

Meningococcal carrier rate before and after hajj pilgrimage: effect of single dose ciprofloxacin on carriage

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معدلات حَمَلَة المَكُورَات السَحَائِيَّة قَبْل وبعْد مَوْسَم الحَجِّ، وَآثَر الجُرْعَة الوَاحِدَة مَن السَّيْبِرُوفْلُو كَسَاسِين عَلَي حَمَلِهَا

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الخلاصة: حددت الدراسة معدلات حمل التيسرية السحائية (المكورة السحائية) قبل وبعد موسم الحج بين مجموعة أولى ضمّت 674 حاجاً إيرانياً اختبروا بصورة عشوائية، وتأثير جرعة مقدارها 500 مغ من السيبروفلو كساسين تُعطى قبل 24 ساعة من العودة إلى الديار، في خفض نسبة حَمَلَة المَكُورَات السَحَائِيَّة بين مجموعة ثانية ضمّت 123 حاجاً اختبروا بصورة عشوائية أيضاً من بين الحجاج الإيرانيين. ولقد جمعت عينات من الحلق قبل ساعة من مغادرتهم متوجهين إلى الحج، ثم في غضون ساعة واحدة فور عودتهم وتم زرعها. وكانت معدلات حمل التيسرية السحائية في المجموعة الأولى 5.2% قبل الحج و 4.6% بعده (P=0.65)، كما حددت ثلاث مجموعات مصلية جديدة فيمن عادوا هي (Z، Z'، K). أما المجموعة الثانية فقد انخفضت فيها المعدلات من 8.1% إلى الصفر قبل الحج وبعده.

ABSTRACT We determined the carriage rate of *Neisseria meningitidis* before and after hajj pilgrimage among a group (1) of 674 randomly selected Iranian pilgrims, and the effect of 500 mg of ciprofloxacin given 24 hours before return on the reduction of meningococcal carriers among another group (2) of 123 randomly selected Iranian pilgrims. Throat specimens taken 1 hour before departure on the hajj and immediately on return were cultured. Carriage rates of *N. meningitidis* in group 1 were 5.2% before and 4.6% after pilgrimage (P = 0.65); 3 new serogroups (Z, Z' and A) were identified on return. In group 2, the carriage rate decreased from 8.1% to zero before and after pilgrimage.

Taux de portage du méningocoque avant et après le Hadj (pèlerinage à La Mecque) et effets d'une dose unique de ciprofloxacin sur le portage

RÉSUMÉ Nous avons déterminé le taux de portage de *Neisseria meningitidis* avant et après le Hadj dans un groupe (1) de 674 pèlerins iraniens sélectionnés au hasard, et les effets d'une administration de 500 mg de ciprofloxacin 24 heures avant le retour sur la diminution du nombre de porteurs du méningocoque dans un autre groupe (2) de 123 pèlerins iraniens sélectionnés au hasard. Les prélèvements de gorge effectués une heure avant le départ au Hadj et dès le retour ont été mis en culture. Les taux de portage de *N. meningitidis* dans le groupe 1 étaient de 5,2 % avant et de 4,6 % après le pèlerinage (p = 0,65) ; 3 nouveaux sérogroupes (Z, Z' et A) ont été identifiés au retour. Dans le groupe 2, le taux de portage est passé de 8,1 % avant le pèlerinage à zéro après.

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Received: 12/06/05; accepted: 04/01/06

Introduction

Meningococcal infections occur worldwide and are associated with considerable fatality. Approximately 2.5 million Muslim people participate in the hajj pilgrimage to Saudi Arabia each year and pilgrims will stay in Saudi Arabia for approximately 30 days. Epidemiological studies show that hajj pilgrimage plays an important role in disease transmission. The first large meningococcal outbreak among hajj pilgrims, which was caused by *Neisseria meningitidis* serogroup A, was reported in 1987 and the disease spread quickly to all countries [1]. Then, some limited epidemics or sporadic cases were reported in 1992 mainly with serogroup A and in 1993 with serogroup W135 [1,2].

The epidemics caused by serogroup W135 in the years 2000 and 2001 during the hajj, which spread to many countries in the world, resulted in the requirement of vaccination with quadrivalent polysaccharide (PS) vaccine before entering Saudi Arabia [3]. Although PS vaccination prevents the disease, it cannot prevent the carriage [4]. Therefore there are many possible meningococcal carriers among pilgrims who return to their home countries every year and can therefore transfer the organism to their close relatives and even to the population of their surrounding community. In 1987 the rate of serogroup A carriers among hajj pilgrims was 11 times higher than other tourists who visited other countries [1]. After the epidemics of 2000 and 2001 the carriage rate of serogroup W135 in Singapore reached 15% [5].

The rate of meningococcal meningitis has been increasing after the hajj pilgrimage in recent years in Shiraz city, Islamic Republic of Iran [6]. A single dose of ciprofloxacin can eradicate *N. meningitidis* at a rate of almost 100%. Administering

ciprofloxacin to hajj pilgrims can reduce transmission to family and other close contacts upon return [7].

