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Side Effect Profile of Meningococcal B Vaccine in Children

Çocuklarda Meningokok B Aşısının Yan Etki Profili

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Abstract

Aim: Invasive meningococcal infections have a clinical picture with a rapid onset and can lead to serious sequelae and death even in individuals who are treated early. The most common causes of related epidemics are serogroups A, B, C, W, Y, and X, and two different vaccines have been developed against serogroups A, C, W, and Y and serogroup B. The serogroup B-containing MenB-4C vaccine (Bexsero®) was licensed in Turkey in 2018 and is still being administered. In this study, the side effects of this vaccine in infants and children followed up in a tertiary pediatric clinic were questioned.

Material and Method: In our study, the local and systemic side effects of the MenB-4C vaccine doses, which were administered between March 1, 2019, and March 1, 2022, at the Child Health Follow-up Outpatient Clinic of Gazi University Faculty of Medicine, were evaluated retrospectively. All infants and children aged 0-18 years who were vaccinated at this clinic on the specified dates (n=102) were recruited, and a questionnaire was completed by calling their parents by telephone and questioning the side effects of the vaccine.

Results: It was determined that a total of 224 doses of the MenB-4C vaccine were administered to 102 children over the three-year study period, Of these vaccines, 21.6% were administered during the year before the pandemic and 78.4% during the two years after the pandemic. According to the total number of doses, the rate of local and systemic side effects was 30.8% (n= 69). It was found that among the 69 doses with side effects, 42 (60.8%) were systemic (fever), and 27 (39.1%) were local (stiffness, redness, and pain at the injection site). Side effects were observed in 41.3% of the patients after the first dose of the vaccine, 23.3% after the second dose, and 25.9% after the third dose.

Conclusion: In our study, no serious post-vaccine reactions, such as anaphylaxis and encephalopathy, were observed following vaccination with MenB-4C, and the most common side effects of this vaccine were fever and local pain, which were only transient and self-limiting, lasting only two to three days at most. Since the MenB-4C vaccine, which has been included in the vaccination schedule of most countries, is a strong tool to help prevent meningococcal infections, every parent presenting to a health institution should be informed by the physician about the necessity of this vaccine, and if possible, conjugated meningococcal vaccines containing not only serogroups A, C, W, and Y but also serogroup B should be added to the national vaccine scheme.

Keywords: Childhood, vaccination, meningococcal type B

Öz

Amaç: İnvazif meningokokal enfeksiyonlar hızlı başlangıçlı bir klinik tabloya sahiptir ve erken tedavi edilen bireylerde dahi ciddi sekellere ve ölüme yol açabilmektedir. İlgili salgınların en yaygın nedenleri serogrup A, B, C, W, Y ve X'tir ve serogrup A, C, W ve Y ile serogrup B'ye karşı iki farklı aşı geliştirilmiştir. Serogrup B'yi içeren MenB- 4C aşısı (Bexsero®) Türkiye'de 2018 yılında ruhsatlandırılmış olup halen uygulanmaktadır. Bu çalışmada üçüncü basamak pediatri kliniğinde takip edilen bebek ve çocuklarda bu aşının yan etkileri sorgulandı.

Gereç ve Yöntem: Çalışmamızda Gazi Üniversitesi Fakültesi Çocuk Sağlığı Takip Polikliniği'nde 1 Mart 2019 ile 1 Mart 2022 tarihleri arasında uygulanan MenB-4C aşı dozlarının lokal ve sistemik yan etkileri araştırıldı. Tıp Fakültesi retrospektif olarak değerlendirildi. Belirlenen tarihlerde (n=102) bu klinikte aşı olan 0-18 yaş arası tüm bebek ve çocuklar çalışmaya dahil edildi ve ebeveynleri telefonla aranarak aşının yan etkileri sorgulanarak anket dolduruldu.

Bulgular: Üç yıllık çalışma süresi boyunca 102 çocuğa toplam 224 doz MenB-4C aşısı uygulandığı belirlendi. Bu aşıların %21,6'sının pandemiden önceki yılda, %78,4'ünün ise iki pandemi döneminde uygulandığı belirlendi. salgından yıllar sonra. Toplam doz sayısına göre lokal ve sistemik yan etki oranı %30,8 (n= 69) idi. Yan etki görülen 69 dozun 42'sinin (%60,8) sistemik (ateş), 27'sinin (%39,1) ise lokal (enjeksiyon yerinde sertlik, kızarıklık, ağrı) olduğu belirlendi. Aşının ilk dozundan sonra hastaların yüzde 41,3'ünde, ikinci dozundan sonra yüzde 23,3'ünde, üçüncü dozundan sonra ise yüzde 25,9'unda yan etki görüldü.

