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Evaluation of Adverse Effects After MenACWY-TT Vaccination in Children and Adults

Çocuk ve Erişkinlerde MenACWY-TT Aşılama Sonrasında Yan Etkilerin Değerlendirilmesi

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Abstract

Objective: *Neisseria meningitidis* infections have high mortality and morbidity (10-20% and 15%, respectively), but can be prevented by vaccination. Conjugated MenACWY-TT vaccine is a safe vaccine approved for use in both children and adults. Knowing the side effects plays an important role in the acceptance of vaccines by both the physician and the society. In our study, it was aimed to evaluate the side effects in children and adults who were vaccinated with MenACWY-TT.

Material and Methods: MenACWY-TT vaccines, which are available for use in pilgrimage and umrah travel vaccinations, at Konya Health Directorate, were administered to healthy volunteers by Selçuk University Faculty of Medicine, Family Medicine and Pediatric Infectious Diseases and Necmettin Erbakan University Meram Medical Faculty Pediatric Infectious Diseases departments. Vaccine recipients were observed for 30 minutes for acute adverse events. After vaccination, a survey research was planned, and contact information of the vaccinated people was obtained. One month after vaccination, demographic information, chronic diseases, and side effects from previous routine vaccinations were recorded for individuals who were contacted by phone and accepted the questionnaire. Local and systemic side effects that developed in the first month period after vaccination were questioned. The volunteer group was examined in two groups as under 18 years old and over.

Results: Six hundred and nineteen individuals (310 children-309 adults) were included in the study. Mean age of the subjects included in the study

Öz

Giriş: *Neisseria meningitidis* enfeksiyonları mortalitesi ve morbiditesi yüksek (sırasıyla %10-20 ve %15), ancak aşı ile önlenebilir hastalıklardandır. Konjuge MenACWY-TT aşısı hem çocuk ve hem de erişkinlerde kullanımı onaylı, güvenli aşılardır. Yan etkilerinin bilinmesi, aşıların hem hekim hem de toplum tarafından kabulünde önemli rol oynamaktadır. Çalışmamızda MenACWY-TT aşılaması yapılan çocuk ve erişkinlerde yan etkilerin değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntemler: Konya Sağlık Müdürlüğünde hac ve umre seyahat aşılamasında kullanılmak üzere bulunan MenACWY-TT aşıları, Selçuk Üniversitesi Tıp Fakültesi Aile Hekimliği ve Çocuk Enfeksiyon Hastalıkları ile Necmettin Erbakan Üniversitesi Meram Tıp Fakültesi Çocuk Enfeksiyon Hastalıkları Bilim Dallarınca, sağlıklı gönüllü bireylere yapılmıştır. Aşı alıcıları 30 dakika akut yan etki açısından gözlenmiştir. Aşılama sonrasında anket çalışması planlanmış, aşılanmış kişilerin iletişim bilgilerine ulaşılmıştır. Aşılamadan bir ay sonra, telefonla ulaşılan ve anket çalışmasını kabul eden bireylerin demografik bilgileri, kronik hastalıkları, daha önceki rutin aşılarda oluşmuş yan etkiler kaydedilmiştir. Aşılamadan sonraki bir aylık süreçte gelişen lokal ve sistemik yan etkiler sorgulanmıştır. Gönüllü grubu 18 yaş altı ve üstü olmak üzere iki grupta incelenmiştir.

Bulgular: Çalışmaya 619 kişi (310 çocuk-309 erişkin) dahil edildi. Bireylerin ortalama yaşı 22.5 ± 18.2 yıldı. Komorbiditesi olan erişkinlerde (n= 37, %12) aşılama oranı çocuklara (n= 22, %7.1) göre daha yüksek saptandı. Aşı yan etkileri 35 (%11.3)'i çocuk, 53 (%17.2)'ü erişkin, toplam 88 (%14.2)

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was 22.5 ± 18.2 years. Vaccination rate was found to be higher in adults with comorbidities (n= 37, %12) than in children (n= 22, %7.1). Vaccine side effects were detected in 88 (14.2%) individuals, 35 (11.3%) were children and 53 (17.2%) were adults. The most common local side effects were pain (n= 43; 6.9%), redness (n= 15, 2.4%) and swelling (n= 11, 1.8%). Pain complaints were statistically higher in adults than in children (p= 0.039). The most common systemic side effects were fever (n= 18, 2.9%), fatigue (n= 9, 1.5%) and nausea (n= 7, 1.1%). There was no statistical difference between children and adults in terms of systemic side effects.

