Surveillance report

HEPATITIS A ANTIBODY PREVALENCE AMONG PEOPLE WITH AN INTELLECTUAL DISABILITY IN IRELAND

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This manuscript aims to determine the prevalence of antibody to and risk factors for hepatitis A virus (HAV) in individuals attending three intellectual disability services through a cross-sectional survey held in Dublin, Ireland. Participants were 636 individuals aged four to 78 years attending three intellectual disability services. The main outcome measure was the measurement of anti-HAV (IgG antibody) in oral fluid swabs using an antibody capture enzyme immunoassay (EIA) technique. Risk factor information was obtained by questionnaire from the individual's medical record. Participants were 362 males and 274 females. The median age was 36 years. The median age of the individuals differed significantly from one institution to another ($P < 0.001$). The prevalence of antibody to HAV was 43% overall but the individual levels for the three institutions were 65%, 30% and 68% respectively, the difference being statistically significant ($P < 0.05$). Although a number of factors were statistically significantly associated with prevalence of antibody on univariate analysis, only age was associated with the prevalence of antibody on multivariate analysis. Among clients living at home, both age and use of respite care were associated with having antibodies to HAV. In conclusion, the prevalence of antibody increased with age and 14% had evidence of infection in the first ten years of life. We recommend that consideration should be given to immunising new entrants to the service with the combined hepatitis A and B vaccine.

Introduction

The seroprevalence of hepatitis A virus (HAV) has been declining in most parts of the world in recent decades, probably due to improvements in living standards [1]. HAV is a notifiable disease in Ireland, and the number of HAV cases notified in this country decreased by 92% between 2000 and 2003, from 309 in 2000 (8.5/100,000), to 112 in 2001, to 25 in both 2002 and 2003 (0.6/100,000). There was an increase again in 2004 to 47 (1.1/100,000) [2]. However, reporting practices changed in 2004, when, for the first time, case definitions were introduced and laboratories were obliged to notify infectious diseases [3]. Provisional figures for 2005 indicate that 48 cases of hepatitis A were reported (1.2/100,000) (Personal communication). A population based prevalence survey conducted in 1991 in an Irish town found a population immunity level to HAV of 43%, with immunity increasing with age [4].

A 1982 study reported that the prevalence of HAV antibody in residents in institutions for intellectual disability was higher than

in the general population [5]. This was attributed to suboptimal hygiene in institutionalised settings [6]. An Irish seroprevalence survey in a non-residential learning disability setting found a 70% prevalence in the early 1990s [7]. However, screening in three Irish intellectual disability schools found an overall prevalence level of HAV antibody of 10% in 1999 among three to 18-year-olds [8]. Individuals with Down's syndrome have been reported to have a higher prevalence than those with other forms of intellectual disability [5]. Factors reported previously to be associated with anti-HAV positivity include age [6, 9-12] and duration of stay in institutions [6, 10, 12]. However in one study in a country of intermediate endemicity, age or length of stay was not found to influence prevalence [13].

Recent immunisation guidelines in Ireland [14] recommend that patients and carers in institutions for those with intellectual disability (including daycare facilities) receive hepatitis B vaccine, and further recommend that staff and residents in institutions for persons with learning disabilities may be considered for immunisation with hepatitis A vaccine. A review of cost-effectiveness of hepatitis A vaccine in developed countries concluded that vaccination is likely to be cost effective in institutions [15]. A systematic review of evidence of risk of HAV infection concluded that there is moderate evidence of risk of contracting HAV among institutionalised subjects [16]. They recommended that the decision to vaccinate should be made locally on the basis of the home or community's ability to maintain adequate standards of hygiene [16]. Similarly, guidelines for England and Wales state that HAV vaccination should be considered for those individuals with special needs whose capacity to maintain good standards of hygiene is limited, and their carers, following a risk assessment [17].

This study was carried out to clarify the need for hepatitis A vaccination in this population.

