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ORIGINAL ARTICLE

Risk factors for invasive meningococcal disease in southern Queensland, 2000–2001

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Abstract

Aim: The aim of this paper is to describe the risk factors for invasive meningococcal disease (IMD) in southern Queensland.

Methods: A case control study during the calendar years 2000–2001 was undertaken.

Results: Eighty-four laboratory-confirmed cases of IMD were notified. Four patients died and were excluded from the present study. Sixty-two (78%) eligible cases and 79 controls selected from the same age group and medical practice as cases, were interviewed. Univariate analysis found that IMD was associated with sharing bedrooms with two or more people (odds ratio (OR) 4.3; 95% confidence interval (CI) 1.2–17.0, $P = 0.01$), any exposure to tobacco smoke (smoker or passive exposure; OR 2.3; 95% CI 1.1–4.8, $P = 0.02$), passive exposure to tobacco smoke (OR 2.4; 95% CI 1.0–5.6, $P = 0.03$) and recent upper respiratory tract infection (OR 1.9, 95% CI 0.9–4.1, $P = 0.06$). Children who were breast-fed were less likely to develop IMD (OR 0.3; 95% CI 0.1–1.1, $P = 0.04$). Attendance at a child-care centre was not associated with an increased risk of IMD. In multivariate analysis, IMD was associated with children under 6 years of age who shared a bedroom with two or more people (OR 7.4; 95% CI 1.5–36.1, $P = 0.01$) or who had a primary carer who smoked (OR 9.1; 95% CI 2.1–39.9, $P = 0.003$).

Discussion: This is the second Australian study that identifies links between risk of IMD and exposure to cigarette smoke. The risk of IMD in young children could be further reduced if primary caregivers did not smoke. This information may contribute a new perspective to antismoking campaigns. (Intern Med J 2004; 34: 464–468)

Key words: invasive meningococcal disease, passive smoking, risk factors.

INTRODUCTION

Invasive meningococcal disease (IMD) is an important cause of morbidity and mortality in children and young adults in Australia. Approximately 600 cases occur nationally with peak incidence in the 0–4 and 15–24 years age groups.[1] Previous research has identified exposure to cigarette smoke as a significant risk factor for IMD, particularly where children are exposed to cigarette smoke in the home.[2–6] Active smoking and the presence of other smokers in the household have been independently associated with meningococcal carriage.[7] Additional risk factors include recent illness, particularly a preceding influenza infection, exposure to environmental dust, overcrowding and association with university campus bars and nightclubs.[2,4,8–10] Breast-feeding might have a protective effect.[2,11]

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The Southern Public Health Unit Network (SPHUN) includes the Brisbane South, South Coast, West Moreton, Darling Downs and south-west regions of Queensland (the 2001 estimated resident population was 1.7 million). In 1998, a survey of 43 cases of IMD by the SPHUN (88% of all notified cases that year) identified children living with a primary caregiver who smoked as a significant potential risk factor (chi squared test = 6.91, $P = 0.01$). A case control study, designed to test this hypothesis, was conducted by the SPHUN during 2000 and 2001.

METHODS

The SPHUN receives notifications of all cases of IMD. For this study, a case of IMD was defined as a person with an onset of illness between 1 January 2000 and 31 December 2001 that met the following laboratory criteria:

- Isolation of *Neisseria meningitidis* from a normally sterile site *OR*
- Detection of Gram-negative intracellular diplococci in blood or cerebrospinal fluid (CSF) *OR*
- Detection of meningococcal antigen in joints, blood or CSF *OR*
- Detection of *N. meningitidis* nucleic acid in joints, blood, CSF, tissue or urine.

Deceased patients were excluded from the study to avoid further distress to family members. Cases and controls were recruited through the cases' medical practitioner. Controls were identified as the next two people to attend that medical practice of the same age group (<1 year of age, 1–5 years of age, 6–12 years of age, 13–17 years of age, 18–29 years of age and >29 years of age), but not gender, as the case. Most were interviewed over the telephone using a standardized questionnaire within 1 month of notification of the case. A small number of cases was interviewed face to face in hospital because of their medical or family circumstances. However, consistency in the method of interview was maintained through joint training of all interviewers in the administration of the questionnaire. The questionnaire was based on published literature review and contact with other researchers, and was validated during the 1998 pilot study. Matched and unmatched univariate analyses were conducted using Epi Info Version 6.04d (Centers for Disease Control and Prevention, Atlanta, GA, USA). Epi Info 2000 (Centers for Disease Control and Prevention, Atlanta, GA, USA) was used to calculate adjusted odds ratios (OR) in the unmatched analysis by including all risk factors with a *P*-value <0.25 in an unconditional logistic regression model.