Conclusion: Local and systemic side effects in children and adults vaccinated with MenACWY-TT were lower than reported in the literature. We think that the low side-effect profile will make a significant contribution to vaccine acceptance.

Keywords: Adult, child, meningococcal vaccine, vaccine safety

kişide saptandı. Lokal yan etki olarak en sık ağrı (n= 43, %6.9), kızarıklık (n= 15, %2.4) ve şişlik (n= 11, %1.8) saptandı. Ağrı şikayeti erişkinlerde çocuklara göre istatistiksel olarak daha yüksekti (p= 0.039). Sistemik yan etkilerden en sık ateş (n= 18, %2.9), yorgunluk (n= 9; %1.5) ve bulantı (n= 7; %1.1) gözlendi, çocuk ve erişkinler arasında istatistiksel anlamlı fark gözlenmedi.

Sonuç: MenACWY-TT ile aşılanan çocuk ve erişkinlerde lokal ve sistemik yan etkiler literatürde bildirilen değerlerden düşük bulunmuştur. Düşük yan etki profilinin aşı kabulüne önemli katkı sağlayacağını düşünmekteyiz.

Anahtar Kelimeler: Erişkin, çocuk, meningokok aşısı, aşı güvenliği

Introduction

Neisseria meningitidis is a gram-negative, encapsulated bacterium that causes a wide spectrum of diseases from isolated infections such as meningitis, pneumonia, arthritis to fulminant septic shock. In our country, it is one of the most common causes of community-acquired meningitis in children (1). *N. meningitidis* is classified into 13 serogroups according to the polysaccharide composition in the capsule, and the most common serotypes causing invasive disease are serogroups A, B, C, W, X, and Y (2). *N. meningitidis* colonizes mucosal surfaces of the nasopharynx. It can be transmitted directly by droplets from patients or asymptomatic carriers. Nasopharyngeal carriage rates are high in adolescents and young adults (8-25%) (3).

In *N. meningitidis* infections, the clinic usually develops rapidly and despite appropriate antimicrobial therapy, morbidity (10-20%) (neurological sequelae, extremity losses, hearing loss, etc.), and mortality (15%) are high (4-5). Early recognition of meningococcal disease, prompt diagnosis and initiation of antimicrobial therapy are life-saving.

Although the incidence of the disease is highest in infants <1 year old, it is also common in adolescents and young adults aged 16-20 (4). According to the surveillance of invasive meningococcal infections in the USA in 2018, the incidence was reported as 0.1/100.000, 0.83/100.000 in infants, 0.18/100.000 in children aged 1-4 years, 0.14/100.000 in children aged ≥65 years, and 0.10/100.000 in adolescents and young adults. Serogroup W was 12.8%, serogroup C was 12%, serogroup Y was 10.8%, and serogroup B was 6.9% (6). In the serotype evaluation of pediatric patients, who constituted 37.5% of the individuals in the invasive meningococcal infections surveillance study conducted by Ceyhan et al. in Türkiye, there were 66.7% (n= 36) MenB, 18.5% (n= 10) MenW, 7.4% (n= 4) MenA, 5.6% (n= 3) MenY, and 1.8% (n= 1) MenX (1).

Viral infection, smoking, being in a crowded environment (dormitory, military service, pilgrimage, umrah), homosexuality in men are important risk factors. Complement deficiency, those using complement inhibitors (eculizumab, ravulizumab), anatomical or functional asplenia, people with acquired immunodeficiency infection, microbiologists working with *N. meningitidis* isolates, individuals traveling to countries where meningococcal disease is hyperendemic or endemic are defined as high risk group for meningococcal infection (7).