Sonuç: Çalışmamızda MenB-4C aşılaması sonrasında aşı sonrası anafilaksi, ensefalopati gibi ciddi bir reaksiyon görülmedi ve bu aşının en sık görülen yan etkileri geçici ve kendiliğinden düzelen, en fazla iki ila üç gün süren ateş ve lokal ağrıydı. Çoğu ülkenin aşılama takviminde yer alan MenB-4C aşısı meningokok enfeksiyonlarını önlemeye yardımcı güçlü bir araç olduğundan, sağlık kuruluşuna başvuran her ebeveynin hekim tarafından bu aşının gerekliliği konusunda bilgilendirilmesi ve mümkünse sadece A, C, W ve Y serogruplarını değil serogrup B'yi de içeren konjuge meningokok aşıları ulusal aşı şemasına eklenmelidir.

Anahtar Kelimeler: Çocuk, Aşılama, Meningokok Tip B

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INTRODUCTION

Meningococci (*Neisseria meningitidis*) have caused endemics and epidemics in many parts of the world since the beginning of the 19th century. Invasive meningococcal infection has a clinical picture with a rapid onset and can lead to serious sequelae and death even in individuals who are diagnosed and treated early.[1] Despite the appropriate treatment, in addition to the mortality rate of 10-15%, one out of every five survivors faces long-term sequelae, such as limb loss, deafness, and problems with the central nervous system.[2]

Thirteen serogroups have been identified to cause meningococcal disease, with the most common being serogroups A, B, C, Y, W, and X. The distribution of these serogroups differs according to the geographical location and age of the evaluated populations.[3] The highest incidence of meningococcal disease across the world is found in the "meningitis belt" of sub-Saharan Africa. Major consequences occur in this region every five to 12 years, and the attack rate reaches 1,000 cases per 100,000 people. The measured annual attack rate, which is lower in other parts of the world, averages 0.3 to 3 per 100,000 people.[4] According to the meningococcal meningitis incidence, the World Health Organization classified countries as those having high endemic (>10 cases /100,000 persons/year), moderately endemic (2-10 cases/100,000 persons/year), and low endemic (<2 cases /100,000 persons/year) rates.[5] It is recommended that meningococcal vaccine be included in a routine immunization program in countries that are moderately endemic for meningococci. Turkey is also in this category. However, the epidemiology of meningococcus in Turkey differs from many other countries, and significant changes have been observed over time. In a multicenter study by Ceyhan et al., in which they evaluated bacterial meningitis agents in Turkey between 2005 and 2012, *N. meningitidis* was found to be the most common causative agent at a rate of 51.6%, and the W (38.1%) and B (26%) strains were mostly identified in the serotype distribution.[6]

Meningococcal infections are among the diseases that can be prevented by vaccination. It is possible to prevent invasive meningococcal infections with two types of vaccines: the first is the inactivated quadrivalent conjugate vaccine for serogroups A, C, W and Y, and the second is the serogroup B vaccine, which is an inactivated bacterial recombinant protein vaccine. Currently, there are two types of vaccines developed against meningococcal B serotype: the MenB-4C (Bexsero®) vaccine approved in Europe, Canada, Australia, and the USA and the MenB-FHbp (Trumenba®) vaccine approved in the USA.[7] In Turkey, the MenB-4C vaccine has been licensed for use after 2 months of age.[8]

The MenB-4C vaccine has been shown to be immunogenic in infants, adolescents, and adults.[9,10] In many clinical studies, the safety and undesirable effects of the MenB-4C vaccine have been investigated. While no problems were found in studies on its safety in adolescents, there are still concerns and a lack of knowledge among parents and even physicians due to the fever and systemic side effects observed in young children.[10,11] In our study, we planned to investigate the side effects and their frequency in pediatric patients who received the MenB-4C vaccine.

