HUMAN VACCINES & IMMUNOTHERAPEUTICS
2019, VOL. 15, NO. 1, 134–140
https://doi.org/10.1080/21645515.2018.1520586

Taylor & Francis
Taylor & Francis Group

RESEARCH PAPER

The attitudes, behaviors, and knowledge of healthcare professionals towards the diagnosis, treatment, and prevention of bacterial meningitis in Turkey

Meltem Dinleyici[a,b], Merve Iseri Nepesov[c], Oguz Resat Sipahi[d], Kursat Bora Carman[e], Omer Kilic[c], and Ener Cagri Dinleyici[a]

[a]Faculty of Medicine, Department of Pediatrics, Eskisehir Osmangazi University, Eskisehir, Turkey; [b]Faculty of Medicine, Department of Social Pediatrics, Eskisehir Osmangazi University, Eskisehir, Turkey; [c]Faculty of Medicine, Department of Pediatric Infectious Disease, Eskisehir Osmangazi University, Eskisehir, Turkey; [d]Faculty of Medicine, Department of Infectious Disease and Clinical Microbiology, Ege University, Izmir, Turkey; [e]Faculty of Medicine, Department of Pediatric Neurology, Eskisehir Osmangazi University, Eskisehir, Turkey

ABSTRACT

Introduction: Bacterial meningitis is one of the leading causes of morbidity and mortality among children and adults. Better understanding of the seroepidemiology of meningitis is critical for both the selection and implementation of an effective meningitis vaccine for the national immunization program. Because physicians play a crucial role in the implementation of this vaccine, the aim of this study was to evaluate the attitudes, behaviors, and knowledge of healthcare professionals in Turkey regarding the diagnosis, treatment and prevention of bacterial meningitis, especially pneumococcal and meningococcal meningitis.

Methods: This study used a cross-sectional electronic survey with a national convenience sample of 339 physicians (171 pediatric age specialists [PAS] and 168 adult patient specialists [APS]) in Turkey. A web-based questionnaire which consisted 28 questions about the definition, diagnosis, and treatment of bacterial as well as knowledge and/or attitudes about meningococcal vaccines, was designed.

Results: Approximately 72.9% (n = 247) of the respondents followed a patient with meningitis in the last year. A 49.5% of participants preferred to perform computerized cranial tomography (CCT) for suspected meningitis cases before lumbar puncture (LP) at 75–100% frequency (27.5% PAS; 72% APS, $p < .01$). In addition 27.1% of the respondents reported using a routine steroid as an adjunctive treatment (19% PAS; 35% APS, $p < .01$). For meningococcal meningitis, 72.5% of the participants preferred to use third-generation cephalosporins (63.1% PAS; 82.1% APS, $p < .05$). For pneumococcal meningitis, approximately 50% of the participants preferred to use a third-generation cephalosporin plus glycopeptide (41.5% PAS; 58.9% APS, $p < .05$). While 32.7% of the sample preferred to administer a 7-day course of antibiotics for meningococcal meningitis, 40.9% preferred a course of 14 days or more. For pneumococcal meningitis, 88.4% of the sample preferred a 10–14 day course of antibiotics. In addition, 67% of the PAS group and 50% ($p < .001$) of the APS group thought that a conjugated meningococcal vaccine should be a part of the National Immunization Program. The top five groups recommended for routine immunization included all children, asplenia/splenectomy patients, immunodeficient patients, those who planned to travel to endemic areas, including Hajj, and military personnel.

Conclusion: In this large convenient sample of physicians in Turkey, we showed that there are heterogenous approaches to the diagnosis and treatment of bacterial meningitis, also differences between pediatricians and non-pediatricians regarding their beliefs and attitudes, which may be due to differences in the epidemiology and clinical presentation between children and adults. We observed appropriate but unnecessary extended courses of antibiotics for meningitis. Most of the participants thought that children are a vulnerable risk group that should potentially be immunized and that meningococcal vaccines should be included in the National Immunization Program. Our results imply that more awareness is needed regarding diagnosis, treatment, and further recommendations for meningitis at the country level in Turkey.

ARTICLE HISTORY
Received 25 July 2018
Revised 13 August 2018
Accepted 29 August 2018

KEYWORDS
meningitis; Neisseria meningitidis; meningococcal infections; vaccine; meningococcal vaccine

Introduction

Bacterial infections of the central nervous system, mainly meningitis, continue to be an important cause of morbidity and mortality in children as well as adults. Etiological causes of meningitis vary by both patient age and geographical location. The widespread use of an available conjugated vaccine, which could include *Haemophilus influenzae type* B (Hib), *Streptooccus pneumoniae, and Neisseria meningitidis*, might also change the etiological causes of meningitis.[1,2] In Turkey, A 7-valent pneumococcal conjugated vaccine was introduced by the National Immunization Program in 2008, but it was switched to a 13-valent conjugated pneumococcal vaccine and has provided a 95% vaccine coverage among the age appropriate vaccine group. Although the quadrivalent conjugated meningococcal vaccine is marketed in Turkey, it has not been included in the National Immunization Program