Today, conjugated and polysaccharide meningococcal vaccines containing invasive infectious serotypes are produced. Polysaccharide vaccines do not produce a strong immune response and are not effective enough to prevent nasopharyngeal carriage. In our country, MPSV4 (A/C/Y/W-135) purified meningococcal capsular polysaccharide vaccines, quadrivalent conjugated meningococcal (MenACWY) vaccines (2012); 1) A, C, W, and Y polysaccharide diphtheria toxoid conjugate vaccine (MenACWY-D); 2) A, C, W and Y oligosaccharide diphtheria CRM197 conjugate vaccine (MenACWY-CRM); 3) Meningococcal groups A, C, W and Y polysaccharide tetanus toxoid (TT) conjugate vaccine (MenACWY-TT, Nimenrix®) and serogroup B meningococcal vaccines (MenB) MenB-4C are used under license.

To prevent the development of invasive meningococcal disease, MenACWY vaccination recommendation of the Advisory Committee on Immunization Practices (ACIP-2020) is as such: adolescents (11-12 years old), individuals ≥2 months at risk for invasive meningococcal disease; those with anatomical or functional asplenia or complement (properdin, factor D, factor H and C5-C9) deficiency, those who are in institutions such as military barracks, boarding schools where the unvaccinated or incompletely vaccinated population is dense, microbiologists at risk of occupational exposure, and those travelling to regions where meningococcal disease is hyperendemic (8).

MenACWY-TT (Nimenrix®) is a TT-conjugated non-viable vaccine containing *N. meningitidis* serotypes A, C, W135 and Y. In Türkiye, in December 2017, consent was obtained for the application in patients older than six weeks. In our country, meningococcal vaccines are special vaccines that are not included in the routine vaccination schedule and are administered with the recommendation of a doctor. In our study, demographic characteristics, comorbidities, local and systemic side effects that developed immediately after vaccination and

within a month of vaccination were evaluated in 619 individuals vaccinated with MenACWY-TT.

Materials and Methods

Due to the novel Coronavirus Disease (COVID-19) pandemic, international travel restrictions had to be made in 2020. Due to the pandemic in our country, Hajj and Umrah trips could not be realized in 2020. MenACWY-TT, which is in the Health Directorate to be used in the pilgrimage and Umrah travel vaccination, had been sent to Selçuk Faculty of Medicine, Family Medicine and Pediatric Infectious Diseases Departments and Necmettin Erbakan University of Meram Faculty of Medicine, Department of Pediatric Infectious Diseases. Vaccines were given to healthy volunteers. Individuals who agreed to be vaccinated with verbal information, did not receive immunosuppressive treatment, and did not have any signs of acute infection were vaccinated. All vaccination was completed within one week, and acute side effects were observed up to 30 minutes after vaccination of vaccine recipients. After vaccination, a survey was planned and contact information of the vaccinated people was obtained. One month after vaccination, demographic information, chronic diseases, and side effects from previous routine vaccinations were recorded of the individuals and parents who accepted telephone questionnaire. Local and systemic side effects that developed in the one-month period after vaccination were questioned.

In this cross-sectional survey study; swelling, pain, temperature increase, redness, hematoma formation at the injection site as local side effects that occurred in people within a month after vaccination and when the complaints occurred after the vaccination and how long they lasted were questioned. Systemic side effects including fever, anorexia, nausea, diarrhea, vomiting, abdominal pain, cough, respiratory distress, nervousness, restlessness, insomnia, seizure, excessive crying, tremor, fatigue, lethargy, headache, earache, itching, rash, myalgia, arthralgia findings were recorded. How many days after vaccination the symptoms began and how long they persisted were recorded. Telephone interviews with the patients were completed in one week by four researchers. Information was given about the follow-up of late side effects (Guillan-Barre, transverse myelitis) that may occur within six months after vaccination, and a phone number where they could apply to the hospital and contact them was given. Individuals were divided into two groups as children (<18 years old) and adults (18≥) and the differences between side effects were evaluated statistically. This study was conducted with the approval of the non-invasive clinical research ethics committee of our hospital (No: 2021/88).