MATERIAL AND METHOD

The study was carried out with the permission of Gazi University Ethics Committee (Date: 27.07.2023, Decision No: 14).

In our study, the frequency of local and systemic side effects of the MenB-4C vaccine doses, which were administered between March 1, 2019, and March 1, 2022, at the Child Health Follow-up Outpatient Clinic of Gazi University Faculty of Medicine, Department of Social Pediatrics, was retrospectively evaluated.

All infants and children aged 0-18 years who were vaccinated at our clinic over the specified period (n=102) were included in the study. The names and telephone numbers of the vaccinated patients were obtained by screening the records. The parents were informed about the study by telephone, and those who provided consent were administered a questionnaire through a telephone interview to determine the side effects of the vaccine.

Using the questionnaire forms, sociodemographic characteristics, chronic disease history, drug use history, number of doses and age at MenB-4C vaccination (cross-checked through the vaccination records of the patients), side effects after vaccination, e.g., fever (body temperature of 38° and over, armpit or ear measurement), restlessness, swelling, redness, limitation of movement, pain, and stiffness at the injection site, duration of side effects, the vaccines included or not included in the national vaccination schedule (NVS) were questioned. In our department, for intramuscularly (IM) injections, in children younger than 1 years, the anterolateral aspect of the upper thigh is the preferred site. In older children, we preferred the deltoid muscle for IM injections.

Statistical Analysis

Data were analyzed using IBM SPSS V23. The conformity of the data to a normal distribution was evaluated with the Kolmogorov-Smirnov and Shapiro-Wilk tests. The Mann-Whitney U test was used to compare the data that were not normally distributed according to paired groups, and multiple comparisons were undertaken with Dunn's test. Pearson's chi-square, Yates' corrected chi-square, Fisher's exact, and Mc Nemar tests were used to compare categorical data. The results of the analyses were presented as mean ± standard deviation and median (minimum–maximum) for quantitative data, and as frequency and percentage for categorical data. The statistical significance level was taken as $p < 0.05$.

RESULTS

Of the total 1,972 patients who presented to the Child Health Monitoring Outpatient Clinic between March 2019 and March 2020 (before the COVID-19 pandemic), 22 (1.1%) received the MenB-4C vaccine. From March 2020, when the first COVID-19 case was reported in Turkey, to March 2022, a total of 2,853 patients presented to our outpatient clinic, and 80 (2.8%) of these patients were vaccinated against Meningococcal B. Accordingly, it was determined that 21.6% of the MenB-4C vaccine doses were administered during the year before the pandemic and 78.4% during the two years after the pandemic.

Demographic characteristics of vaccinated children and their families are given in Table 1. It was seen through the system that all the children included in our study were fully vaccinated according to their age and other vaccines in the NVS. It has been observed that 50% of the patients who received the MenB-4C vaccine were above 2 years of age when the first dose of vaccine was given. It was determined that 92.2% (n=94) of the children who received the meningococcal B vaccine had complete vaccine doses according to their age. It was observed that 7.8% (n=8) of them did not complete their vaccinations (**Table 1**). The families of the children whose vaccine dose was not completed were interviewed and the reason was asked. One of them stated that he did not have the other doses due to the high fever he experienced in the first dose, two families stated that they could not have it done due to financial reasons, while five families said that they delayed it due to the pandemic.

When the administration rates of other vaccines not included in the NVS were questioned, it was determined that 93.1% of the patients had received the meningococcal ACYW vaccine, 59.4% had received the rotavirus vaccine, 10.9% had received the influenza vaccine, and 6.9% had received the HPV vaccine. Of the parents, 19.4% stated that they also had their other children vaccinated with MenB-4C.

It was found that 95% of the parents had been informed about the vaccine and its possible side effects before vaccination. The MenB-4C vaccine was administered alone in 98% of the cases and simultaneously with the Men ACYW vaccine in two patients, and no side effects were observed in these two patients.