CONTACT Ener Cagri Dinleyici, MD, PhD timboothtr@yahoo.com Faculty of Medicine, Department of Pediatrics, Eskisehir Osmangazi University, Eskisehir TR-26480, Turkey

to date. This vaccine is recommended for those who are traveling to the areas of Hajj and/or Umrah, and vaccine routinely applicated for military personnel. No meningococcal B vaccine are currently available in Turkey.[3-5] In children, after widespread use of the Hib and 13-valent conjugated pneumococcal vaccines among children, incidences of bacterial meningitis decreased, while *N. meningitidis* is a leading cause of meningitis in children (mainly due to serogroups W and B), followed by *S. pneumoniae*. No Hib meningitis cases have been reported since 2012, after the introduction of the Hib conjugated vaccine in 2008.[4,6,7] In adults, *S. pneumoniae* and *N. meningitidis* (*N. meningitidis*) are the major yielded bacteria among patients with bacterial meningitis.[8]

Better understanding of the seroepidemiology of meningitis is critical for both the selection and implementation of an effective meningitis vaccine in the national immunization program. Therefore, adequate surveillance is paramount for accurate epidemiological data and the subsequent initiation of appropriate prevention strategies.[4,9] A lumbar puncture (LP), which is the mainstay therapeutic approach for the diagnosis of bacterial meningitis, is crucial for making a differential diagnosis between bacterial meningitis and aseptic meningitis. A timely LP and appropriate cerebrospinal fluid (CSF) examination assist in proper treatment choices as well as the surveillance of potential causes of meningitis.[10] While there are official guidelines for the diagnosis and treatment of meningitis among children and adults, there is limited data about the beliefs, behavior's, and attitudes of physicians and their adherence to these guidelines. The European Society of Clinical Microbiology and Infectious Diseases (ESCMID) published a guideline in 2016 for central system infections, and the Infectious Disease Society of America published their recommendations in 2004 [10,11]; however, although meningitis is relevant in Turkey, no official guidelines have been developed there. Because different healthcare specialists have different attitudes about proper care, which are often due to their medical education and specialties, harmonization of procedures and treatment for meningitis are vital. The aim of this study was to evaluate the attitudes, behaviors, and knowledge of healthcare professionals in Turkey regarding the diagnosis and treatment of bacterial meningitis, including meningococcal/pneumococcal meningitis, and meningococcal vaccines.

Results

After a self-completion questionnaire was sent via email, including a SurveyMonkey questionnaire link, to a random selection of 600 physicians during the years 2017–2018, 406 physicians completed and returned the questionnaire; 67 participants were excluded because they did not follow-up with a meningitis case during their routine daily work.

We evaluated the completed questionnaires of 339 physicians aged 24–70 years (mean age 37.6 ± 8 years). Of the 339 participants, 171 were from the PAS group (107 pediatricians, 33 pediatric infectious disease specialists, and 31 pediatric intensive care or emergency specialists), and 168 were from the APS group (142 were infectious disease specialists, 17 were emergency specialists, and 9 were internal medicine specialists). Both the mean age and gender distributions of the PAS and APS groups were $p > .05$. In addition, 37.1% (126/339) of the physicians had attended educational activities about meningitis and/or vaccines for meningitis within the last three years.

Per the survey's results, approximately 72.9% (n = 247) of the respondents followed a patient with meningitis during the last year, and 71.9% (n = 244) of those had performed an LP as part of the diagnosis. Regarding meningococcal meningitis cases, while 25% of the PAS group had followed those cases within the last year, only 12% of the APS group had done so ($p < .01$). Similarly, 25% of the PAS group had followed meningococcemia cases during the last year, while 9.5% of the APS group had done so ($p < .001$).

Cranial computerized tomography (CCT) prior to an LP

The respondents were also asked how often they perform radiological tests (CCT) before conducting an LP. As shown in Table 2, 49.5% of the respondents preferred to use CCT 75–100% of the time for suspected meningitis cases before performing an LP. Notably, 36.5% (n = 171) of the PAS group preferred to perform CCT on <25% (n = 12) of their meningitis cases before performing an LP. While 27.5% of the PAS group (n = 47) performed cranial imaging 75–100% of the time before conducting an LP, this rate was significantly higher (72%, n = 121) among the APS group (Table 1).

Table 1. Percentage of ordering CCT before LP among physicians.

CCT before LP	PAS Group (n = 171)	APS Group (n = 168)	Total (n = 339)
<10%	n = 47 (27.5%)*	n = 12 (7%)	n = 59 (17.4%)
10–25%	n = 16 (9%)	n = 2 (1%)	n = 18 (5.3%)
25–50%	n = 25 (15%)	n = 13 (8%)	n = 38 (11.2%)
50–75%	n = 36 (21%)	n = 20 (12%)	n = 56 (16.5%)
75–100%	n = 47 (27.5%)	n = 121 (72%)*	n = 168 (49.6%)

*p < 0.05; PAS group vs. APS group.

Table 2. First-line antibiotic choice of physicians for meningococcal meningitis and pneumococcal meningitis.