Statistical Analysis

The data obtained in the study were statistically analyzed with SPSS version 22.0 for Windows. Quantitative variables were expressed as mean ± standard deviation, and categorical variables as numbers (n) and percentages (%). Pearson's chi-square test, Fisher's exact test and Yates corrected chi-square test were used for the analysis of qualitative data in statistical evaluations. Mann-Whitney U test was used in the analysis of quantitative data. Statistical significance was determined as $p< 0.05$.

Results

Demographic Characteristics of the Vaccinated Individuals and Local Vaccine Side Effects

MenACWY-TT vaccine was given to 820 people on a voluntary basis in Selcuk University Faculty of Medicine, Department of Family Medicine and Pediatric Infectious Diseases, and Necmettin Erbakan University Meram Faculty of Medicine, Department of Pediatric Infectious Diseases. Verbal consent was obtained from the parents of the children. Side effects that may have developed for 30 minutes after vaccination were observed, but no side effects were detected. Eight hundred twenty people who were vaccinated were called one month after vaccination, and 619 people who could be reached were questioned in terms of vaccine side effects.

Of those vaccinated, 50.1% (n= 310) were children and 49.9% (n= 309) were adults. None of the vaccinated individuals had any predisposing factors for meningococcal infection except age, and none of them had previously received meningococcal vaccine. Mean age of all individuals was 22.5 ± 18.2 years, 7.4 ± 4.6 years for children and 37.7 ± 13.5 years for adults. There was no statistically significant difference between the sexes in both groups.

Comorbidity was present in 59 (9.5%) of the vaccinated individuals. Adult asthma (n= 8), diabetes (n= 6), hypertension (n= 5), coronary artery disease (n= 4), malignancy (n= 3), rheumatoid arthritis (n= 2), autoimmune hepatitis (n= 2), unspecified immunodeficiency (n= 1), arrhythmia (n= 1), vertigo (n= 1), Hashimoto's thyroiditis (n= 1), multiple sclerosis (n= 1), chronic renal failure (n= 1), history of ventriculoperitoneal shunt (n= 1) were detected. Autoimmune hepatitis (n= 6), asthma (n= 4), unspecified immunodeficiency (n= 3), epilepsy (n= 2), rheumatoid arthritis (n= 1) were comorbidities in 7.1% (n= 22) of the children. Crohn's disease (n= 1), chronic renal failure (n= 1), cystic fibrosis (n= 1), growth retardation (n= 1), atopy (n= 1) and bronchopulmonary dysplasia (n= 1) were detected. While the incidence of local vaccine side effects was statistically higher in those with comorbidities (p= 0.08), no significant difference was found in terms of systemic side effects (p= 0.629). While 12% of the adults (n= 37) had a comorbid disease, 7.1% (n= 22) of the children had a comorbid disease, and a statistically significant difference was found between the groups (p= 0.039).

Non-serious local side effects, which were remembered in the previous routine non-meningococcal vaccinations, were reported in 10 (1.6%) people, in six (1.9%) children and four (1.6%) adults.

In the first month after the MenACWY-TT vaccine, side effects were detected in 35 (11.3%) children and 53 (8.6%) adults, in a total of 88 (14.2%) individuals. There was no statistically significant difference between adults and children in the frequency of side effects. In 53 (8.6%) of the vaccinated individuals, local side effects were detected in 22 (7.1%) of the children and 31 (10%) of the adults. The most common side effects were pain (n= 43, 6.9%) and redness (n= 15, 2.4%). While the rate of pain complaints was statistically higher in adults than in children (p= 0.039), no significant difference was found in other side effects. Demographic characteristics and local side effects of vaccinated children and adults are summarized in Table 1.

Evaluation of Systemic Side Effects of the Vaccinated Individuals

Systemic side effects that may occur in vaccinated individuals include fever, fatigue, nausea, restlessness, lethargy, headache, myalgia, diarrhea, abdominal pain, cough, nervousness, insomnia, excessive crying, tremor, rash, and myalgia, and their findings were evaluated. Systemic side effects were detected in 6.8% (n= 42) of those who were vaccinated. A systemic side effect developed in 8.1% of adults (n= 25) and 5.5% of children (n= 17).