The 102 children received a total of 224 doses of the MenB-4C vaccine, and the rate of those with side effects according to the total number of doses was found to be 30.8% (n=69). It was determined that of the 69 side effects, 42 (60.8%) were systemic, and 27 (39.1%) were local. Only fever was seen as a systemic side effect and lasted two days in two of the 42 patients and three days in one patient. Fever was self-limiting and resolved within 24 hours in 92.8% (n=39) of the patients with this side effect. As a local reaction, stiffness, redness, and pain were observed at the injection

Table 1: Descriptive characteristics of the study group

	n	(%)
Gender		
Male	45	44.1
Female	57	55.9
Maternal education level		
Primary school	20	19.6
High school	15	14.7
University	67	65.7
Maternal working status		
Working	43	42.2
Not working	59	57.8
Paternal education level		
Primary school	12	11.9
High school	19	18.8
University	70	69.4
Paternal working status		
Working	3	3
Not working	98	97
Family Type		
Nuclear	99	97.1
Extended	3	2.9
Number of children		
1	45	44.1
2	34	33.3
≥3	23	22.5
Order of child who vaccinated		
1	70	68.6
2	21	20.6
≥3	11	10.8
Income level		
≤450$	11	10.8
450-900 $	46	45.1
≥900$	45	44.1
Chronic disease		
Absent	62	60.8
Present	40	39.2
Drugs		
Absent	90	88.2
Present	12	11.8
Immunosuppressive drug use		
Absent	9	75
Present	3	25
Hospitalization		
Absent	97	95.1
Present	5	4.9
Age at first dose		
2-5 months	5	4.9
6-12 months	33	32.3
13-24 months	13	12.7
2-10 years	25	24.5
>10 years	26	25.4
Vaccines in the national vaccination schedule		
Complete	102	100
Completed primary series for 4CMenB?		
No	8	7.8
Yes	73	71.6
Not vaccinated yet	21	20.6
	n / Medium ± S.deviation	**Median (min. - maks.)**
Maternal age	37.43 ± 6.74	38 (25 - 59)
Paternal age	40.18 ± 7.61	40 (26 - 65)

site, which regressed within 24-48 hours, except in one patient. Stiffness at the injection site, which was seen in only one patient, continued for seven to 10 days. Side effects occurred in 41.3% of the patients after the first dose of the MenB-4C vaccine, 23.3% after the second dose, and 25.9% after the third dose. When the relationship between the doses was examined in terms of side effects, statistically significant side effects were not observed at the second dose in patients who had not experienced any side effects after the first dose, but no such relationship was found for the third dose (**Table 2**). Of the 224 doses, 41.5% (n=93) were administered intramuscularly from the leg (to children under 1 year old) and the remaining 58.4% (n=131) from the arm (over 1 year of age) by the same nurse.

Considering the frequency of side effects according to the age of the children, fever was observed more frequently in those aged two years and younger (37.2%, 22,4% and 22%, after the first, second and third dose, respectively) compared to those aged over two years (5.8% after the first dose and 6.5% after the second dose) (**Table 3**).

The rate of antipyretic administration before the first dose of vaccination was 31.4% for the first dose, 26.6% for the second dose, and 27.6% for the third dose. When the effect of pre-vaccination antipyretic administration on the post-vaccination side effects status was examined, no statistically significant result was obtained (**Table 4**).

Table 3. Comparison of the second- and third-dose side effects according to the first-dose side effect status

	First-dose side effects		p*
	Absent	Present	
Second-dose side effects			
No	56 (96.6)	17 (45.9)	0.001
Yes	2 (3.4)	20 (54.1)	
Third-dose side effects			
No	14 (82.4)	6 (60)	0.508
Yes	3 (17.6)	4 (40)	

*McNemar test

Table 4. Evaluation of antipyretic effects before vaccination

	Pre-vaccination administration of antipyretics		p
	Absent n (%)	Present n (%)	
First-dose side effects			
Absent	38 (55.1)	22 (66.7)	0,369*
Present	31 (44.9)	11 (33.3)	
Second-dose side effects			
Absent	54 (79.4)	19 (73.1)	0,702*
Present	14 (20.6)	7 (26.9)	
Third-dose side effects			
Absent	16 (84.2)	4 (50)	0,145**
Present	3 (15.8)	4 (50)	