The aims of this study were to: determine the meningococcal carriage rate in pilgrims just before and after hajj pilgrimage; evaluate the entrance of new serogroups; and evaluate the effect of a single dose of ciprofloxacin taken by pilgrims 24 hours before returning to the Islamic Republic of Iran from Saudi Arabia.

Methods

This study was conducted from 21 January to 24 February 2003. The total number of pilgrims participating in hajj pilgrimage from Fars province, Islamic Republic of Iran is approximately 4500 annually (unpublished report). The sample size was estimated for single proportion ($\alpha = 0.05$ with 95% confidence interval). There were 11 hajj caravans from Shiraz in 2003 from which we randomly selected 3 as our sampling frame. From these 3 caravans, 674 hajj pilgrims were randomly selected at the airport as group 1 in our study (mean age of 52.9 years); 392 (58.2%) were male and 282 (41.8%) were female.

Cotton swab specimens of the posterior pharynx were taken from the pilgrims in Shiraz airport 1 hour before their flight to Saudi Arabia and were directly cultured on modified Thayer–Martin medium agar (MTMM) plates and incubated at 37 °C in candle jars (5%–7% CO₂) for 48 hours. Each colony suspected of being *N. meningitidis* (Gram-negative diplococci and oxidase-positive colonies) was subcultured on sheep blood agar and pure culture was obtained. For each pure colony, Gram stain, oxidase, catalase and rapid carbohydrate utilization tests were performed.

Biochemically positive colonies of *N. meningitidis* were evaluated for serogroups by specific polyvalent and monovalent antisera (Difco).

Pilgrims travel in "caravans" with an assigned serial number, a leader and date of return. Thus we were able to know when individuals in group 1 returned to the Islamic Republic of Iran. On arrival, therefore, another throat sample was taken at the airport and the same process was repeated. The pilgrims also filled in a questionnaire about any antibiotic use during the hajj.

To study the usefulness of ciprofloxacin prescription to eradicate meningococcal carriage, another group of 123 pilgrims was selected as group 2 and throat cultures before departure from the Islamic Republic of Iran and after return were taken in the same way as group 1. This group, however, was treated with a single dose of 500 mg ciprofloxacin 24 hours before they returned to the Islamic Republic of Iran. This was dispensed by the authors who also observed the pilgrims taking the dose.

All individuals in both groups had received the quadrivalent PS meningococcal vaccine before departure from the country (according to their required vaccination card signed by health centres).

The results were statistically analysed using the chi-squared, Fischer exact and McNemar tests.

Results

Out of 674 pilgrims in the first group, 35 (23 males and 12 females) were infected by different strains of meningococci before departure from the Islamic Republic of Iran. No correlation was found between sex and carriage rate ($\chi^2 = 1.18$, $P = 0.45$). Serogrouping showed that 10 strains (28.6%) were non-serogroupable [8], 9 (25.7%) were serogroup B, 5 (14.3%) were serogroup C, 5

(14.3%) were serogroup D, 5 (14.3%) were serogroup Y and 1 (2.8%) was serogroup W13 (Table 1).

When the individuals in group 1 returned to the Islamic Republic of Iran, we were able to retest all of them (100% retesting).

The results show that 31 pilgrims were infected with different strains of *N. meningitidis*; 21 strains (67.7%) were non-serogroupable, 2 (6.4%) were serogroup B, 1 (3.2%) was serogroup W135, 3 (9.7%) were serogroups Z,Z', 1 (3.2%) was serogroup A, 1 (3.2%) was serogroup C and 2 (6.4%) were serogroup Y. Although none of the pilgrims in group 1 had a history of recent antibiotic use before leaving the Islamic Republic of Iran, 392 (58.2%) had received antibiotics because of respiratory infections during the hajj pilgrimage (based on the questionnaires), 222 (32.9%) pilgrims had not received any antibiotics and 60 (8.9%) had no reliable history of antibiotic use (they had taken some medication but did not know what type). Out of the 31 infected returning pilgrims in group 1, 15

Table 1 Distribution of *Neisseria meningitidis* serogroups in Iranian hajj pilgrims (group 1) before departure for Saudi Arabia

Serogroup	No. infected before departure (n = 674)	%
A	0	0.0
B	9	1.3
C	5	0.7
D	5	0.7
Y	5	0.7
W135	1	0.1
Non-serogroupable	10	1.5
Z	0	0.0
Z'	0	0.0
Total	35	5.2

had received antibiotics, another 15 had not so the carrier rate was the same ($P = 0.14$) and 1 pilgrim had no reliable history.

Carriage rates of *N. meningitidis* in group 1 were 5.2% and 4.6% before leaving and after arriving in the country, respectively, a non-significant difference ($P = 0.65$) but entrance of new serogroups (A, Z and Z') was epidemiologically significant as they have the capability to cause outbreaks (Table 2) [9]. Group 2 had a 8.1% carriage rate before leaving the Islamic Republic of Iran (with serogroups B,C,D,X and Y), which reduced to zero when they arrived back in the country having taken 500 mg ciprofloxacin 24 hours before they returned ($P = 0.002$) (Table 3).