Fever [18 (2.9%)] was the most common side effect, starting one day after vaccination and continuing for 2.5 ± 1.5 days. When the signs of loss of appetite, vomiting, respiratory distress, seizures, ear pain, itching, and arthralgia were questioned, it was stated that there were no signs in any of the patients. The frequency of systemic side effects was similar in children and adults (p= 0.197). Findings of systemic side effects of vaccinated children and adults are summarized in Table 2.

Table 1. Evaluation of demographic characteristics and local side effects of children and adults vaccinated with men ACWY-TT

Age groups	Children (n= 310)	Adults (n= 309)	Total (n= 619)	p
Age (X ± SS)	7.4 ± 4.6	37.7 ± 13.5	22.5 ± 18.2	-
Sex				
Female, n (%)	162 (52.3%)	170 (55.0%)	332 (53.6%)	0.491*
Male, n (%)	148 (47.7%)	139 (45.0%)	287 (46.4%)	
Comorbidity				
Present, n (%)	22 (7.1%)	37(12.0%)	59 (9.5%)	**0.039***
Absent, n (%)	288 (92.9%)	272 (88.0%)	560 (90.5%)	
Previous history of vaccine side effect				
Present, n (%)	6 (1.9%)	4 (1.3%)	10 (1.6%)	0.752**
Absent, n (%)	304 (98.1%)	305 (98.7%)	609 (98.4%)	
MenACWY-TT side effect, n (%)	35 (11.3%)	53 (17.2%)	88 (14.2%)	0.037*
Vaccine local side effect, n (%)	22 (7.1%)	31 (10%)	53 (8.6%)	0.192*
Pain, n (%)	15 (4.8%)	28 (9.1%)	43 (6.9%)	**0.039***
Day (after vaccine) (X ± SS)	1.1 ± 0.3	1.1 ± 0.3	1.1 ± 0.3	0.667****
Duration (X ± SS)	2.4 ± 1.2	3.0 ± 1.9	2.8 ± 1.7	0.317****
Redness, n (%)	10 (3.2%)	5 (1.6%)	15 (2.4%)	0.299***
Day (after vaccine) (X ± SS)	1.1 ± 0.3	1.0 ± 0.0	1.1 ± 0.3	0.480****
Duration (X ± SS)	2.7 ± 1.6	3.4 ± 1.9	2.9 ± 1.7	0.489****
Swelling, n (%)	5 (1.6%)	6 (1.9%)	11 (1.8%)	0.996***
Day (after vaccine) (X ± SS)	1.4 ± 0.5	1.0 ± 0.0	1.2 ± 0.4	0.134****
Duration (X ± SS)	3.8 ± 1.6	3.6 ± 1.5	3.7 ± 1.5	0.914****
Increase in temperature, n (%)	2 (0.6%)	2 (0.6%)	4 (0.6%)	1.000**
Day (after vaccine) (X ± SS)	1.5 ± 0.7	1.0 ± 0.0	1.3 ± 0.5	0.317****
Duration (X ± SS)	3.5 ± 2.1	1.5 ± 0.7	2.5 ± 1.7	0.221****

*Pearson's chi-square test.
**Fisher's Exact test.
***Yates corrected chi-square test.
****Mann-Whitney U test.

Discussion

The MenACWY-TT vaccine formulation contains 0.5 mg each of the four polysaccharides conjugated to 44 mg TT to which sucrose and trometamol are added. It is in the form of a sterile lyophilized white powder in a single-dose bottle (8). MenACWY-TT vaccine was approved for use in individuals older than one year in Europe in 2012 and in infants older than six weeks in November 2016. It is administered in two doses at two months apart in infants at 6-12 weeks of age, and as a booster dose at 12 months, and as a single dose for children over one year old and adults. In phase 2 and 3 studies, MenACWY-TT was found to be highly immunogenic and safe for all four serogroups in the first dose or booster applications. In addition, it is known that both vaccines can be administered together with other routine vaccines without adversely affecting their immunogenicity or safety (9).

While the most common reactions reported after MenACWY-TT vaccination are pain, redness, and swelling in infants, irritability, lethargy, anorexia, and fever are reported between 1-5 years of age, and headache, fatigue, gastrointestinal symptoms, and fever are reported in older age groups (10).