	Penicillin	Third-generation cephalosporins	Third-generation cephalosporins + glycopeptide	Other
Meningococcal meningitis	13.2%	72.5%	2.9%	11.5%
TOTAL	(n = 45)	(n = 246)	(n = 10)	(n = 38)
Meningococcal meningitis	15.2%	63.1%	4%	17.5%
PAS group	(n = 26)	(n = 108)	(n = 7)	(n = 30)
Meningococcal meningitis	11.3%	82.1%	1.7%	4.7%
APS group	(n = 19)	(n = 138)	(n = 3)	(n = 8)
Pneumococcal meningitis	2.0%	29.7%	50.1%	20.6%
TOTAL	(n = 7)	(n = 101)	(n = 170)	(n = 61)
Pneumococcal meningitis	2.3%	25.1%	41.5%	30.9%
PAS group	(n = 4)	(n = 43)	(n = 71)	(n = 53)
Pneumococcal meningitis	1.7%	34.5%	58.9%	4.7%
APS group	(n = 3)	(n = 58)	(n = 99)	(n = 8)

CSF fluid examination

Approximately half (50.4%) of the sample performed a gram stain to evaluate the CSF when meningitis was suspected. While 77.3% of the participants preferred to evaluate the WBC with direct microscopy without using stain. 28% used an automatic cell counter. In addition, 69.6% of the respondents used the BACTEC blood culture system for bacteriological culture of the CSF sample, whereas 37.5% used an agar culture at the patient's bedside. Only 34% (115/339) used a PCR for routine detection of meningitis pathogens.

Corticosteroid use

In total, 27.1% of the respondents reported using routine steroids as an adjunctive treatment: 19% (33/171) PAS; 35% (59/168) APS ($p < .01$).

Treatment choice and duration for bacterial meningitis

The respondents' first-line antibiotic choices for meningococcal meningitis and pneumococcal meningitis are shown in Table 2. For meningococcal meningitis, 72.5% of the participants preferred to use third-generation cephalosporins (63.1% PAS; 82.1% APS, $p < .05$), and 13.2% preferred to use penicillin (15.2% PAS; 11.3% APS, $p > .05$). For pneumococcal meningitis, approximately 50% of the participants preferred to use third-generation cephalosporins plus glycopeptide (41.5% PAS; 58.9% APS, $p < .05$).

32.7% of the respondents preferred using a 7-day course of antibiotics for meningococcal meningitis, with similar percentages found between the PAS and APS groups ($p > .05$). However, 40.9% of the participants preferred to use a course of 14 days or more. For pneumococcal meningitis, 64.3% of the respondents preferred to use a 14-day course of antibiotics, while 24.1% preferred 10 days. The pneumococcal meningitis treatment duration preference was similar between the PAS and APS groups ($p > .05$). (Table 3)

Meningococcal vaccine

When we asked about conjugated meningococcal vaccination, 56.3% of the respondents stated that they recommend vaccination in their daily practice, while 74% said that meningococcal vaccination should be on the national vaccination schedule (67% PAS; 50% APS, $p < .001$). We asked all participants about their thoughts regarding risk groups and the routine use of meningococcal vaccines. Although the majority thought that children are a vulnerable risk group for potential immunization, the age for targeted immunization varied. In the PAS group, all children (0–18 years), children < 2 years of age, children < 1 year of age, and adolescent age groups were the most recommended groups. In the APS group, asplenia/splenectomy patients comprised the most recommended risk group, followed by immunodeficient patient, all children, and those who plan to travel to endemic areas, including Hajj. In both groups, the top five groups that were recommended for routine immunization included all children, asplenia/splenectomy patients, immunodeficient patients, those who planned to travel to endemic areas, including Hajj, and military personnel (Table 4).

Comparisons of the subgroups of physicians

When we compare the questionnaire results of infectious diseases specialists (n = 145) and pediatric infectious disease specialists (n = 33) regarding their attitudes, behaviors, and knowledge of about the management of bacterial meningitis. Approximately 83.4% (n = 123) of the infectious disease specialist followed a patient with meningitis during the last year, while all pediatric infectious disease specialist followed ($p > .05$). There are no difference between infectious disease specialist and pediatric infectious disease specialist for the percentage of performing LP procedure (80% vs. 96.9; $p > .05$). Percentage of pediatric infectious disease specialist followed a patient with meningococcemia or meningococcal meningitis is significantly higher than infectious disease specialist (37.5% vs 8.2% and 43.7% vs. 11.7% respectively. 73.7% (n = 107) of the adult infectious disease specialist preferred to use CCT 75–100% of the time for suspected meningitis cases before performing an LP while this rate is 30.3% among pediatric infectious disease specialist ($p < 0.001$). There are no difference for CSF fluid examination and adjunctive corticosteroid use between these groups ($p > .05$). There are also no difference between the groups for the treatment choice and duration for bacterial meningitis. When we asked about conjugated meningococcal vaccination, 72.7% of the pediatric infectious disease specialist stated that they recommend vaccination in their daily practice, and 75.7% said that meningococcal vaccination should be on the national vaccination schedule, and these rates are significantly higher than infectious disease specialist (72.7% vs. 26.8 and 75.7% vs 52.4; $p < .001$ and $p < .05$ respectively).