* Chi-square test with Yates correction, **Fisher's exact chi-square test

Table 2: Side effects by age groups

Age	Total number of children	Number of children with side effects	Systemic side effects		Local side effects		
	n	n (%)	Fever*	Restless	Redness at the injection site	Stiffness at the injection site	Pain at the injection site
First dose							
2-5 month	5	1 (20)	1				
6-12 month	33	17 (51.5)	15		1	1	
13-24 month	13	5 (38.5)	3			1	1
2-10 month	25	9 (36)	2			5	2
>10 month	26	9 (34.6)	1				8
	Total 102						
Second dose							
2-5 month	5	2 (40)	2				
6-12 month	31	9 (29)	8			1	
13-24 month	13	2 (15.3)	1				1
2-10 month	22	4 (18.1)	2				2
>10 month	24	4 (16.6)	1				3
	Total 95						
Third dose							
2-5 month	1	1 (100)	1				
6-12 month	18	5 (27.7)	5				
13-24 month	8	1 (12.5)					1
2-10 month	0	-					
>10 month	0	-					
	Total 27						

* Body temperature of 38° and over (armpit or ear measurement)

DISCUSSION

In our study, in which we retrospectively evaluated the local and systemic side effects of MenB-4C vaccines administered in the Child Health Follow-up Outpatient Clinic, no serious reactions such as post-vaccine anaphylaxis and encephalopathy were observed. It has been found that it has self-limiting features within 2-3 days at most.

Although local and systemic reactions are mostly self-limiting and transient after MenB-4C vaccination, fever has been reported more frequently in infants. But in adolescent pain at the injection site has been reported more frequently and, fever less frequently.[12] In the study with the largest adolescent cohort to date, 58,637 doses of 4CMenB vaccine were administered to 30,522 students (median age 16 years) during 2017–2018. Most common side effects were injection site reaction (126/193), headache (99/193) and nausea (61/193). Reported side effects declined with increasing age. It was found to be well tolerated in adolescent.[7] In a study conducted in Quebec, after the administration of a total of 43,000 doses of the MenB-4C vaccine, the incidence of fever was found to be higher in children under the age of two years (14-15%) than in those aged 2-4 years (12%) or five and over (6-8%).[13] Similarly, in our study, fever was observed more frequently in children aged two years and younger and less frequently in those over two years of age.

MenB-4C has been associated with increased rates of fever and other vaccine-related reactions, especially within the first 24-72 hours, when administered with other routine infant vaccines.[9] In vaccine side-effect studies, it can be very difficult to determine which vaccine is associated with the side effect that occurs due to the simultaneous administration of multiple vaccines.[14,15] Therefore, most studies have performed statistical analyses by attributing side effects to all vaccines in the presence of multiple vaccinations. In one of these studies, fever was detected at a rate of 26-41% when MenB-4C was administered alone, 23-36% after routine vaccinations alone, and 51-61% after the co-administration of MenB-4C and routine vaccines.[16] In our study, 98% of the patients having been administered the MenB-4C vaccine alone helped monitor the side effects specific to this vaccine in a more reliable manner.

England was the first country to include the MenB-4C vaccine in the national immunization program. In September 2015, the vaccine was started to be administered to infants to protect them from meningococcal B infections, and since then, studies have been published to prove the vaccine's safety and effectiveness.[9,17] In a meta-analysis conducted in 2018, it was reported that a high fever and local and systemic reactions were observed at a higher rate after the MenB-4C vaccine compared to other vaccines, but they were mild-moderate, short-term, and self-limiting.[18] Among the 43,000 doses of vaccine administered under the Quebec national immunization program, only two cases of bronchospasm were reported as serious vaccine-related reactions, and fever and local pain were the most common side effects.[13]

In a prospective cohort study conducted in the United Kingdom, approximately three million doses of vaccine were administered to 1.29 million children aged 0-18 months, and side effects were reported at a rate of 0.03% (n=902). The most common side effects were fever (41%, n=366), local reactions (40%, n=364), convulsions (6%, n=55), Kawasaki disease (<1%, n=3), and sudden infant death (<1 %, n=5).[19] In another study conducted in United Kingdom to investigate safety of 4CMenB, a total of 107,231 children aged 1–18 months received one doses of 4CMenB vaccination. Most 4CMenB exposure (93%) was on the same day as other vaccines within a complete national immunisation program stage. Adjusted incidence rate ratios including all 4CMenB exposures were 1.43 (95%CI: 1.02–2.02) for seizures and 1.72 (95%CI: 1.08–2.75) for febrile seizures. This study shows few cases of the outcomes after vaccination including 4CMenB with an increased risk of seizures and febrile seizures. But it is not possible to attribute the finding to one specific vaccination as the majority of 4CMenB was given with other vaccinations.[20] Such serious reactions were not observed in our study, and the vaccine side effects in our patients were acceptable, transient, and self-limiting.