The questionnaire sought information on medical history, socioeconomic indicators and attendance at nightclubs, high intensity exercise, stressful life events, exposure to dust and exposure to tobacco smoke in the previous 4 weeks. A current smoker was defined as a person who smoked at least one cigarette in the previous 4 weeks.[2] Passive exposure to tobacco smoke was defined as exposure for at least 1 h per day during the previous 4 weeks. For children aged less than 6 years, details were sought on attendance at childcare facilities in the previous 4 weeks and duration of breast-feeding. Analysis was age stratified where risk factors were known or assumed to vary by age group of the exposed.

The study was approved by the Princess Alexandra Hospital Ethics Committee.

RESULTS

There were 84 laboratory-confirmed cases of IMD notified to the SPHUN in 2000 and 2001. There were 43 male cases and 41 female cases. These included 50 (60%) serogroup B, 24 (29%) serogroup C, 3 (3%) serogroup Y, and 7 (8%) ungroupable. Ages ranged from 4 weeks to 84 years with a median age of 18 years. Four cases died and were excluded from the study.

Sixty-two (78%) cases and 79 controls were interviewed for the study. There were 30 male and 32 female cases. These included 39 (63%) serogroup B, 16 (26%) serogroup C, 2 (3%) serogroup Y and 5 (8%) ungroupable. The age distribution of cases included in the study ranged from 4 weeks to 75 years with a median age of 17 years. This age distribution was similar to notified cases in Queensland during the last 5 years. The notification date of cases included in the study reflected the seasonal pattern of all IMD cases in the SPHUN and in Queensland, peaking in late winter/early spring.

Forty-five cases were matched to 79 controls of similar age group and recent attendance at the same medical practice. The matched analysis revealed little difference between crude and matched OR, indicating that confounding by age and medical practice was not significant and that univariate analyses and unconditional logistic regression can be performed on the unmatched data.[12,13] Therefore, in order to improve the power of the study, unmatched univariate analysis was performed for all 62 cases and 79 controls interviewed. The results of the unmatched analysis for selected risk factors in adults and children are shown in Tables 1–3.

Unmatched univariate analysis of all cases found that IMD was associated with sharing a bedroom with two or more people (OR 4.3, 95% confidence interval (CI) 1.2–17.0, $P = 0.01$) and upper respiratory tract infection within the last 4 weeks (OR 1.9, 95% CI 0.9–4.1, $P = 0.06$). Among adults, there was no association between IMD and antibiotic use, stressful events, attendance at nightclubs, high intensity exercise or exposure to tobacco smoke in the previous 4 weeks. Among children under the age of 6 years, IMD was more likely in those sharing a bedroom with two or more people (OR 6.3, 95% CI 1.2–36.3, $P = 0.01$). A history of breast-feeding was protective (OR 0.3, 95% CI 0.1–1.1, $P = 0.04$). The median duration of breast-feeding

Table 1 Results of unmatched univariate analysis for all ages (cases, $n = 62$; controls, $n = 79$)

Exposure	Proportion exposed		Odds Ratio	95% Confidence interval	*P*-value
	Cases (*n* (%))	Controls (*n* (%))			
Recent upper respiratory tract infection	30 (48)	26 (33)	1.9	0.9–4.1	0.06
Antibiotic	6 (10)	10 (13)	0.7	0.2–2.3	0.53
Chronic condition	13 (21)	17 (22)	1.0	0.4–2.4	0.94
Dusty environment	13 (21)	14 (18)	1.2	0.5–3.1	0.63
Sharing bedroom	27 (44)	30 (40)	1.2	0.6–2.5	0.63
Sharing bedroom with two or more persons	12 (19)	4 (5)	4.3	1.2–17.0	0.01
Tobacco exposure (active or passive)	42 (68)	38 (48)	2.3	1.1–4.8	0.02
Passive tobacco exposure	28 (45)	24 (30)	2.4	1.0–5.6	0.03

Table 2 Results of unmatched univariate analysis for ages 15 years and older (cases, $n = 36$; controls, $n = 45$)

Exposure	Proportion exposed		Odds Ratio	95% Confidence interval	*P*-value
	Cases (*n* (%))	Controls (*n* (%))			
High-intensity exercise	4 (11)	10 (22)	0.4	0.1–1.8	0.19
Recent stressful event	8 (22)	6 (13)	1.9	0.5–7.0	0.30
Attendance at night clubs	21 (58)	18 (40)	2.1	0.8–5.7	0.10
Current smoker	14 (39)	14 (31)	2.1	0.6–7.3	0.18
Passive tobacco exposure	13 (36)	12 (27)	2.3	0.7–8.3	0.15

Table 3 Results of unmatched univariate analysis for ages 5 years and younger (cases, $n = 21$; controls, $n = 28$)

Exposure	Proportion exposed		Odds Ratio	95% Confidence interval	*P*-value
	Cases (*n* (%))	Controls (*n* (%))			
Breast-fed	11 (52)	21/26† (81)	0.3	0.1–1.1	0.04
Sharing bedroom with two or more persons	9 (43)	3 (11)	6.3	1.2–36.3	0.01
Attendance childcare	8 (38)	9/26† (35)	1.2	0.3–4.6	0.80
Carer smokes	12 (57)	5 (18)	6.1	1.4–28.4	0.01
Passive tobacco exposure	14 (67)	11 (39)	3.1	0.8–12.2	0.06

†Missing data ($n = 26$).

was 3 months in cases compared with 6 months in controls. Attendance at childcare in the previous 4 weeks was not associated with IMD (OR 1.2, 95% CI 0.3–4.6, $P = 0.8$).