The aims of the study were to:

- (a) determine the prevalence of HAV antibodies in individuals attending three intellectual disability services,
- (b) document factors associated with prevalence
- (c) provide information for planning of future vaccination programmes.

The study was carried out between April 2003 and January 2004.

Methods

Study population

The study was carried out in three large centres for people with an intellectual disability in Dublin. All three centres provide services for all levels of intellectual disability

Sample size

The sample was chosen to ensure a 95% confidence interval around an estimated seroprevalence of 50% would be $\pm 5\%$. The sample was as follows: All residents on campus of institution A (178), and all residents in institution C (148), were invited to take part. In institution B, which is a multicentred institution, a random computer-generated sample of 600 people (of 1420 who were enrolled in the institution) were invited to take part. They all attended a service on a daily basis, and some of them were living in community residential settings. A total of 926 individuals from the three institutions were invited to participate.

Eligibility criteria were:

- No documented previous hepatitis A vaccination
- No immunoglobulin administered in the previous six months

Written consent to participate was obtained from the client where possible, and from their parents and/or guardians

Study instruments

We used a questionnaire to obtain basic demographic data and other information relevant to the spread of HAV from each client's medical records. Each institution also had to complete a brief questionnaire on total numbers of people in the institution and on whether any outbreaks of HAV had occurred there. Measurement of anti-HAV (IgG antibody) using an antibody capture enzyme immunoassay (EIA) technique from oral fluid samples was undertaken using a modification of a method used previously in the same laboratory which included specimen validation [18]. 'Comparison of anti-HAV results for 50 matched serum and oral fluid specimens showed sensitivity and specificity greater than 95% for this modification' (personal communication). Oral fluid was collected according to manufacturer's instructions. One of the authors (SB) carried out the data collection in two institutions while a staff member did data collection in the third.

Ethics

Participation was voluntary. Study approval was received from the Research Ethics Committee of the Faculty of Public Health Medicine of the Royal College of Physicians of Ireland.

Conduct and management of the study

A steering committee comprising the authors of this paper guided the study.

Analysis

Analysis (χ^2 test and logistic regression) was carried out using the statistical package R.

Results

The response rate was 69% (636/926) overall. There was no record of any of the participants being given immunoglobulin (in the previous six months) or hepatitis A vaccine (ever), so all questionnaires were eligible for inclusion. No outbreaks of HAV were known to have occurred in any of the services. Not all questions were answered, and so the denominator is below 636 for some

results. The response rate by institution was as follows: 73% (130/178) in institution A, 69% (415/600) in institution B and 61% (91/148) in institution C. The vast majority (95%:251/265) of the non-responders did not return the form with the remaining 5% saying no.

The median age of responders was 36 years, and of non-responders, 38 years ($P=0.06$, Wilcoxon rank-sum test). Further analysis showed a strong interaction between age and institution, $= 26.8$, $p = 2.8e-7$). For this reason, analysis of non-response was

TABLE 1

Analysis of response rate by institution, age and sex, Dublin, Ireland, April 2003 - January 2004

Institution	Gender		Age	
	M	F	≤ 36 years	> 36 years
A	70%	62%	60%	73%
B	72%	74%	69%	77%
C	56%	53%	88%	43%

Median = 36 years

done separately for each institution. The response rate by age and gender by institution is shown in Table 1.

The 636 responders included 362 males and 274 females. The participants' median age differed significantly ($P<0.001$) from one institution to another with individuals attending service B substantially younger than those in institution A or C. The level of disability of the respondents was as follows: mild (86/634:13%), moderate (258/634:41%) and severe (290/634:46%). Twenty nine per cent (181/628) had Down's syndrome. The majority attended a day unit such as a school or a workshop (601/635:95%).

The residence of the respondents was as follows: home (308/635:49%), institution (225/635:35%) and community home (102/635:16%). Of the 308 who lived at home, 290 (94%) replied to the question about respite care: 82% of these made use of it. Almost a quarter (23%: 144/631) had incontinence.

