



Safety and Acceptance of HPV Vaccine: A Hospital - Based Survey at Tertiary Care Centre

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Abstract

Objective: If really safety of HPV vaccines is the concern for non-acceptability for HPV vaccines in northern India or there are some other obstacles. This was the question. So study was done to evaluate the safety of HPV vaccines in individuals who have accepted it and also to assess the factors responsible for low acceptance for vaccine.

Material and Methods: A pilot intervention study was done from June 2016 to June 2017 in the Department of Obstetrics and Gynecology of King George Medical University, Lucknow, Uttar Pradesh, India. First acceptability was determined by filling questionnaire by taking face to face interview and subjects who accepted for the vaccines, were provided vaccines (Cervarix). Various side effects in terms of pain at injection site, erythema, induration, fever, myalgia etc. were assessed after every injection. The study was ethically approved from the Institutional Ethical Committee of the KGMU, Lucknow, Uttar Pradesh, India (1689/Ethics/R cell/17). Mean with standard deviation was used for continuous variables. Frequencies and percentages were noted for categorical variables.

Results: Face to face interviewers were taken for 302 cases. Out of these 302, amongst 70 cases showed acceptability (23%). Total Cervarix doses given were 196. Most common side effect was pain at injection site followed by induration 3.5% and 1.5% respectively.

Conclusion: HPV vaccines are quite safe and safety is not a major concern for non-acceptability of HPV vaccines.

Keywords: Carcinoma cervix; Cervarix; Gardasil; HPV vaccine

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Introduction

Sexually transmitted Human Papilloma Virus (HPV) infection is the most important causative risk factor for Cervical Intraepithelial Neoplasia (CIN) and invasive cervical cancer. HPV has got more than 100 strains. 90% of high-grade intraepithelial lesions and cancer are caused by following strains, HPV16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68 out of these HPV 16 is most common one and most virulent one [1,2]. Strong association of HPV infection in causation of cervical cancer gives an opportunity for primary prevention by providing HPV vaccines. Bivalent (Cervarix) and quadrivalent (Gardasil) are available vaccines. Efficacy of these vaccines in prevention of malignancy is in tune of 70%. This efficacy reaches up to 97% in 9 valent vaccine which additionally caters 31, 33, 45, 52 and 58 strains. In spite of good efficacy uptake of HPV vaccines is very less than other recommended vaccines. This is probably due to low acceptability. However, this varies worldwide being as low as 10% to as high as 70% [3].

Indian government has not introduced HPV vaccine in universal immunization program of India till now probably showing concern about its safety and cost. So, this study was done to evaluate the safety profile of these vaccines and to find out if safety is a real concern for non-acceptability of these vaccines at population level?

Subjects and Methods

A pilot interventional study was conducted over a period of one year from June 2016 to June 2017 in Obstetrics and Gynecology department of KGMU, Lucknow. This study was ethically approved by ethical committee of university and approval No. was 1689/Ethics/R.cell-17. Target sample size was 245 from the formula:

$N = z^2 p(1-p)/e^2$, N=sample size, Z=1.96 at 5% alpha error and 20% beta error, P= power of study (80%), e= error allowance (5%), Cases were selected with following inclusion and exclusion criteria.

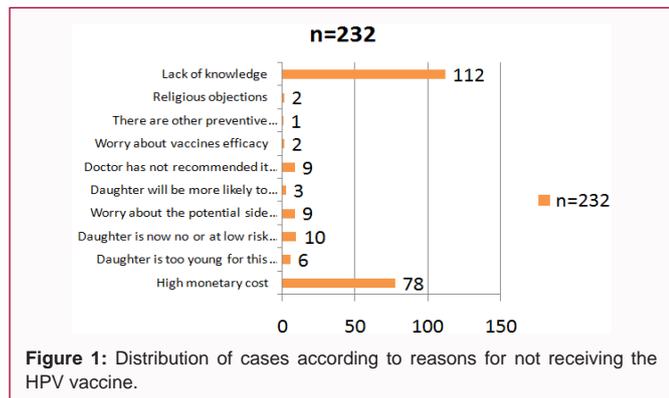


Figure 1: Distribution of cases according to reasons for not receiving the HPV vaccine.

Inclusion criteria

- Individuals giving the consent to participate
- Females of age >15 years
- Outdoor patients, their attendants and hospital employees.

Exclusion criteria

- Individuals not giving the consent to participate.