Discussion

In this large convenient sample of physicians in Turkey, we showed that there is a heterogenous approach to the diagnosis

Table 3. Duration of antibiotic treatment preference for meningococcal meningitis and pneumococcal meningitis.

	7 days	10 days	14 days	21 days	Other
Meningococcal meningitis TOTAL	32.7% (n = 111)	26.2% (n = 89)	28.9% (n = 98)	9.1% (n = 31)	2.9% (n = 10)
Meningococcal meningitis PAS group	30.9% (n = 53)	27.4% (n = 47)	26.3% (n = 45)	13.4% (n = 23)	1.7% (n = 3)
Meningococcal meningitis APS group	34.5% (n = 58)	25% (n = 42)	31.5% (n = 53)	4.7% (n = 8)	4.1% (n = 7)
Pneumococcal meningitis TOTAL	2.3% (n = 8)	24.1% (n = 82)	64.3% (n = 218)	7.6% (n = 26)	1.4% (n = 5)
Pneumococcal meningitis PAS group	2.3% (n = 4)	28.0% (n = 48)	59.0% (n = 101)	9.9% (n = 17)	0.58% (n = 1)
Pneumococcal meningitis APS group	2.3% (n = 4)	20.2% (n = 34)	69.6% (n = 117)	5.3% (n = 9)	2.3% (n = 4)

Table 4. Ten risk groups who are recommended for routine meningococcal vaccines.

	PAS Group (n = 171)	APS Group (n = 168)	Total (n = 339)
1	All children 16.3%	Asplenia/splenectomy patients 16.8%	All children 14.4%
2	Children < 2 years of age 5.8%	Immunodeficient patients 13.0%	Asplenia/splenectomy patients 9.7%
3	Children < 1 year of age 5.8%	All children 8.9%	Immunodeficient patients 9.7%
4	Adolescents 5.8%	Travel to endemic areas, Hajj/Umrah 8.3%	Travel to endemic areas, Hajj/Umrah 6.7%
5	Asplenia/splenectomy patients 5.2%	Dormitory 6.5%	Military service 3.8%
6	Children < 5 years of age 5.2%	Military service 5.9%	Children < 5 years of age 3.5%
7	Travel to endemic areas, Hajj/Umrah 4.6%	Nursing home* 4.7%	Children < 2 years of age 3.5%
8	Immunodeficient patients 4.0%	> 65 years of age 4.1%	Children < 1 year of age 3.2%
9	All age groups 4.0%	Healthcare professionals 2.9%	Dormitory 3.2%
10	Healthcare professionals 2.9%	HIV 2.3%	Adolescents 2.9%

and treatment of bacterial meningitis. In this cohort, 72.9% of the participants had treated bacterial meningitis, while 72% had performed an LP within the last year. Regarding meningococcal meningitis and meningococcemia cases, 25% of the PAS group had followed meningococcal meningitis and meningococcemia patients, while 12% of the APS group had followed meningococcal meningitis, and 9.5% of APS group had followed meningococcemia during the last year. Therefore, it can be said that participants of this survey are representative of physicians who routinely deal with meningitis in their daily practice. Percentage of pediatric infectious disease specialist followed a patient with meningococcemia or meningococcal meningitis is significantly higher than infectious disease specialist and this situation might be related with majority of the invasive meningococcal disease have been observed during childhood.[3]

A lumbar puncture is crucial for the diagnosis and the physician must decide if cranial imaging is warranted to reduce the risk of cerebral herniation before LP. According to ESCMID's 2016 guideline indications for cranial imaging before performing an LP are focal neurologic deficits, new-onset seizures, severely altered mental status, and immunosuppression.[10] In this study, 49.6% of the participants preferred to use CCT 75–100% of the time for suspected meningitis cases before performing and LP. While only 27.5% in the PAS group chose this route, the rate was significantly higher (72%) in the APS group. Also, 30% of pediatric infectious disease specialist preferred to use CCT 75–100% of the time for suspected meningitis cases before performing an LP while the rate was 74% among the adult infectious disease. In cases of childhood bacterial meningitis, seizures have been reported in 10–56% of children, while altered mental status was reported in 13–56%, and focal neurologic deficits were reported in 11–16% of patients upon hospital admission. However, altered mental status in adults with bacterial meningitis has been reported at 30–69%, while focal neurologic deficits have been reported at 15–34%.[10] The difference in clinical presentation between adults and children may be the reason why the sampled non-pediatrician physicians ordered significantly more cranial imaging. One reason why pediatricians use less cranial imaging may be due to the open fontanel in children below one year of age and the low risk of causing a hernia during an LP. Importantly, cranial imaging prior to an LP delays the administration of antibiotics and thus increases mortality.[12] Heckenberg and colleagues'[13] prospective study results among adult patients with meningitis showed that antibiotics were not initiated before a CCT in 83% of patients who underwent cranial imaging prior to an LP. Therefore, future recommendations for cranial imaging should consider not only radiation exposure but possible treatment delays.