HAV antibody level

There were 635 oral fluid samples received. The overall prevalence of HAV antibody was 43% (271/635), with the individual levels for three institutions being 65% (institution A), 30% (institution B) and 68% (institution C). The differences were statistically significant ($P<0.05$). A comparison of antibody prevalence by age group in this study and in the population study [4] is shown in the figure. A comparison test between the two studies found no significant difference in overall antibody prevalence but there was an obvious difference in the 0-9 year age group.

The prevalence of antibody in those living at home was 25%, compared with 60% for those living in either an institution or a community dwelling ($P<0.001$). The distribution of HAV antibody status with respect to the variables in the questionnaire is shown in table 2. The non-significant factors are gender, use of respite care and type of incontinence. Univariate logistic regression is outlined in table 3. Multivariate logistic regression analysis for the entire study group and for those living at home is outlined in tables 4a and 4b. The only factor significantly associated with prevalence of HAV antibody on multivariate analysis for the whole group was age. Among those living at home, in addition to age, the use of respite care was also associated with prevalence of antibody.

FIGURE

Comparison between level of antibody to Hepatitis A virus in current study and in previous population study in an Irish town in 1991

* Source: [4]

Discussion

We examined the prevalence of HAV antibody and risk factors for HAV in those with an intellectual disability in three centres in Ireland. The rate is much lower than in an Irish non-residential setting in the early 1990s [7]. The overall level of 10% among those aged 3-18 years in special schools in 1999 [8] is similar to the rate of 10.9% found in those aged 0-19 years here. Our overall response rate was good, the prevalence of HAV may have been somewhat underestimated in institution C as the non-responders there were older and the overall response rate for that institution was poorer. The epidemiology of HAV has changed fundamentally with the advent of hepatitis A vaccine [19]. Before that it was primarily cyclical but this is now changing in the US [19], the UK and Scandinavia [20]. We are not yet in a position to say whether this cyclical pattern has also disappeared in Ireland. We note that the rates have been at their lowest level over the past four to five years but we do not know what will happen to the cyclical pattern in the years to come.

There is a paucity of studies available on this topic and many of those available are old. Comparisons may not be valid given the change in social circumstances. The overall prevalence of antibody of 43% is similar to that found in two US studies in 1970 and in 1994-95 [9,12]. Given the decline in the prevalence of HAV in recent decades, the timing of the studies will have a very significant impact on the antibody level. The only European studies in the intellectual disability setting found were in France (1992-3: anti-HAV prevalence of 50%) and in Spain (1996-7: 54%) [11,13]. These rates were marginally higher than we found but the Spanish study was carried out in an area of intermediate endemicity.

As found previously, the prevalence of antibody significantly increased with age [6, 9-12] on both univariate and analysis. While a number of factors were significantly associated with anti-HAV on both univariate and analyses, the only factor significantly associated with HAV antibody on multivariate logistic regression analysis for the whole group was age, reflecting the fact that people do not lose their immunity and that older people are more likely to have been infected during their lifetime. Down's syndrome was found to be negatively associated, contrary to the findings of other studies [5]. In countries with a low prevalence of anti-HAV, studies have found a close correlation with age and duration of institutionalisation and

TABLE 2

Distribution of hepatitis A virus antibody among individuals using χ^2 analysis, Ireland, April 2003 - January 2004

