ISSN: 1813-1638

The Medical Journal of Tikrit University

Available online at: www.mjotu.com

العراقية
المجلات الاكاديمية العلمية
IRAQI
Academic Scientific Journals

Evaluation of the immune response toward Neisseria meningitidis in displaced people receiving A.C.W.Y-meningococcal vaccine.

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***Keywords*:**

Immune response
Neisseria meningitidis
Meningococcal vaccine
ACWY antibodies
ELISA

ARTICLE INFO

Article history:

Received 08 Sep 2018
Accepted 01 Feb 2019
Available online 01 June 2019

ABSTRACT:

Background Meningococcal vaccine refers to any of the vaccines are used to prevent infection by Neisseria meningitidis.

Patients & Methods: The present study was carried out from 15th of January 2018 to 15th of June 2018. The number of previously vaccinated for N. meningitidis individuals under study was 68 displaced individuals whose ages were between 5-60 years old. These individuals were living in Laylan refugee camps. The control group who were matched to the patients studied, included 22 blood donors. The blood was collected from each individual enrolled in this study for estimation of anti-meningococcal group ACWY antibodies (IgG, IgM and IgA) level by ELISA technique.

The Results: The study showed that the mean of anti-meningococcal IgA-Abs in previously vaccinated persons (0.116 pg/ml), which was higher than that of the control group (0.014 pg/ml), the highest mean of anti-meningococcal IgM-Abs was occurred in previously vaccinated persons (0.2962 IU/ml) comparing with the control group (0.0064 IU/ml) and the highest rate of IgG positive result was (5.88%) present in previously vaccinated persons comparing with the control. The study showed that there was no significant relation of anti-meningococcal antibodies with sex and the highest mean level of anti-meningococcal IgM was recorded among males. This study showed that there was no significant relation of anti-meningococcal antibodies with age and the highest mean level of anti-meningococcal IgA was recorded among the age group 5-16 years. The study showed that the highest mean level of anti-meningococcal IgA, IgM and IgG antibodies were observed among the group of 1-2 months after vaccination (0.1341, 0.3089 and 0.0483 pg/ml respectively).

DOI: http://dx.doi.org/10.25130/mjotu.25.01.05

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Introduction

Meningitis is an inflammation of the protective membranes covering the brain and spinal cord. A bacterial or viral infection of the fluid surrounding the brain and spinal cord usually causes the swelling [1]. Bacteria that enter the bloodstream and travel to the brain and spinal cord cause acute bacterial meningitis. Bacterial meningitis, results from a complex multistep interaction between the host and the pathogen. These sequential steps are important for the development of bacterial meningitis [2]. Several strains of bacteria can cause acute bacterial meningitis: Streptococcus pneumoniae, Haemophilus influenzae, Listeria monocytogenes and Neisseria meningitidis (meningococcus) [3 .[

These bacteria commonly cause an upper respiratory infection but can cause meningococcal meningitis when they enter the bloodstream. This is a highly contagious infection that affects mainly teenagers and young adults. It may cause local epidemics in college dormitories, boarding schools and military bases. A vaccine can prevent infection [4]. Neisseria meningitidis, is a diplococcus Gram negative bacterium it is the cause of the endemic form of meningitis[1]. The polysaccharide capsule that surrounds the bacteria is important for the classification of N. meningitidis into 12 serogroups. Out of these 12 serogroups, only 6 are responsible for most of the infections in human: A, B, C, W135, X and Y The serogroups are widely distributed around the globe[5]. Meningococcal vaccine refers to any of the vaccines used to prevent infection by Neisseria meningitidis. Different versions are effective against some or all of the following types of meningococcus: A, C, W-135, and Y. The vaccines are between 85 and 100% effective for at least two years[4]. They result in a decrease of meningitis and sepsis among populations where they are widely used [6]. The study was conducted for the determination of immunity status toward Neisseria meningitidis vaccine in displaced individuals in Kirkuk city.

Patients and methods

The study was carried out from 15th of January 2018 to 15th of June 2018. The number of previously vaccinated for N. meningitidis individuals under the study was 68 displaced individuals at ages between 5-60 years. These individuals were living in Laylan refugee camps. The control group who were matched to the patients studied, included 22 blood donors individuals who visited to Kirkuk main blood bank for blood donation. Five ml of blood was collected from each individual enrolled in this study.