Cerebrospinal fluid examination is crucial and the gold standard in confirming bacterial meningitis and identifying the pathogen.[1,2,10] The leukocyte count, CSF gram stain, glucose, and total protein level are all needed to confirm bacterial meningitis. A CSF gram stain is a quick and useful method for identifying the pathogen, especially in patients who were treated with antibiotics prior to an LP. In many studies, gram staining was positive in more than half the tested patients.[14] In our study, only half the participants were routinely using the gram stain technique. In a prospective study, 5/258 patients with CSF culture-proven meningococcal meningitis had a normal CSF analysis. In three of these five patients, gram staining of the CSF showed bacteria.[13]

CSF cultures are positive in 60–90% of bacterial meningitis patients; however, for patients who have received antibiotic treatment before an LP, the yield of the CSF culture decreases by 10–20%.[10] PCR is also a useful diagnostic test due to its adequate sensitivity and excellent specificity in the diagnosis of bacterial meningitis, especially in patients with a negative CSF culture.[15] In a study that included 1,924 patients with invasive meningococcal disease, 57.1% of the cases were confirmed by PCR only, while 22.5% were confirmed by culture only.[16] Similarly, in a Turkish study that included 79 patients with meningitis (46 were purulent), 58.6% of the bacterial meningitis cases were confirmed by PCR, while 21.7% were confirmed by culture only.[17] In our study, only 33.9% of the participants were able to utilize molecular techniques, such as PCR. This number must be improved because the PCR method is also effective at differentiating viral infections

from bacterial infections to prevent the unnecessary use of antibiotics. A reference laboratory for PCR confirmation of specimens would be extremely beneficial in Turkey. Notably, the Meningococcal Reference Unit at Public Health England provides free nonculture PCR confirmation of meningococcal diagnosis for all clinical specimens routinely in England.[18]

There are different opinions about the use of steroids in the treatment of meningitis. In 2015, a Cochrane meta-analysis stated that, although adjunctive corticosteroids were found to reduce hearing loss and neurological sequelae significantly in bacterial meningitis, they did not reduce overall mortality. The effect of dexamethasone was most prominent in pneumococcal meningitis, in which it reduced mortality, neurological sequelae, and hearing loss. In Hib meningitis, steroids have been shown to reduce hearing loss, but they have had no beneficial effect on meningococcal meningitis.[19] In the ESCMID 2016 guidelines, the use of corticosteroids in patients with bacterial meningitis beyond the neonatal age is recommended.[10] Surprisingly, only 34% of our respondents used routine adjunctive dexamethasone treatment. While 19% of the PAS group preferred to use routine steroid treatment, in the APS group, the presence of corticosteroid use was %35 which is significantly higher.

Notably, there has been a major decrease in pediatric Hib and pediatric pneumococcal meningitis cases after routine immunization changes were implemented as part of the Turkish National Immunization Program. The most common causative organisms of pediatric meningitis are *N. meningitidis* in our country. [3-7] However, the most common pathogen in adult bacterial meningitis cases is *S. pneumoniae*.[8] Therefore, differences in steroid use may be due to the difference between the etiologic agent of meningitis in children and adults.

S. pneumoniae is the second most common causative microorganism in childhood cases beyond the neonatal age.[2] Reduced susceptibility or resistance to penicillin for *S. pneumoniae* is a growing problem worldwide, and there are great differences in resistance rates between countries. For example, the percentage of penicillin resistance to pneumococci in invasive isolates are < 1% in Denmark, France, and Germany, while they are 61% in Romania.[20] Therefore, although treatment should be based on local resistance rates, there is a limited number of studies regarding the antibiotic susceptibility of *S. pneumoniae* in Turkey. Thus, additional studies in Turkey should be initiated. Ceyhan and colleagues' prospective study on pneumococcal strains causing invasive pneumococcal disease in children in Turkey during the period when the PCV7 vaccine was newly included to national immunization program, found that 33.7% of invasive isolates were penicillin non-susceptible.[21] Soysal and colleagues' prospective study results among children in Turkey showed that the prevalence of pneumococcal carriage was 6.4%. In addition, while 62% of the isolates were resistant to penicillin, 13% were non-sensitive to ceftriaxone.[22] The Survey of Antibiotic Resistance study (SOAR 2002–2009) found a statistically significant reduction in susceptibility to antibiotics since 2002. From 2002–03, 74.7% of pneumococci were susceptible to penicillin, although this decreased to 47.2% by the years 2007–2009.[23] In an adult study, the rate of pneumococci strains' intermediate resistance to penicillin was reportedly 2%, while it was 3% for cefotaxime, and 25% of isolated pneumococci strains in invasive disease were resistant to erythromycin.[24]

Ongoing surveillance of pneumococcal diseases is essential for close monitoring of resistance rates and the proper determination of the best treatment options. Different attitudes regarding the proper treatment of pneumococcal meningitis are seen among physicians worldwide. In pneumococcal meningitis, combination therapy with third-generation cephalosporin and glycopeptides is significantly higher compared to treatment for meningococcus. This could be due to physicians' awareness regarding penicillin and cephalosporin resistance in pneumococci. We also observed that the duration of antibiotic treatment of meningococcal meningitis varies. While most of our participants preferred to use the recommended antibiotics for meningococcal meningitis (penicillin or third-generation cephalosporins), approximately 41% preferred to use antibiotics for 14 days or more, which is longer than the recommended 7 days. A small number of physicians are administering combination therapy for meningococcal meningitis; however, we observed longer durations of antibiotics, which appeared unnecessary, and further recommendations are needed at the country level in Turkey.