After taking a written informed consent and fulfilling the set criteria for this study a questionnaire was filled by face to face interview by doctors with cases as selected by the set criteria. The questionnaire covered following points: Demographic profile, knowledge about HPV infection and cervical cancer, belief about perceived benefits and barriers to vaccination, perception about whether their daughter might be at risk of HPV infection, parental informational need in relation to HPV vaccination, belief concerning the severity of HPV related diseases including cervical cancer, apprehension regarding side effects of vaccine, and difference of attitude towards vaccination in context of monetary issues. Participants who consented for vaccination for themselves or their daughters were vaccinated. Since, the age group for vaccination was between 9 to 26 years so the cases between the age group of 15 to 18 years (minor) who were also the part of acceptability study were vaccinated only after getting a written parental consent for vaccination. Immediate side effects were noted within 15 min, and they were asked to report remote events telephonically. Satisfaction of clients regarding HPV vaccine was assessed at 3 and 6 months post vaccination as to whether they were satisfied or not and would they recommend it to others.

Results

The present study was conducted from June 2016 to June 2017 in the Department of Obstetrics and Gynecology, KG Medical University, Lucknow, Uttar Pradesh, India with the objective to evaluate the safety of HPV vaccine.

A total of 302 cases were interviewed amongst which 70 cases showed acceptability and 232 did not accept the vaccine. Out of 70 acceptors, 20 cases accepted vaccine for themselves and remaining 50 accepted for their daughters/sisters of which 4 cases had 2 daughters each and both of them got vaccinated so the total number of clients for vaccination were 74. Clients with age 13 years or less were given 2 doses of vaccine and 3 doses were given to cases with age greater than 13 years. No of clients receiving 2 doses=26 and 3 doses=48 so the total doses given were 196. Reasons for not receiving HPV vaccines were assessed and Figure 1 shows the distribution of cases according to reasons for not receiving the HPV vaccine. Lack of knowledge

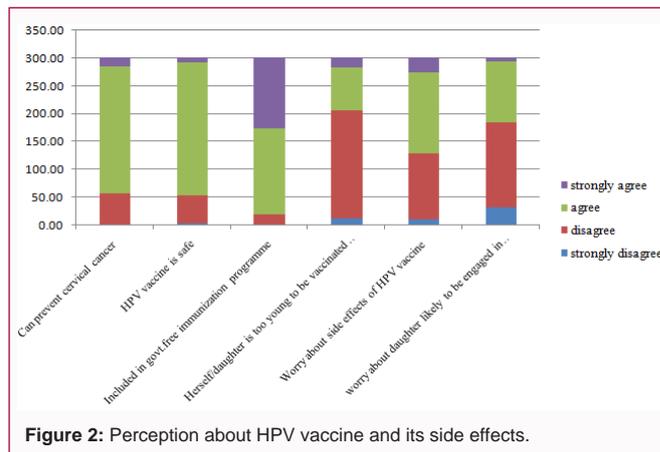


Figure 2: Perception about HPV vaccine and its side effects.

Table 1: Side Effects.

S NO.	Side Effects	No.	Percentage	
1	Pain at injection site	Mild*	7	3.6
		Moderate	4	2
2	Erythema#	2	1	
3	Induration#	3	1.5	
4	Fever	1	0.5	
5	Myalgia	1	0.5	
6	Nausea/Vomiting	0	0	
7	Diarrhoea	0	0	
8	Numbness/Tingling	0	0	
9	Seizure	0	0	
10	Syncope	0	0	

(48.3%) and high monetary cost (33.6%) were the most common reasons not to receive HPV vaccine. Only 3.6% (9 cases) had worry about serious side effects. Maximum patients had positive perception about HPV vaccine efficacy and safety. Figure 2 details about it and it was found that most of subjects agree that HPV vaccine is safe. Out of 196 doses of HPV vaccine, side effects were observed in 18 cases (9%). Mild to moderate injection site pain was the most common adverse effect noted after giving HPV vaccines (61%). Other rare side effects were fever (0.5%) and myalgia (0.5%). Safety assessment was done at 3 months and 6 months post vaccination. No long- term side effects were noted. Majority of the cases were satisfied and would like to recommend it to others. These symptoms were transient and resolved spontaneously (Table 1 and 2).

Discussion

HPV infection is the cause of nearly all cases of cervical cancer. HPV vaccines are expected to prevent up-to 70% of all cervical and anal cancer cases caused by HPV16/18 infection and >95% of genital warts (quadrivalent vaccine) in both women and men globally. Worldwide HPV vaccines have been introduced in immunization programmers; however, it is not widely accepted in India.

A questionnaire was filled by face to face interview for assessment of acceptability of HPV vaccine and all cases which opted for vaccination were given bivalent vaccine (Cervarix). Only bivalent vaccine was given because it was available in our institution. In this study 302 cases were interviewed, out of which 70 cases accepted the HPV vaccine. So, the acceptability rate in this study was 23%. The

Table 2: Distribution of side effects according to doses of vaccination (n=196).