The obtained sera were then aspirated and transferred into clean test tubes for estimation of anti-meningococcal group ACWY antibodies (IgG, IgM and IgA) level by ELISA technique.

Statistical analysis

Computerized statistically analysis was performed using IBM SPSS ver. 23.1 statistic program. Comparison was carried out the P value .

Results.

Table 1 shows that the mean of anti-meningococcal IgA-Abs in previously vaccinated persons (0.1162 pg/ml) was higher than that of the control group (0.0142 pg/ml). The result was statistically highly significant. In relation of anti-meningococcal IgM-Abs with vaccination ،

Table 2 shows that the highest mean of anti-meningococcal IgM-Abs was occurred in previously vaccinated persons (0.2962 IU/ml) comparing with the control group (0.0064 IU/ml). The result was highly significant. Table 3 shows that the highest rate of IgG positive results (5.88%) was present in previously vaccinated persons comparing with control. The study showed that there was no significant relation of anti-meningococcal antibodies with sex and the highest mean level of anti-meningococcal IgM was recorded among males. The study showed that there was no significant relation of anti-meningococcal antibodies with age and the highest mean level of anti-meningococcal IgA was recorded among the age group 5-16 years, the highest mean level of anti-meningococcal IgM was recorded among the age group 37-46 years and the highest mean level of anti-meningococcal IgG was recorded among age group 47-60 years (Table 5). The study showed that the highest mean level of anti-meningococcal IgA was recorded among the group of 1-2 months (0.1341 pg/ml), the highest mean level of anti-meningococcal IgM was recorded among the group1-2 years (0.3089 pg/ml) and the highest mean level of anti-meningococcal IgG was recorded among the group 1-2 years (0.0483 pg/ml), Table 6. Statistical Analysis: The present results are analyzed by the following statistical method which includes: Statistical descriptive tables, relative frequencies (percent), arithmetic mean and standard deviation (SD). The suitable statistical tests are used as follows: T-test, Qi-square test.

Table 1: Anti-meningococcal IgA-Abs level in vaccinated persons and the control group

Anti-meningococcal IgA pg/ml	Vaccinated persons (n:68)	Control (n:22)
Mean	0.1164	0.0142
S.D	0.0734	0.0051
T test = 42.199 P= 0.00001 P < 0.01 Highly Significant(HS)		

Table 2: Distribution of anti-meningococcal IgM-Abs in vaccinated persons and the control group.

Anti-meningococcal IgM pg/ml	Vaccinated persons (n:68)	Control (n:22)
Mean	0.2962	0.0064
S.D	0.1605	0.0051
T test = 71.149 P= 0.00001 P < 0.01 Highly Significant(HS)		

Table 3: Frequency of anti-meningococcal IgG-Abs in previously vaccinated persons and the control group.

Anti-meningococcal IgG	Vaccinated persons (n:68)		Control	
	No.	%	No.	%
+ve	4	5.88	0	0
-ve	64	94.12	22	100
Total	68	100	22	100
X^2 = 7.372 P= 0.025 P < 0.05 Significant(S)				

Table 4: Frequency of anti-meningococcal Abs in previously vaccinated persons in relation to sex.

Anti-meningococcal Abs pg/ml		Male (n:31)	Female (n:37)	T Test	*P. Value*
IgA	Mean	0.0241	0.0231	0.198	0.65 NS
	S.D	0.0094	0.0091		
IgM	Mean	0.3064	0.2878	0.22	0.63 NS
	S.D	0.1648	0.1587		
IgG	Mean	0.0374	0.0343	0.21	0.64 NS
	S.D	0.0254	0.0274		

Table 5: Frequency of anti-meningococcal Abs in previously vaccinated persons in relation to age.

Anti-meningococcal Abs pg/ml		Duration after vaccination (months)					*P. Value*
		5-16	17-26	27-36	37-46	47-60	
No.		27	19	7	11	4	
IgA	Mean	0.0254	0.0235	0.0183	0.0221	0.0252	0.43
	S.D	0.0079	0.0109	0.0072	0.0083	0.0137	NS
IgM	Mean	0.2744	0.3089	0.2517	0.3866	0.2769	0.33
	S.D	0.1365	0.1957	0.1081	0.1807	0.1226	NS
IgG	Mean	0.0172	0.0149	0.0169	0.0175	0.018	0.31
	S.D	0.0076	0.0089	0.0055	0.0082	0.012	NS

Table 6: Frequency of anti-meningococcal Abs with the duration of protection.