Following the first dose of prophylactic paracetamol given immediately before or during MenB-4C vaccine administration, two additional doses four to six hours apart have been shown to reduce the frequency of post-vaccination fever and other related vaccine reactions without altering the immune response.[21] In a previous study, it was shown that while the use of the MenB-4C vaccine and prophylactic antipyretic in children under two years of age decreased the incidence of fever by 44%, there was a decrease of 22% in older children (five to 16 years old).[22] In our study, no statistically significant results were obtained when the effect of antipyretic administration before vaccination was examined according to the side effect status. This was attributed to our patients not using prophylactic paracetamol. Although the patients included in our study had received paracetamol before vaccination, they did not require any additional doses in the absence of side effects in the post-vaccination period.

In our Child Health Follow-up Outpatient Clinic before administration of MenB-4C, the parents were informed about common mild side effects of vaccination. For only one of the eight patients who did not complete their MenB-4C vaccine doses, the reason for discontinuation was related to the side effects experienced after the first dose. In a study conducted in 2016 to evaluate the views of parents and adolescents regarding the acceptability of the vaccine during the vaccination campaign initiated with the MenB-4C vaccine in Quebec, a serogroup B endemic region, a telephone interview was conducted with families. They reported that the main reasons for the refusal or discontinuation of vaccination were a lack of information about vaccination or time constraints. Negative perceptions of vaccine safety or the reporting of adverse events after the administration of a vaccine dose were not associated with vaccine rejection.[23]

In a study examining the attitudes of parents to vaccination in the United Kingdom, the majority of participants chose immunization with MenB-4C because they could not afford to risk invasive meningococci despite high fever rates.[24] In our study, it was observed that only one patient did not complete the vaccination schedule due to side effects, and that 92.2% (n=94) of the children received complete vaccine doses scheduled according to their age.