Side effects		Dose 1 st (n=74)	Dose 2 nd (at 1 month) (n=48)	Dose 2 nd (at 6 th month) (n=26)	Dose 3 rd 9n=48)
Pain	Mild*	5	1	0	1
	Moderate	1	1	1	1
Erythema#		0	1	1	0
Induration#		1	1	1	0
Systemic	Fever	0	0	1	0
	Myalgia	0	1	0	0

*mild pain (<48 h to 72 h) #erythema or induration >5 mm in diameter

HPV vaccine was given from 9 to 26 years age group.

Out of 74 girls who were vaccinated, 33 (44.5%) were between the age of 9 to 15 years and the remaining 41 were between 15 to 26 years. The client population for acceptability in this study was the cases between the age group 15 to 26 years and the parental population was taken above 26 years. The client acceptability was seen to be higher (48.8%) as compared to parental acceptability which was only 19.2%.

In our study pain at injection site was the most common adverse event which is similar to other studies like Stan et al. [4], described the safety of quadrivalent HPV vaccine using updated clinical trial data and summarized up-to 3 years of post-licensure surveillance and found that 8 subjects out of 21,480 girls/women experienced a treatment related serious adverse effect (0.05% vaccine; 0.02% placebo). Of 18 deaths (0.1% vaccine; 0.1% placebo), no death was associated with study vaccines. Because of autoimmunity, new conditions were reported in 2.4% of both vaccine and placebo recipients. Pain was the most common injection-site adverse event and it was in 81% vaccine; 75% placebo aluminium; 45% placebo-saline respectively. The most common non serious adverse effects-headache and pyrexia were found to be similar. Also The Vaccine Adverse Event Reporting System has found it to be very safe, with only 7% being serious adverse effects, about half the average reported for licensed vaccines in general in 14,072 reports.

Dominique et al. [5] conducted a review of clinical trials of Human Papilloma Virus Prophylactic Vaccines and it was found that both vaccines exhibited excellent safety profiles in the clinical trials. The most common adverse events in Cervarix and Gardasil vaccines were injection site pain, headache and fatigue. In vaccine group, Injection-site pain was present in 83.0% to 93.4% and from 75.5% to 87.25% in control groups. Fatigue and headache were common and were reported in 50% to 60% participants in both groups. Symptoms were mild and transient in nature. They even did not increase with increase in number of cases. Presence of past or present infection does not lead to difference in side effect profile. For comparison of injection site pain from both the injections, a RCT was done which showed that Gardasil causes less pain. Cervarix group had Grade 3 severity in 17.4% and Gardasil group had 3.4% participants. The more grade 3 severe lesion in Cervarix is due to adjuvant present in Cervarix, which is MPL, an immune reacting agent.

Macartney et al. [6], reported high rates of injection site reactions particularly pain, that usually resolved spontaneously. In our study also pain resolved spontaneously. Systemic reactions were reported in few cases, which were mild and self-limited. Rosa et al. [7] reported that incidence of unsolicited adverse effects reported within 30 days after any dose of HPV vaccine was similar between the HPV vaccinated and control groups. In our study there was no case of anaphylaxis however, Gee et al. [8], in his study estimated 1.7 to be

rate of the estimated anaphylaxis based on doses of HPV vaccine given in Australia [8]. HPV vaccines are absolutely safe as their rate of anaphylaxis is similar to other vaccines ranging from 0 to 3.5 per million doses [9].

Conclusion

Conclusion of our study was that HPV vaccines are quite safe and safety is not a major concern for non-acceptability of HPV vaccine however lack of knowledge and awareness and monetary issues are major obstacles.

Synopsis

HPV vaccines are quite safe and safety is not a major concern for non acceptability of HPV vaccine however lack of knowledge and awareness and monetary issues are major obstacles.

Key Messages

HPV vaccines are quite safe and safety is not a major concern for non-acceptability of HPV vaccines. Lack of awareness and monetary issues are most important barriers for non-acceptability.

Declaration

Acknowledgement

I sincerely acknowledge my thanks to all the patients who gave their consent for participating in the study.

Contribution

Concepts: Verma ML, Singh U. Design: Verma ML, Singh U, Sachan R, Sankhwar PL. Definition of intellectual content: Verma ML, Singh U, Sachan R, Sankhwar PL. Literature search: Singh U, Rai P. Clinical studies: Singh U. Experimental studies Data acquisition: Rai P. Data analysis: Singh U, Rai P. Statistical analysis: Rai P. Manuscript preparation: Singh U, Rai P Manuscript editing: Verma ML. Manuscript review: Verma ML, Singh U, Sachan R, Sankhwar PL. Guarantor: Singh U.

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