We asked all participants for their thoughts about risk groups and the routine use of meningococcal vaccines. Most of the participants thought that children are a vulnerable risk group that should potentially be immunized; however, the targeted age varied among the participants. Among the PAS group, all children were recommended the most, followed by children below five years of age, children below one year of age, and adolescents. In the APS group, asplenia/splenectomy patients were the most recommended group, followed by immunodeficient patients, all children, and those who planned to travel to endemic areas, including Hajj. Between both groups, the top five that were recommended for routine immunization were all children, asplenia/splenectomy patients, immunodeficient patients, those who planned to travel to endemic areas, including Hajj, and military personnel. Interestingly, long-term facilities for people > 65 years of age were also defined as at-risk groups that were recommended for routine immunization. For both groups, healthcare professionals selected risk groups that had been previously defined for invasive meningococcal infections, including all children, asplenia/splenectomy patients, immunodeficient patients, those who planned to travel to endemic areas, including Hajj, and military personnel. Mameli et al.[25] evaluated the acceptability of the meningococcal B vaccine among 291 healthcare workers in Italy and pediatricians who considered meningitis a disease with a higher mortality rate risk than non-pediatricians. These pediatricians considered the 4CMenB vaccination a priority for all newborns, unlike non-pediatricians. Regarding the healthcare professionals' response, children were an important target group for immunization. More than 80% of the healthcare workers thought that meningitis is a disease with either a high (56.9%) or very high (23.3%) mortality rate and either a high (65.4%) or very high risk of permanent damage (20.7%). The majority (61.9%) also thought that meningitis is a disease of utmost importance for public health, while 35.94% thought that, although it is important, meningitis is not a public health

priority. The majority of these healthcare workers (77.6%) had received information about the European Medical Agency's approval of the 4CMenB vaccine, and 73% considered the new 4CMenB vaccine a priority in infants' immunization schedules. Finally, 26.3% agreed that immunization with this vaccine should be evaluated on a case-by-case basis.[25]

Our study has some limitations. Sample size is slightly lower than we expected however we excluded physicians who did not follow-up with a meningitis case during their routine daily work. For this reason we have a chance to evaluate the real world data of the meningitis diagnosis and treatment. We only ask the physicans, how often they perform radiological tests before conducting an LP however we did not evaluate the indications of CCT (e.g. loss of consciousness, focal neurological signs etc.). We also evaluate routine corticosteroid use for bacterial meningitis however we did not evaluate subgroup analysis for pneumococcal or meningococcal meningitis.

Advocating for vaccines needs to be contextually sensitive; therefore, it should have different objectives by region and country. Many steps must precede the introduction of a vaccine into national immunization programs, including surveillance of invasive meningococcal disease, seroepidemiology, and cost-effectiveness analyses; importantly, the benefit of these steps will increase awareness about meningitis, groups that are at risk for the disease, and routine immunization via meningococcal vaccines[4] In this study, 37.1% of the physicians had attended educational activities about meningitis and/or vaccines for meningitis within the last three years. Further education about diagnosis, treatment and prevention of meningitis will increase the knowledge and also harmonize the clinical approach for all medical specialities.

This is the first and largest survey conducted to collect data on current knowledge, attitudes, and beliefs of Turkish physicians regarding bacterial meningitis, including its diagnosis, treatment, and prevention. Our results imply that more awareness is needed about meningitis diagnosis and treatment, including the protective effect of the meningococcal vaccine, to ensure adequate immunity in the community.

Methods

This study used a cross-sectional electronic survey with a national convenience sample of physicians in Turkey. A web-based questionnaire, which consisted of 28 questions about the definition, diagnosis, and treatment of bacterial meningitis (especially meningococcal and pneumococcal meningitis) as well as knowledge and/or attitudes about meningococcal vaccines was designed. A cover letter and questionnaire were electronically mailed via SurveyMonkey to the convenience sample. For the PAS group, we included general pediatricians, pediatric infectious disease specialists, and pediatric emergency care and intensive care specialists. For the APS group, we sent this survey to infectious disease (ID), internal medicine, and emergency care specialists. The included cover letter explained the study's details, identified the purpose and confidentiality, and reminded all potential participants that their participation was voluntary. Anonymity was ensured by not requiring names on the questionnaire, and no financial incentives were provided for participation. Exclusion criteria is the physicians who did not follow-up with a meningitis case during their routine daily work.