In our study, we tried to evaluate local and systemic side effects in children and adults vaccinated with MenACWY-TT. No serious systemic side effects such as respiratory distress, anaphylaxis, angioedema were detected in vaccinated children and adults. There was no significant difference in vaccine systemic side effects between healthy and comorbid individuals. For late-stage side effects, individuals were informed about serious systemic side effects that may occur in the first six months after vaccination, new-onset chronic diseases, and hospital admission was recommended, and there was no application during this period. Baxter et al.'s 784 adolescents and young adults vaccinated with MenACWY-TT were followed up for side effects at six months post-vaccination. Rash was reported in 2.4% of the individuals and serious systemic side effects were reported at a rate of 0.9% (hypotension, shock, anaphylaxis, etc.), but it was later found that systemic findings were not related to the vaccine, and no mortality was observed (11).

When the literature is evaluated, local and systemic effects found in children and adults in our study were similar, but the frequency of side effects was found to be low in our study. Although the onset time of systemic side effects is generally defined in the first week, it was observed in our study that side effects appeared in the first four days after vaccination. Although the data on the duration of side effects are limited in the literature, the duration of the findings in our patients is summarized in Table 1 and Table 2.

In the study of Merino Arribas et al., local and systemic side effects have been detected most frequently in the first eight days after vaccination in infants aged 6-12 weeks (n= 2095) vaccinated with MenACWY-TT. The most common local side effects have been reported as redness (29%), pain (27%), swelling (17%) at the injection site, while the most common systemic side effects have been established as restlessness (60%), lethargy (44%), anorexia (36%), and fever (28%). In the study of Borja-Tabora et al. (n= 374), urticaria has been detected eight days after vaccination in one patient and completely resolved (12-13).

Although the use of MenACWY-TT vaccine is stated as six weeks-55 years in clinical studies, it has been found to be safe in 274 individuals over 56 years of age who were vaccinated with one dose (14). The youngest of the vaccinated individuals in our study was six months old, and the oldest was 84 years old. No local or systemic side effects were detected in both. In children, total side effects were 11.3% (n= 35), local side effects were 7.1% (n= 22), and systemic side effects were 5.5% (n= 17). Pain and redness were the most common local side effects. Among the systemic side effects, fever was 2.6% (n= 8), fatigue, nausea, and headache were 0.6%, restlessness was 1%, diarrhea, abdominal pain, nervousness, insomnia, excessive crying, and rash were 0.3%. In the study of Klein et al., fever has been found at a rate of 3.3% in infants older than nine months and has not been measured above 40°C in any patient (15). In the study of Vannice et al., fever has been found frequently on the third and seventh days after conjugated meningococcal A vaccination (16).

In the study of Bona et al., a total of 202 healthy 12-15 months old children have received a dose of MenACWY-CRM or MenACWY-TT vaccine, and similar local and mild systemic findings have been found seven days after vaccination. The most common local side effects have been reported as pain (26%), swelling (4%), and redness (2%) in those who had MenACWY-TT. Systemic side effects have been found at a rate of 56.4%, and it has been reported that the most common side effects were restlessness (39.4%) fever (13%), insomnia-anorexia (26%), diarrhea (18.2%), and vomiting (9.1%). Antibody response and persistence have been found to be similar between the two groups, and it has been stated that both vaccines were well tolerated and no safety concerns were detected (17).

In the study of Ostergaard et al., in 175 adult individuals vaccinated with MenACWY-TT, pain has been detected to be the most common local side effect; and fatigue and headache have been found to be the most common systemic side effects (18). The most common local side effects in adolescent-young adults (10-55 years) are pain (35-45%), redness (5%), swelling (4-5%); systemic side effects were reported as myalgia (27-36%), headache (27-30%), fatigue (19-26%), fever (1%). Similar side effects were found in individuals aged ≥56 years with other age groups (19-20).