Analysis of all cases found that IMD was associated with regular smoking or passive exposure to tobacco smoke (OR 2.3, 95% CI 1.1–4.8, $P = 0.02$). Passive exposure to cigarette smoke was also independently associated with IMD (OR 2.4, 95% CI 1.0–5.6, $P = 0.03$). IMD in children under 6 years of age was more likely if the child had a primary caregiver who smoked (OR 6.1, 95% CI 1.4–29.4, $P = 0.01$).

In multivariate analysis, most of the above-mentioned findings were not confirmed. However, for children under 6 years of age, the risk of IMD was higher in those sharing a room with two or more people (OR 7.4; 95% CI 1.5–36.1, $P = 0.01$) or if the child had a primary caregiver who smoked (OR 9.1; 95% CI 2.1–39.9, $P = 0.003$).

DISCUSSION

Passive exposure to tobacco smoke has been recognized as a factor in the development of bacterial meningitis in children.[14,15] This study confirms previous findings of the association between exposure to tobacco smoke and the risk of IMD. The finding that children under 6 years of age have a higher risk of IMD if their primary caregiver smokes, although not new, further adds to the Australian published literature on this subject.[2] Cigarette smoke might influence the risk of IMD by increasing carriage of *N. meningitidis* in the oropharynx of smokers.[7,16] Children whose primary caregiver smokes are thus more likely to be exposed to carriage of *N. meningitidis* and placed at greater risk of acquiring the disease.

This suggests that cases of IMD in young children might be prevented through reduction in smoking among primary caregivers of young children. However, this risk will not be reduced by simple avoidance of smoking around the child, as it is exposure to the increased carriage in smokers that is the risk factor of importance.[7,16] This information could contribute to antismoking campaigns, particularly targeting parents of young children.

The findings on the protective effects of breast-feeding, though not confirmed in multivariate analysis, warrant further study as they have potential to contribute additional public health messages to the efforts to improve breast-feeding rates. The finding that sharing a bedroom with two or more people was associated with a higher risk of IMD in young children is consistent with other studies that describe the association between crowding and IMD and might reflect an association with lower socioeconomic status.[2,4,17] In very young infants, this association was found in the context of placing the child in the bedroom with parents during the first months of life.

Evidence for an association between IMD and attendance at childcare centres is not clear. A Belgian study suggested a higher attack rate among childcare contacts than the general community and recommended the use of chemoprophylaxis in these settings.[18] Although the evidence was 'weak', the Public Health Laboratory Service of the United Kingdom issued guidance in 1992 to provide chemoprophylaxis to nursery contacts following a single case in those settings.[19] This was not always successful in preventing further cases.[20] Other

studies have suggested that attendance at childcare centres is not associated with a risk of meningococcal disease and might reduce the risk of IMD by removing young children from close and prolonged contact with adults (carriers).[21,22] Australian guidelines limit chemoprophylaxis in childcare settings to children and staff in the same room group attended by a single index case.[23] This is on the basis of same room ('household') contact for a period of more than 4 h in the 7-day period preceding onset of IMD in the case. The finding of this study that attendance at childcare was not associated with IMD suggests that limiting chemoprophylaxis to household-type contacts of single cases within this setting is a reasonable approach at this time.

The cases in this study were similar in age, gender, serogroup and onset to the rest of the SPHUN cases and Queensland cases, which suggests these results may be applicable to the wider Queensland community. Potential weaknesses in this study include the response rate for cases (78%) and the low number of controls per case. This was because some patients declined to participate and some medical practitioners were unable or unwilling to provide controls. The lack of confounding by age or medical practice demonstrated in the comparison of matched and unmatched analyses suggests that unmatched data are suitable for analysis.

Recall bias might be a factor in this study as the severe nature of the infection might promote a different level of recall in cases than to that of controls. However, many controls indicated that they were already aware of meningococcal disease prior to the interview. Recall bias was further reduced by interviewing cases and controls within 1 month of the onset of IMD in the case. Interviewer bias was reduced by training the interviewers in the administration of the open-ended questions in the questionnaire.

Meningococcal disease remains a rare but important public health problem in Australia. This study confirms an established association between risk of IMD and exposure to cigarette smoke and highlights the risk to young children from primary caregiver smoking. The risk of IMD in young children could be further reduced if primary caregivers did not smoke. There is an opportunity to use this message in targeted antismoking campaigns. Such campaigns might have more impact during peak periods of IMD (late winter/early spring). With the funding of the National Meningococcal Conjugate C vaccination programme, it is timely to consider such strategies to further reduce the incidence of IMD. The role of breast-feeding is amenable to further study.

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