



# The change of meningococcal carriage rate and serogroup among military trainees since the introduction of meningococcal vaccine, and the genetic characterization of the carriage isolates

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## INTRODUCTION

Monovalent meningococcal conjugate vaccines against serogroups A or C have resulted in significant reduction of pharyngeal carriage rates against the vaccine serogroups. In Korea, Republic of Korea (ROK) Armed Forces Medical Center has instituted a meningococcal vaccination program for its recruits since 2013 due to consistent outbreak of meningococcal disease within the military force. However, the effect of the quadrivalent meningococcal conjugate vaccine on meningococcal carriage has not yet been evaluated. Therefore, we assessed changes in pharyngeal carriage rates of *Neisseria meningitidis* after vaccination with quadrivalent meningococcal conjugate vaccine among Korean military recruits.

## METHODS

### Study design

Prospective observational study

### Collection of oropharyngeal samples

We enrolled ROK army in the first week of March, 2013 and 2014. Two rounds of oropharyngeal swabs of Korean military trainees were obtained at the beginning and at the end of the army training period. The first oropharyngeal swabs were collected prior to Men ACWY-CRM (Menveo, 0.5mg intramuscular, GlaxoSmithKline) vaccination; the second round was performed 5 weeks later.

### Culture and characterization of isolates

Oropharyngeal swabs were directly inoculated onto blood agar plate and Modified Thyer-Martin (MTM) media. Strains were confirmed to be *N. meningitidis* by conventional methods.

### PCR-based serogrouping of isolates

Serogrouping by polymerase chain reaction (PCR) was performed.

## Multi-locus sequence typing (MLST) analysis for isolates

The isolates were further analyzed by MLST, using 7 housekeeping gene (*abcZ, adk, aroE, fumC, gdh, pdhC, pgm*).

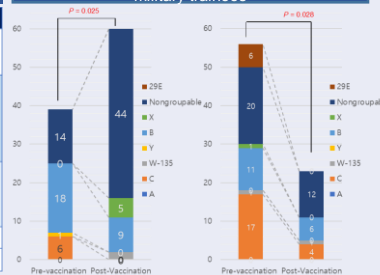
## RESULTS

- A total of 434 and 443 conscripts were enrolled in 2013, and 2014, respectively.
- A total of 178 carriage isolates were obtained among the 877 recruits.
- In 2013, the overall *N. meningitidis* carriage rate was higher at the end of the training period (13.8%, 60 of 434 participants) than upon entry into military service (8.9%, 39 of 434 participants). Although the carriage rates of non-groupable and serogroup X isolates increased over the 5-week interval, carriage of the serogroup strains included in the quadrivalent meningococcal vaccine was decreased from 7 to 2 isolates, after vaccination. (Table.1, Fig.1)
- However, in 2014, the overall carriage rate of *N. meningitidis* was significantly lower at the end of the training period (5.2%, 23 of 443 participants) than on entry into military service (12.6%, 56 of 443 participants) ( $p = 0.028$ ). (Table.1, Fig.1) Only the carriage of serogroups included in quadrivalent meningococcal vaccine significantly decreased over the 5-week interval ( $p=0.006$ )
- The aggregate of data obtained in 2013 and 2014 found reduced overall meningococcal carriage rate after vaccination (10.9% vs 9.5%), but it was not statistically significant ( $p=0.34$ ). However, carriage rate of vaccine serogroups included in vaccine decreased significantly after vaccination (2.9% vs. 0.8%,  $p<0.001$ )

Table 1. Meningococcal carriage rate before and after Menveo® vaccination in military trainees

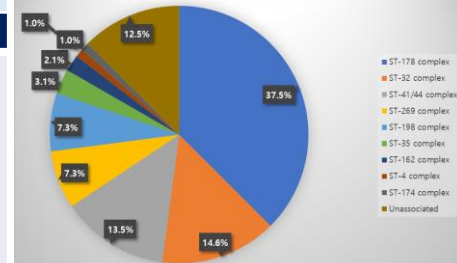
	2013			2014		
	Entry date <sup>a</sup>	5 weeks later <sup>b</sup>	<i>p</i> value	Entry date <sup>a</sup>	5 weeks later <sup>b</sup>	<i>p</i> value
	No. of carriage isolates (%)			No. of carriage isolates (%)		
Serogroups included in quadrivalent vaccine	Serogroup A	0 (0)	0 (0)	0 (0)	0 (0)	0.177
	Serogroup C	6 (15.4)	0 (0)	17 (30.4)	4 (11.4)	
	Serogroup W135	0 (0)	2 (3.3)	1 (1.8)	1 (4.3)	
	Serogroup Y	1 (2.6)	0 (0)	0 (0)	0 (0)	
Serogroups not included in quadrivalent vaccine	Serogroup B	18 (46.1)	9 (15.0)	11 (19.6)	6 (26.1)	0.009
	Serogroup 29E	0 (0)	0 (0)	6 (10.7)	0 (0)	
	Serogroup X	0 (0)	5 (8.3)	1 (1.8)	0 (0)	
	Nongroupable	14 (35.9)	44 (73.4)	20 (35.7)	12 (52.2)	
<b>Total</b>	<b>39/434 (8.9)</b>	<b>60/434 (13.8)</b>	<b>0.025</b>	<b>56/443 (12.6)</b>	<b>23/443 (5.2)</b>	<b>0.028</b>

Figure.1. Meningococcal carriage rate before and after Menveo® vaccination in military trainees



- By MLST, 39 different sequence types(STs) were identified among 178 carriage isolates with complete MLST profiles. They fell into 9 previously known clonal complexes.
- Isolates belonging to the ST-178 (37.5%), ST-32(14.6%) and ST-41/44(13.5%) were the most frequently identified clonal complex (Fig.2.)

Figure.2. Distribution of carriage isolates profiles within clonal complexes



## CONCLUSION

- Meningococcal vaccination in Korean military recruits lead to reduced oropharyngeal carriage rates of meningococcal serogroups included in quadrivalent meningococcal vaccine.
- An association between invasive meningococcal disease and oropharyngeal carriage of certain virulent strains is known.
- Thus, these findings highlight the importance of quadrivalent meningococcal conjugate vaccination of military recruits.
- Further study should be needed to evaluate the long term efficacy of quadrivalent meningococcal vaccination.

## REFERENCES

- Im JH et al., Effectiveness of a single dose of the quadrivalent meningococcal conjugate vaccine, MenACWY-CRM, in the Korean Armed Forces. *Vaccine*. 2020 Jan 22;38(4):730-732
- Junio U et al., Genotypic and phenotypic characterization of carriage and invasive disease isolates of *Neisseria meningitidis* in Finland. *J Clin Microbiol*. 2012 Feb;50(2):264-73.