Table 2. Evaluation of systemic side effects in children and adults vaccinated with men ACWY-TT

Age groups	Children (n= 310)	Adults (n= 309)	Total (n= 619)	p
Systemic side effect, n (%)	17 (5.5%)	25 (8.1%)	42 (6.8%)	0.197***
Fever, n (%)	8 (2.6%)	10 (3.2%)	**18 (2.9%)**	0.627***
Day (after vaccine) (X ± SS)	1.0 ± 0.0	1.0 ± 0.0	1.0 ± 0.0	1
Duration (X ± SS)	2.4 ± 1.2	2.5 ± 1.7	2.5 ± 1.5	0.879
Fatigue, n (%)	2 (0.6%)	7 (2.3%)	**9 (1.5%)**	0.107**
Day (after vaccine) (X ± SS)	1.5 ± 0.7	1.1 ± 0.4	1.2 ± 0.4	0.312
Duration (X ± SS)	1.0 ± 0.0	2.1 ± 0.7	1.9 ± 0.8	0.06
Nausea, n (%)	2 (0.6%)	5 (1.6%)	**7 (1.1%)**	0.286**
Day (after vaccine) (X ± SS)	2.0 ± 0.0	1.0 ± 0.0	1.0 ± 0.0	1
Duration (X ± SS)	2.0 ± 0.0	2.0 ± 0.7	2.0 ± 0.6	1
Discomfort, n (%)	3 (1.0%)	-	**3 (0.5%)**	0.249**
Day (after vaccine) (X ± SS)	2.0 ± 0.0	-	2.0 ± 0.0	-
Duration (X ± SS)	2.7 ± 0.6	-	2.7 ± 0.6	-
Lethargy, n (%)	-	3 (1.0%)	**3 (0.5%)**	0.124**
Day (after vaccine) (X ± SS)	-	1.0 ± 0.0	1.0 ± 0.0	-
Duration (X ± SS)	-	6.0 ± 7.0	6.0 ± 7.0	-
Headache, n (%)	2 (0.6%)	1 (0.3%)	**3 (0.5%)**	1.000**
Day (after vaccine) (X ± SS)	1.0 ± 0.0	1.0	1.0 ± 0.0	1
Duration (X ± SS)	3.5 ± 2.1	2.0	3.0 ± 1.7	0.480
Myalgia, n (%)	-	3 (1.0%)	**3 (0.5%)**	0.124**
Day (after vaccine) (X ± SS)	-	1.3 ± 0.6	1.3 ± 0.6	-
Duration (X ± SS)	-	2.7 ± 1.2	2.7 ± 1.2	-
Diarrhea, n (%)	1 (0.3%)	-	**1 (%0.2)**	1.000**
Day (after vaccine) (X ± SS)	2.0	-	2.0	-
Duration (X ± SS)	1.0	-	1.0	-
Abdominal pain, n (%)	1 (0.3%)	-	**1 (0.2%)**	1.000**
Day (after vaccine) (X ± SS)	2.0	-	2.0	-
Duration (X ± SS)	1.0	-	1.0	-
Cough, n (%)	-	1 (0.3%)	**1 (0.2%)**	0.499**
Day (after vaccine) (X ± SS)	-	1.0	1.0	-
Duration (X ± SS)	-	3.0	3.0	-
Irritability, n (%)	1 (0.3%)	-	**1 (0.2%)**	1.000**
Day (after vaccine) (X ± SS)	1.0	-	1.0	-
Duration (X ± SS)	3.0	-	3.0	-
Insomnia, n (%)	1 (0.3%)	-	**1 (0.2%)**	1.000**
Day (after vaccine) (X ± SS)	2.0	-	2.0	-
Duration (X ± SS)	3.0	-	3.0	-
Excessive crying, n (%)	1 (0.3%)	-	**1 (0.2%)**	1.000**
Day (after vaccine) (X ± SS)	2.0	-	2.0	-
Duration (X ± SS)	3.0	-	3.0	-
Shivering, n (%)	-	1 (0.3%)	**1 (0.2%)**	0.499**
Day (after vaccine) (X ± SS)	-	1.0	1.0	-
Duration (X ± SS)	-	4.0	4.0	-
Rash, n (%)	1 (0.3%)	-	**1 (%0.2)**	1.000**
Day (after vaccine) (X ± SS)	2.0	-	1.0 ± 0.0	-
Duration (X ± SS)	1.0	-	3.5 ± 2.1	-

*Pearson's chi-square test.
**Fisher's exact test.
***Yates corrected chi-square test.

