic threat level and the need to vaccinate a high percentage of the population in order to minimize the risk of illness through the virus spreading via sick and contaminated personnel. No severe long-term adverse effects of the vaccine were found on HNoMS Fridtjof Nansen's operations in the Gulf of Aden.

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