The questionnaire included questions regarding the following topics: (1) evaluation of the participants' approach to meningococcal infections mainly meningitis and meningococcemia in routine daily practice, (2) radiological tests completed prior to an LP, (3) routine CSF examination tests, (4) treatment choices and duration for pneumococcal meningitis and meningococcal meningitis, and (5) their beliefs about meningococcal vaccines in general as well as their implementation into the National Immunization Program.

A statistical analysis of the data was carried out using the Statistical Package for the Social Sciences, Chicago, IL, for Windows 11.5 software program. Normal distribution of the demographic data was analyzed with the Shapiro Wilks test, and the results were summarized as means and standard deviations. The categorical data were presented as percentages, and both the chi-square test and paired-t test were used for comparisons. A p value of <0.05 was considered statistically significant.

Abbreviations

APS:	Adult patient specialist
CCT:	Computerized cranial tomography
CSF:	Cerebrospinal fluid
ESCMID:	European Society of Clinical Microbiology and Infectious Diseases
Hib:	Haemophilus influenzae type B
LP:	Lumbar puncture
PAS:	Pediatric age specialist

Compliance with ethical standards

All analysis performed in this trial were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Informed consent was obtained, when the physicians agree to fulfill the electronic version of questionnaire.

Disclosure of potential conflicts of interest

No potential conflicts of interest were disclosed.

Acknowledgments

We thank all the participants to this study during their busy work schedule.

Author contributions

Dr. M Dinleyici, Dr Iseri Nepesov, Dr Kilic and Dr EC Dinleyici, participated in protocol development, statistical analysis, primary data analysis, interpretation and wrote the first version of the manuscript and also finalized the manuscript. Dr Sipahi and Dr Carman participated in interpretation and wrote the first version of the manuscript and also finalized the manuscript and writing the manuscript.