In our study, pain at the vaccination site was found to be statistically higher in adults, and unlike children, diarrhea and abdominal pain were not observed. When other local and systemic side effects were evaluated in adults and children, no significant difference was found. Side effects were found in 53 (17.2%) individuals, local side effects were detected in 31 (10%) and systemic side effects in 25 (8.1%) individuals. Among the local side effects, pain was detected as 9.1% (n= 28), redness as 1.6% (n= 5), swelling as 1.9% (n= 6), and temperature increase as 0.6% (n= 2). There were fever at a rate of 3.2% (n= 10), fatigue at a rate of 2.3% (n= 7), 1.6% (n= 5), lethargy at a rate of 1% (n= 3), headache at a rate of 0.3% (n= 1), myalgia at a rate of 1% (n= 3), and cough and shivering at a rate of 0.3% (n= 1).

In the study of Barjo-Tabora et al., 500 previously healthy individuals (11-55 years old) have been vaccinated with MenACWY-TT (n= 374) or meningococcal polysaccharide vaccine (n= 126), and immune response and side effects have been evaluated. It has been observed that systemic and local side effects were common in the four-day period after vaccination in the one-month follow-up related to vaccine side effects. Pain at the injection site was the most common local side effect with a rate of 38.6% in MenACWY-TT recipients and 32.3% in Men-PS recipients. The most common systemic side effect was headache in both groups (17.5% for MenACWY-TT, 12% for Men-PS). Redness and swelling at the injection site were higher in the MenACWY-TT group (15.4%; 11.4%) compared to Men-PS (6.5%, 3.2%). The reason for the frequent occurrence of local side effects in conjugated vaccines is thought to be due to the TT component. Fatigue (15%), fever (5%), and gastrointestinal findings (4%) were found in the MenACWY-TT group (12).

In the survey conducted by Elitok et al. on meningococcal vaccination in 2019, 59.4% of mothers (n= 426) who had children aged 3-59 months stated that they knew that the meningococcal vaccine was protective against meningitis, 3.5% did not find the vaccine safe, and 1.6% did not get vaccinated due to serious side effects of the vaccine. The rate of meningococcal vaccination was found to be 24.9% in the study, and it was reported that most of the mothers had their children vaccinated after being informed about the vaccine (21). In our country, where vaccine rejection has become widespread recently, it is very important for physicians to give sufficient information to the individuals in the community about the protection and safety of routine or private vaccines in vaccine preference. In our study, we think that the evaluation of the side effects that may occur in adults and children after mass vaccination is valuable in informing the society and health workers.

Limitations of Our Study

MenACWY-TT vaccines available in the health directorate of two university hospitals in Konya were administered to volunteering children and adults. After the vaccination was completed, it was decided to conduct a questionnaire study to evaluate the side effects of the vaccine. Due to the COVID-19 pandemic, the questioning of the side effects that developed in the first month after vaccination in individuals was made over the phone. The fact that the study was planned after vaccination may have biased the data accuracy due to the memory status of parents of vaccinated adults and children or due to lack of attention to the subject.

In our study, 619 individuals were vaccinated in two centers over a one-week period, which is a significant mass vaccination. After vaccination, individuals were observed for only 30 minutes. Although verbal information was given about the side effects, no written document was given on this subject. However, we did not receive any application due to any side effects associated with the vaccine. In addition, it could not be objectively evaluated whether the side effects reported by those vaccinated or their parents were due to causes other than the vaccine. In our study, antibody response levels could not be evaluated.

Conclusion

Conjugated meningococcal vaccines seem to be the most important weapon against the disease in severe meningococcal infections that can be prevented by vaccination. Knowing the low side-effect profile of the vaccine, which is not in the routine vaccination schedule, by clinicians and patients will play an important role in increasing the confidence in the vaccine and keeping the vaccination rates high.

Ethics Committe Approval: This study was approved by Selçuk University Rectorate Local Ethics Committee (Decision no: 24.02.2021, Date: 2021/88).

Informed Consent: Patient consent was obtained.

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