CONCLUSION

Similar to the literature, we determined that local and systemic reactions after MenB-4C administration were mostly self-limiting and transient. The MenB-4C vaccine, which is currently licensed in many countries and has also taken its place in the vaccination guidelines of most countries, will lead to significant progress in the fight against meningococcal B infections. Healthcare professionals have a significant role in increasing vaccine acceptance and the vaccination rates of vaccines that are not included in the NVC. Therefore, we believe that providing information about the vaccine and its side effects to every family presenting to a health institution, regardless of their income or the age of their children, will increase the vaccination rates.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Gazi University Ethics Committee (Date: 27.07.2023, Decision No: 14).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Ladhani SN, Campbell H, Parikh SR, Saliba V, Borrow R, Ramsay M. The introduction of the meningococcal B (MenB) vaccine (Bexsero®) into the national infant immunisation programme--New challenges for public health. J Infect. 2015;71(6):611-4. (
2. Edmond K, Clark A, Korczak VS, Sanderson C, Griffiths UK, Rudan I. Global and regional risk of disabling sequelae from bacterial meningitis: a systematic review and meta-analysis. Lancet Infect Dis. 2010;10(5):317-28.
3. Jafri RZ, Ali A, Messonnier NE, et al. Global epidemiology of invasive meningococcal disease. Popul Health Metr. 2013;11(1):17.
4. Centers for Disease Control and Prevention. Meningococcal home. Meningococcal disease in other countries. (Accessed August 30, 2022, available at https://www.cdc.gov/meningococcal/global.html)
5. Ceyhan M, Yildirim I, Balmer P, et al. A prospective study of etiology of childhood acute bacterial meningitis, Turkey. Emerg Infect Dis. 2008;14(7):1089-96.
6. Meningitis caused by Neisseria Meningitidis, Hemophilus Influenzae Type B and Streptococcus Pneumoniae during 2005-2012 in Turkey. A multicenter prospective surveillance study. Hum Vaccin Immunother. 2014;10(9):2706-12.
7. Marshall HS, Koehler AP, Wang B, et al. Safety of meningococcal B vaccine (4CMenB) in adolescents in Australia. Vaccine. 2020;38(37):5914-22.
8. Manolya, K. and A. SOMER. Meningokok Aşıları. Çocuk Derg 19 (2): 51-9.
9. Vesikari T, Esposito S, Prymula R, et al. Immunogenicity and safety of an investigational multicomponent, recombinant, meningococcal serogroup B vaccine (4CMenB) administered concomitantly with routine infant and child vaccinations: results of two randomised trials. Lancet. 2013;381(9869):825-35.
10. Santolaya ME, O'Ryan ML, Valenzuela MT, et al. Immunogenicity and tolerability of a multicomponent meningococcal serogroup B (4CMenB) vaccine in healthy adolescents in Chile: a phase 2b/3 randomised, observer-blind, placebo-controlled study. Lancet. 2012;379(9816):617-24.
11. U Özdemir, T Çelik, et al. Pediatristlerin meningokok enfeksiyonları ve aşıları ile ilgili bilgi düzeyleri ve tutumları. J Pediatr Inf 12 (2018): 58-64.
12. Toneatto D, Pizza M, Masignani V, Rappuoli R. Emerging experience with meningococcal serogroup B protein vaccines. Expert Rev Vaccines. 2017;16(5):433-51.
13. De Serres C, Gariépy M-C, Billard M-N, Rouleau I. Initial dose of amulticomponent serogroup B meningococcal vaccine in the Saguenay-Lac-Saint-Jean region, Québec, Canada: an interim safety surveillance report. 2014. https://www.inspq.qc.ca/pdf/publications/1902_SerogroupB_Meningococcal_Vaccine.pdf (accessed Dec 24, 2022).
14. Varricchio F, Iskander J, Destefano F, et al. Understanding vaccine safety information from the Vaccine Adverse Event Reporting System. Pediatr Infect Dis J. 2004;23(4):287-94.
15. McMahon AW, Iskander J, Haber P, et al. Adverse events after inactivated influenza vaccination among children less than 2 years of age: analysis of reports from the vaccine adverse event reporting system, 1990-2003. Pediatrics. 2005;115(2):453-60.
16. Gossger N, Snape MD, Yu LM, et al. Immunogenicity and tolerability of recombinant serogroup B meningococcal vaccine administered with or without routine infant vaccinations according to different immunization schedules: a randomized controlled trial. JAMA. 2012;307(6):573-82.
17. Parikh SR, Andrews NJ, Beebeejaun K, et al. Effectiveness and impact of a reduced infant schedule of 4CMenB vaccine against group B meningococcal disease in England: a national observational cohort study. Lancet. 2016;388(10061):2775-82.
18. Flacco ME, Manzoli L, Rosso A, et al. Immunogenicity and safety of the multicomponent meningococcal B vaccine (4CMenB) in children and adolescents: a systematic review and meta-analysis. Lancet Infect Dis. 2018;18(4):461-72.
19. Bryan P, Seabroke S, Wong J, et al. Safety of multicomponent meningococcal group B vaccine (4CMenB) in routine infant immunisation in the UK: a prospective surveillance study. Lancet Child Adolesc Health. 2018;2(6):395-403.
20. Hall GC, Douglas I, Heath PT, et al. Postlicensure observational safety study after meningococcal B vaccine 4CMenB (Bexsero) vaccination within the routine UK immunisation program. Vaccine. 2021;39(24):3296-330.
21. N. Prymula R, Esposito S, Zuccotti GV, et al. A phase 2 randomized controlled trial of a multicomponent meningococcal serogroup B vaccine (I): effects of prophylactic paracetamol on immunogenicity and reactogenicity of routine infant vaccines and 4CMenB. Hum Vaccin Immunother. 2014; 10:1993–2004.
22. Insititut National de Sante Publique du Quebec. Rapport final de surveillance de la Securite de la vaccination des jeunes de 20 ANS et Moins Contre Le Meningococque de Serogroupe B Au Saguenay-Lac-Saint-Jean, 2016.
23. E Dubé, D Gagnon, M Ouakki, et al. Meningococcal B vaccine acceptability: Results of a longitudinal study in Quebec (Canada). Vaccine Reports, 2016;6:29-35.
24. Jackson C, Yarwood J, Saliba V, Bedford H. UK parents' attitudes towards meningococcal group B (MenB) vaccination: a qualitative analysis. BMJ Open. 2017;7(4):e012851. Published 2017 May 4.