Discussion

We evaluated the carriage rate of *N. meningitidis* among Iranian pilgrims before and after the hajj pilgrimage. Meningococcal carriers are asymptomatic and are a reser-

voir for the organism. Pilgrims are commonly in contact with many people after returning to the Islamic Republic of Iran because of the custom of visiting relatives post hajj.

According to our data, the carriage rate of *N. meningitidis* in group 1 reduced from 35 cases (5.2%) to 31 cases (4.6%) after the pilgrimage, but this was not statistically significant. This finding is contrary to our first hypothesis that the carriage rate would increase after the hajj pilgrimage, but concurs with other studies [5,10]. However, in our study 3 new serogroups, Z, Z' and A, were found among the returning pilgrims. A study from Ghana reported the occurrence of a serogroup X *N. meningitidis* outbreak in northern Ghana [11] which highlights the potential of unusual serotypes of *N. meningitidis* to cause outbreaks.

There are several reasons that could explain the lack of significant changes in the carriage rate of *N. meningitidis* in group 1 pilgrims after the hajj. First, the use of

Table 2 Distribution of *Neisseria meningitidis* serogroups in 674 Iranian hajj pilgrims after returning from Saudi Arabia by use of antibiotics while on hajj

Serogroup	No antibiotic (n = 222)		Received antibiotic (n = 392)		Unknown (n = 60)	
	No.	%	No.	%	No.	%
A	1	0.45	0	0.0	0	0.0
B	2	0.9	0	0.0	0	0.0
C	0	0.0	1	0.25	0	0.0
D	0	0.0	0	0.0	0	0.0
Y	1	0.45	1	0.25	0	0.0
W135	0	0.0	1	0.25	0	0.0
Non-serogroupable	8	3.6	12	3.06	1	1.7
Z	1	0.45	0	0.0	0	0.0
Z'	2	0.9	0	0.0	0	0.0
Total	15	6.8	15	3.8	1	1.7

Table 3 Distribution of *Neisseria meningitidis* serogroups in Iranian hajj pilgrims (group 2 – ciprofloxacin group) before departure for Saudi Arabia

Serogroup	No. (n = 123)	%
A	0	0.0
B	2	1.6
C	1	0.8
D	2	1.6
X	1	0.8
Y	2	1.6
W135	0	0.0
Non-serogroupable	2	1.6
Z	0	0.0
Z'	0	0.0
Total	10	8.1

After returning to the Islamic Republic of Iran having taken 500 mg ciprofloxacin 24 hours before, the carriage rate was zero ($P = 0.002$).

antibiotics could play a role as 58.2% of the pilgrims had taken antibiotics during their stay in Saudi Arabia but none had done so before leaving. Most of the pilgrim who had taken antibiotics had done so without a prescription from a physician as it is customary among pilgrims to start self-therapy when they develop a cough or fever. Secondly, it is possible that the absence of outbreaks in other countries might have led to a decrease in the carrier rate on arrival in Saudi Arabia. Finally, vaccination may play a role; vaccination decreases meningococcal disease in the pilgrims and thus vaccinated pilgrims will have less active disease and will be less likely to infect others.

In a study in 1978 on African people who were in contact with patients with meningococcal infection, the effect of rifampin, ciprofloxacin and ceftriaxone on eradication of carriage was 96.5%, 97.6% and 88% respectively [12], while it was

100% in our study. Thus ciprofloxacin appears to be effective in eliminating the chance of carriage.

The cost of admission of patients with uncomplicated meningitis in teaching hospitals in the Islamic Republic of Iran is approximately US\$ 500 for 10 days for each patient (based on the approved fees of the Iranian Ministry of Health and Medical Education), while each tablet of ciprofloxacin is about 10 US cents. Considering that about 92 000 pilgrims go for hajj from the Islamic Republic of Iran each year, US\$ 9200 would be needed for meningococcal prophylaxis for all Iranian pilgrims. This is equal to the cost of admission of about 18 patients with uncomplicated meningitis in hospitals.

As meningococcal disease has high fatality rate and the cost of hospitalization of such infected patients is very expensive, and disease outbreaks are very likely after hajj pilgrimage in some years, it would appear to be cost-effective to prescribe 500 mg of ciprofloxacin as single dose to all pilgrims to be taken 24 hours before arrival in their home country. This would serve to prevent the transfer of new serogroups, decrease carriage rate and finally prevent possible outbreaks in their countries.

Acknowledgements

A part of this project was supported financially by the Centre for Disease Control (Islamic Republic of Iran).

We would like to thank Dr B. Oboodi, Dr M. Ziyaeyan, Mr M. Kalani, Mr J. Nasiri and Mr M. Hayati for the contribution to this study. We would also like to thank Dr Christofer Nelson for basic revision of the paper, Dr Peiravi for his support and all Shiraz airport personnel for their collaboration.

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