Variable		Hepatitis A virus antibody		P value
		Positive	Negative	
Gender	Male	144 (40%)	217 (60%)	N.S.
	Female	127 (46%)	147 (54%)	
Institution	A	84 (65%)	45 (35%)	P = 0.000 *
	B	125 (30%)	290 (70%)	
	C	62 (68%)	29 (32%)	
Age group	0-9 yrs	8 (14%)	49 (86%)	P = 0.000 *
	10-19 yrs	13 (10%)	122 (90%)	
	20-29 yrs	17 (27%)	46 (73%)	
	30-39 yrs	54 (53%)	47 (47%)	
	40-49 yrs	76 (56%)	59 (44%)	
	50-59 yrs	75 (71%)	30 (29%)	
	60-69 yrs	24 (71%)	10 (29%)	
	70-79 yrs	4 (100%)	0 (0%)	
Day unit	Attendee	247 (41%)	353 (59%)	P = 0.001*
	Non-attendee	24 (69%)	11 (31%)	
Day unit type	Workshop	103 (57%)	79 (43%)	P = 0.000*
	Day activation unit/ local centre	106 (54%)	89 (46%)	
	Adult special care/ nursing care unit	12 (57%)	9 (43%)	
	Children's developmental day unit	6 (13%)	40 (87%)	
	School	12 (8%)	134 (92%)	
	Other	7 (78%)	2 (22%)	
Residence	Home	77 (25%)	231 (75%)	P = 0.000*
	Institution	148 (66%)	76 (34%)	
	Community	46 (45%)	56 (55%)	
Respite	Made use of	60 (26%)	170 (74%)	N.S.
	Not made use of	12 (20%)	48 (80%)	
Disability level	Mild	39 (45%)	47 (55%)	P = 0.000*
	Moderate	85 (33%)	173 (67%)	
	Severe	146 (51%)	143 (49%)	
Diagnosis	Down's syndrome	64 (36%)	116 (64%)	P = 0.020*
	Non-Down's syndrome	204 (46%)	243 (54%)	
Incontinence	Present	51 (35%)	93 (65%)	P = 0.043*
	Absent	218 (45%)	263 (55%)	
Incontinence type	Urinary	2 (100%)	0 (0%)	N.S.
	Faecal	6 (40%)	9 (60%)	
	Both	38 (34%)	74 (66%)	

N.S.: not significant

* Significant $p < 0.05$

a high prevalence of anti-HAV in institutionalised intellectually disabled patients [6, 10]. Among those living at home, both age and the use of respite care were significantly associated with HAV antibody.

Neither the World Health Organization nor the Centers for Disease Control and Prevention in Atlanta (USA) lists people in institutions for intellectual disabilities as a high-risk group needing hepatitis A vaccine [19,21]. However, this client group is vaccinated in a number of European countries according to the findings of the EUROHEP.NET project [22]. A large US study conducted in the 1990s concluded that the current need for such an intervention is not clearly demonstrated [12]. Changes in living arrangements, universal precautions and other changes may have substantially decreased the contemporary risk for HAV [12]. While acknowledging that the population prevalence study was done 15 years ago, there was a much higher prevalence of antibody in the 0-9 year age group in our study. It would be useful to have ongoing seroprevalence studies for the Irish population.

The primary course of the adult combined hepatitis A and B vaccine (3 doses) in Ireland currently (GlaxoSmithKline, personal communication, March 2006) costs €102.84, compared with €57.15 for hepatitis B vaccine. The equivalent paediatric costs are €57.15 and €41.88 respectively. So, the differential is very small for the paediatric vaccine. As it is current policy that those attending intellectual disability services receive hepatitis B vaccine [14], and given the higher level of immunity in this study in the 0-9 years age group in comparison to the previous population study [4], consideration should be given to offering new entrants the combination vaccine. A high uptake of the combined vaccine among special schools' pupils was achieved with one school having an 86% uptake of first and second dose (n=19) and the second having a 97% uptake (n=30). The third school was offered hepatitis A vaccine only in response to an outbreak in that school [8]. 'This vaccine is safe [23] and easy to administer with hepatitis B'. It must be remembered that a single lapse of appropriate hygiene during exposure to the virus is sufficient to cause infection [15].

These results will be available to Irish vaccination policy makers and thus can be used to formulate future policy. In particular, we recommend that consideration should be given to immunising new entrants to the intellectual disability service with the combined hepatitis A and B vaccine. In the interim, strict hygiene and infection control policies should be maintained in the work and living areas of those with an intellectual disability.