Anti-meningococcal Abs pg/ml		Duration of protection (months) (n:68)			*P. Value*
		1-2	3-4	5 and more	
No.		3	11	54	
IgA	Mean	0.1341	0.1174	0.1124	0.87
	S.D	0.104	0.0612	0.0745	NS
IgM	Mean	0.3089	0.2987	0.1362	0.23
	S.D	0.1704	0.1153	0.1038	NS
IgG	Mean	0.0483	0.0316	0.0334	0.22
	S.D	0.0202	0.0247	0.0266	NS

Discussion

Adults and older children who become colonized with Neisseria meningitidis develop bactericidal antibodies against strains of homologous and heterologous serogroups, suggesting the carriage plays a role in induction and maintenance of antibodies to meningococci [4,5]. Gold et al [7] found that 40% of perons who carried N. meningitidis had increased titers of bactericidal antibodies reactive with meningococcal isolates of serogroups A, B and C. Zorgani et al [8] study, bactericidal antibodies to capsulate strains of meningococci were associated with high levels of IgG to N. meningitidis. Kremastinou et al [9] in a study of detection of IgG and IgM to meningococcal outer membrane proteins in relation to carriage of Neisseria meningitidis or Neisseria lactamica, found high titers of IgG and IgM against meningococci. Wedege et al [10] showed a higher antibody response in adult patients that had previously been immunized with the vaccinated Norwegian persons when

compared to non-immunized patients. Milagres et al [11] found similar results of the current study and showed that a complex specificity of antibody response of patients with meningococcal disease.

Salih et al [12] found that the titer of anti-meningococcal IgG, IgM and IgA would increased with increasing of the age of patients enrolled in their study and the highest means were observed in children 10-14 years. Heyderman et al [13] found that the incidence of meningococcal disease tends to be higher in males than females which was in agreement of the current study. Meningococcal carriage prevalence is generally higher in males than females and particularly high rates of carriage have been observed in closed or partially closed communities [14]. Males and females differ in their immunological responses to foreign and self-antigens and show distinctions in innate and adaptive immune responses. Goldschneider et al [15] demonstrated that incidence was usually highest in children aged less than 5 years, with infants under 1 year of age being at highest risk. Often there is a smaller secondary peak in disease incidence in teenagers and young adults, likely due to increased exposure and transmission of meningococci in this age group [16]. Duration of the antibody response is limited, especially among children, and intervention studies have shown that effectiveness of the C component of these vaccines is very limited in the youngest members of the population [17]. Coen et al [18] showed that the age-related increases in levels of salivary IgA to N. meningitidis in line with age-related increases in the prevalence. Several studies done earlier denoted that the quadrivalent (A, C, Y, W-135) and bivalent (C, Y) meningococcal conjugate vaccines are in phase 3 immunogenicity trials in the younger age group, but these vaccines may not produce a robust immune response until after the second or third dose (at 4–6 months of life) as well as, the activity of vaccine would decrease with increase of time after vaccination [19-21]. A study done by Blakebrough et al [22] reported that period of immune response may be transient or last for many months. The duration of immune response toward meningococci was not well established as few longitudinal studies of carriage have been performed. Studies in Europe have suggested periods of nine or more months, whereas other study estimated a much shorter duration of three months [23-25]. Duration of the antibody response is limited, especially among children, and intervention studies in Quebec have shown that effectiveness

of the C component of these vaccines is very limited in the youngest members of the population. The serogroup A component of the vaccine appears to be immunogenic from a few months of age and may therefore be unlike other polysaccharide vaccines, which do not offer relevant protection before 2 years of age [26]. Plotkin et al [27] found that bactericidal antibody levels declining more rapidly with the increasing of the duration of protective immunity which induced by polysaccharide antigens. Cohn et al [28] concluded in their study that the anti-meningococcal vaccine was effective in the first year after vaccination but effectiveness declined 3 to <8 years post vaccination. The results of the presented study were consistent with immunogenicity data of previos studies that revealed decreasing levels of serum bactericidal antibody 3 to 5 years postvaccination [29,30].

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