References

1. McGill F, Heyderman RS, Panagiotou S, Tunkel AR, Solomon T. Acute bacterial meningitis in adults. Lancet. 2016 Dec 17;388 (10063):3036–3047. doi:10.1016/S0140-6736(16)30654-7.
2. Swanson D. Meningitis. Pediatr Rev. 2015 Dec;36(12):514–524. doi:10.1542/pir.36-12-514.
3. Dinleyici EC, Ceyhan M. The dynamic and changing epidemiology of meningococcal disease at the country-based level: the experience in Turkey. Expert Rev Vaccines. 2012 May;11(5):515–518. doi:10.1586/erv.12.29.
4. Borrow R, Caugant DA, Ceyhan M, Christensen H, Dinleyici EC, Findlow J, Glennie L, Von Gottberg A, Kechrid A, Vázquez Moreno J, et al.; Global Meningococcal Initiative (GMI). Meningococcal disease in the Middle East and Africa: findings and updates from the Global Meningococcal Initiative. J Infect. 2017 Jul;75(1):1–11. doi:10.1016/j.jinf.2017.04.007.
5. Ceyhan M, Dagan R, Sayiner A, Chernyshova L, Eç D, Hryniewicz W, Kulcsár A, Mad'arová L, Pazdiora P, Sidorenko S, et al. Surveillance of pneumococcal diseases in Central and Eastern Europe. Hum Vaccin Immunother. 2016 Aug 2;12(8):2124–2134. doi:10.1080/21645515.2016.1159363.
6. Ceyhan M, Ozsurekci Y, Gürler N, Karadag Oncel E, Camcioglu Y, Salman N, Celik M, Emiroglu MK, Akin F, Tezer H, et al. Bacterial agents causing meningitis during 2013-2014 in Turkey: A multi-center hospital-based prospective surveillance study. Hum Vaccin Immunother. 2016 Nov;12(11):2940–2945. doi:10.1080/21645515.2016.1209278.
7. Ceyhan M, Gürler N, Ozsurekci Y, Keser M, Aycan AE, Gurbuz V, Salman N, Camcioglu Y, Dinleyici EC, Ozkan S, et al. 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):2706–2712. doi:10.4161/hv.29678.
8. Arda B, Sipahi OR, Atalay S, Ulusoy S. Pooled analysis of 2,408 cases of acute adult purulent meningitis from Turkey. Med Princ Pract. 2008;17(1):76–79. doi:10.1159/000109595.
9. Li J, Shao Z, Liu G, Bai X, Borrow R, Chen M, Guo Q, Han Y, Li Y, Taha MK, et al. Meningococcal disease and control in China: findings and updates from the Global Meningococcal Initiative (GMI). J Infect. 2018 May;76(5):429–437. doi:10.1016/j.jinf.2018.01.007.
10. van de Beek D, Cabellos C, Dzupova O, Esposito S, Klein M, Kloek AT, Leib SL, Mourvillier B, Ostergaard C, Pagliano P, et al.; ESCMID Study Group for Infections of the Brain (ESGIB). ESCMID guideline: diagnosis and treatment of acute bacterial meningitis. Clin Microbiol Infect. 2016 May;22(Suppl 3):S37–62. doi:10.1016/j.cmi.2016.01.007.
11. Tunkel AR, Hartman BJ, Kaplan SL, Kaufman BA, Roos KL, Scheld WM, Whitley RJ. Practice guidelines for the management of bacterial meningitis. Clin Infect Dis. 2004 Nov 1;39(9):1267–1284. doi:10.1086/425368.
12. Proulx N, Fréchette D, Toye B, Chan J, Kravcik S. Delays in the administration of antibiotics are associated with mortality from adult acute bacterial meningitis. QJM. 2005 Apr;98(4):291–298. doi:10.1093/qjmed/hci047.
13. Heckenberg SG, de Gans J, Brouwer MC, Weisfelt M, Piet JR, Spanjaard L, van der Ende A, van de Beek D. Clinical features, outcome, and meningococcal genotype in 258 adults with meningococcal meningitis: a prospective cohort study. Medicine (Baltimore). 2008 Jul;87(4):185–192. doi:10.1097/MD.0b013e318180a6b4.
14. Yadhav Ml K. Study of bacterial meningitis in children below 5 years with comparative evaluation of gram staining, culture and bacterial antigen detection. J Clin Diagn Res. 2014 Apr;8(4): DC04–6. doi:10.7860/JCDR/2014/6767.4215.
15. Brouwer MC, Thwaites GE, Tunkel AR, van de Beek D. Dilemmas in the diagnosis of acute community-acquired bacterial meningitis. Lancet. 2012 Nov 10;380(9854):1684–1692. doi:10.1016/S0140-6736(12)61185-4.
16. Heinsbroek E, Ladhani S, Gray S, Guiver M, Kaczmarski E, Borrow R, Ramsay M. Added value of PCR-testing for confirmation of invasive meningococcal disease in England. J Infect. 2013 Nov;67(5):385–390. doi:10.1016/j.jinf.2013.06.007.
17. Kahraman H, Tünger A, Şenol Ş, Gazi H, Avcı M, Örmen B, Türker N, Atalay S, Köse Ş, Ulusoy S, et al. [Investigation of bacterial and viral etiology in community acquired central nervous system infections with molecular methods]. Mikrobiyol Bul. 2017 Jul;51(3):277–285. doi:10.5578/mb.57358.
18. Edge C, Waight P, Ribeiro S, Borrow R, Ramsay M, Ladhani S. Clinical diagnoses and outcomes of 4619 hospitalised cases of laboratory-confirmed invasive meningococcal disease in England: linkage analysis of multiple national databases. J Infect. 2016 Nov;73(5):427–436. doi:10.1016/j.jinf.2016.07.016.
19. Brouwer MC, McIntyre P, Prasad K, van de Beek D. Corticosteroids for acute bacterial meningitis. Cochrane Database Syst Rev. 2015 Sep 12;(9):CD004405. doi:10.1002/14651858.CD004405.pub5.
20. European Centre for Disease Prevention and Control. Antimicrobial resistance surveillance in Europe 2011. Annual Report of the European Antimicrobial Resistance Surveillance Network (EARS-Net). Stockholm: ECDC; 2012.
21. Ceyhan M, Gurler N, Yaman A, Ozturk C, Oksuz L, Ozkan S, Keser M, Salman N, Alhan E, Esel D, et al. Serotypes of Streptococcus pneumoniae isolates from children with invasive pneumococcal disease in Turkey: baseline evaluation of the introduction of the pneumococcal conjugate vaccine nationwide. Clin Vaccine Immunol. 2011 Jun;18(6):1028–1030. doi:10.1128/CVI.00526-10.
22. Soysal A, Karabağ-Yılmaz E, Kepenekli E, Karaaslan A, Cagan E, Atıcı S, Atınkanat-Gelmez G, Boran P, Merdan S, Hasdemir U, et al. The impact of a pneumococcal conjugate vaccination program on the nasopharyngeal carriage, serotype distribution and antimicrobial resistance of Streptococcus pneumoniae among healthy children in Turkey. Vaccine. 2016 Jul 19;34 (33):3894–3900. doi:10.1016/j.vaccine.2016.05.043.
23. Torumkuney D, Gur D, Soyletir G, Gurler N, Aktas Z, Sener B, Tunger A, Bayramoglu G, Koksal I, Yalcin AN, et al. Results from the Survey of Antibiotic Resistance (SOAR) 2002-09 in Turkey. J Antimicrob Chemother. 2016 May;71(Suppl 1):i85–91. doi:10.1093/jac/dkw067.
24. Öksüz L, Gürler N. [Serotype distribution and antibiotic resistance of Streptococcus pneumoniae strains isolated from the adult patients in a Turkish university hospital]. Mikrobiyol Bul. 2017 Jul;51(3):195–208. doi:10.5578/mb.48638.
25. Mameli C, Faccini M, Mazzali C, Picca M, Colella G, Duca PG, Zuccotti GV. Acceptability of meningococcal serogroup B vaccine among parents and health care workers in Italy: a survey. Hum Vaccin Immunother. 2014;10(10):3004–3010. doi:10.4161/21645515.2014.971602.