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TABLE 3

Prevalence of hepatitis A, univariate logistic regression, Dublin, Ireland, April 2003 - January 2004

Variable	Unadjusted odds ratio	95% confidence interval
Gender - NS	1.30	0.95 - 1.79
Institution *		
Institution A	1.00	-
Institution B	0.23	0.15 - 0.35
Institution C	1.15	0.65 - 2.03
Age group *		
0 - 9 years	1.00	-
10 - 19 years	0.65	0.62 - 0.69
20 - 29 years	2.26	2.21 - 2.31
30 - 39 years	7.04	5.17 - 9.57
40 - 49 years	7.89	5.51 - 11.30
50 - 59 years	15.31	9.52 - 24.62
60 - 69 years	14.7	7.30 - 29.61
Day unit *	0.32	0.12 - 0.84
Day unit type *		
Workshop	1.00	-
Day activation unit/local centre	0.91	0.44 - 1.88
Adult special care/nursing care unit	1.02	0.32 - 3.24
Children's developmental day centre	0.12	0.09 - 0.14
School	0.07	0.05 - 0.09
Other	2.68	0.16 - 45.15
Residence *		
Home	1.00	-
Institution	5.84	4.00 - 8.53
Community	2.46	1.54 - 3.93
Respite - NS	1.41	0.70 - 2.84
Disability level *		
Mild	1.00	-
Moderate	0.59	0.44 - 0.80
Severe	1.23	0.44 - 3.45
Having Down's syndrome*	0.66	0.56 - 0.77
Incontinence - NS	0.67	0.45 - 1.01
Incontinence type *	1.94	1.29 - 2.92
Urinary		
Faecal		
Both		

* Significant p<0.05, N.S. = non-significant

TABLE 4A

Multivariate logistic regression for entire study group (n=636), Dublin, Ireland, April 2003 - January 2004

Variable	Odds ratio	P> z	95% Confidence interval
Intercept	0.16		0.07-0.39
Age group		0.00	
0 - 9 years	1.00	-	-
10 - 19 years	0.50		0.20 - 1.25
20 - 29 years	1.83		0.78 - 4.41
30 - 39 years	6.06		2.89 - 13.63
40 - 49 years	6.36		3.05 - 14.24
50 - 59 years	12.83		5.76 - 30.65
60 - 69 years	11.53		4.27 - 33.90
70 - 79 years	8.2 x 10 ⁶		0.00 - Not defined
Disability		0.65	
Mild	1.00	-	-
Moderate	0.97		0.54 - 1.76
Severe	1.20		0.67 - 2.15
Gender	1.30	0.17	0.89 - 1.89
Down's syndrome	0.80	0.31	0.52 - 1.23
Incontinent	1.13	0.64	0.68 - 1.90

TABLE 4B

Multivariate logistic regression for those living at home (n=308), Dublin, Ireland, April 2003 - January 2004

Variable	Odds ratio	P> z	95% confidence interval
Intercept	0.10		0.02 - 0.53
Age group		0.00	
0 - 9 years	1.00	-	-
10 - 19 years	0.46		0.18 - 1.18
20 - 29 years	2.83		1.02 - 8.03
30 - 39 years	3.42		1.35 - 9.10
40 - 49 years	7.07		2.49 - 21.36
50 - 59 years	9.08		0.72 - 221.5
60 - 69 years	1.75		0.07 - 21.22
70 - 79 years *	-	-	-
Disability		0.73	
Mild	1.00	-	-
Moderate	0.74		0.32 - 1.74
Severe	0.95		0.27 - 3.36
Gender	1.23	0.50	0.67 - 2.26
Respite	2.36	0.03	1.09 - 5.44
Down's syndrome	1.12	0.75	0.57 - 2.22
Incontinent	1.09	0.87	0.36 - 3.48

* Due to the small number of people included in this category (n=4), the regression estimates were not calculated

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