ELSEVIER

Vaccine 19 (2001) 844–849

Vaccine

www.elsevier.com/locate/vaccine

Prevalence of hepatitis A virus infection in sewage plant workers of Central Italy: is indication for vaccination justified?

P. Bonanni [a,*], N. Comodo [a], R. Pasqui [a], U. Vassalle [b], G. Farina [b], A. Lo Nostro [b], V. Boddi [c], E. Tiscione [a]

[a] *Department of Public Health and Epidemiology, University of Florence, Florence, Italy*
[b] *Operative Unit of Hygiene and Health in the Workplace, Local Health Agency No. 11, Empoli, Italy*
[c] *Department of Experimental Pathology and Oncology, University of Florence, Florence, Italy*

Received 29 March 219; received in revised form 8 June 2000; accepted 27 June 2000

Abstract

Prevalence of antibodies to hepatitis A virus (HAV) was studied in a group of 65 sewage plant workers living in Tuscany, Central Italy. In order to evaluate the effect of several confounders (age, place of birth, income, educational degree, sea-food consumption, etc.), subjects under study were matched with 160 other workers residing in the same area. Anti–HAV was detected in about 51% of sewage workers and 44% of other employees. The difference was not statistically significant. Both univariate and multivariate analysis showed that the main variables related to previous HAV infection were increasing age ($P < 0.001$), birth in Southern Italy ($P < 0.01$) and lower educational degree ($P < 0.001$). Although other studies in Northern and Central Europe showed a slightly higher risk of infection in sewage workers versus general population, lack of evidence of occupational risk in Italy might be explained by the relative importance of a higher degree of viral circulation in the past. The changing epidemiology of HAV infection in Italy with increasing numbers of susceptibles in adults and the potential occupational risk suggest that the present indication to immunize sewage plant workers against hepatitis A should be maintained.

Keywords: Hepatitis A; Seroprevalence; Sewage plant workers; Vaccination

1. Introduction

Hepatitis A virus (HAV) is the causative agent of one of the most widespread infections transmitted via the faecal-oral route.

In recent decades, the circulation of the virus has substantially decreased in many countries as a consequence of improvements in the treatment of sewage and general hygiene conditions. In Italy, the increase of susceptibility in older children, adolescents and young adults has already given rise to outbreaks and even to a large epidemic in a south-eastern region in 1996 [1]. Hepatitis A inactivated vaccine has been available in the country since 1994. In 1995, a Consensus Conference held in Rome identified some risk groups for which immunization was recommended. Sewage plant workers were among those subjects who, due to the potential risk of infection connected to work with water and aerosols contaminated by faecal materials, were considered for vaccination.

However, there is no recently published study on the prevalence of anti-HAV in sewage plant workers in Italy where all possible confounders (age, place of birth, socio-economic status, educational degree, sea-food consumption, travels to endemic areas, etc.) have been controlled.

Our work aimed at studying the prevalence of antibodies to hepatitis A virus in workers of a single sewage plant in Tuscany, Italy in comparison with other workers matched for the main potentially confounding variables.

* Corresponding author. Present address: Viale G.B. Morgagni, 48 – 50134 Florence, Italy. Tel.: +39-055-432729; fax: +39-055-4222541.

E-mail address: bonanni@dsp.igiene.unifi.it (P. Bonanni).

0264-410X/00/$ - see front matter
PII: S0264-410X(00)00227-9

2. Materials and methods

A 4-month study was carried out on anti-HAV prevalence in workers of a sewage plant, for whom potential exposure to fluids and aerosols containing faecal materials was an occupational hazard. In order to verify possible differences in seroprevalence with the open population, a control group of workers living in the same area but with no potential exposure was identified. Subjects to be enrolled in the control group were randomly selected among all employees of the same municipality where the sewage plant was located and were matched with sewage plant workers for age and place of birth.

All subjects were informed of the aim of the research and gave consent to participate in the study.

Overall, the study group (sewage workers) consisted of 65 subjects (61 males and four females). The control group was made up of 160 subjects (111 males and 49 females).

A blood sample (5 ml) was collected from each subject. Sera were stored at −20°C until testing. Anti-

STUDY ON HAV PREVALENCE - DATA COLLECTION FORM

Subject identification (code).....

Date of birth.....

Place of birth.....**Province**.....

Residence.....**Province**.....

Educational degree ❑ primary school ❑ low. secondary school ❑ high. secondary school ❑ university degree

Company.....**Length of service**.....

Occupation.....

Raw shellfish (fish) consumption:
❑ never ❑ sometimes ❑ often

Number of household members.....

Overall family yearly income (sum-up income of husband, wife and working siblings) (It. Liras):

❑ < 20 million ❑ 20-30 million
❑ 30-40 million ❑ 40-50 million
❑ 50-70 million ❑ 70-100 million
❑ >100 milioni

Travels abroad:
❑ never ❑ rarely ❑ rather frequent (1-2/year)
❑ very frequent (> 2/year)

Destination of travels (indicate all destinations of the last years):
❑ Western Europe ❑ Eastern Europe
❑ North America or Australia ❑ Japan
❑ Asia (except for Japan) ❑ Africa ❑ South America

Other occupations in the past.....

Date.....

Fig. 1. Data collection form for the study of anti-HAV prevalence in sewage plant workers and in other workers.

bodies to HAV were detected using the commercial ELISA kit HAV Ab (Nuclear Laser Medicine s.r.l., Milan, Italy). Reading was performed with a photometer at 450 nm (reference background filter: 620 nm). The cut-off value was calculated according to the manufacturer's instructions as follows: (mean optical density of negative controls + mean optical density of positive controls): 2. Samples whose optical density was lower than the cut-off were classified as positive.

Subjects enrolled in the study were asked questions regarding date and place of birth, length of work in sewage plants (study group only) and information on possible confounders (socio-economic and educational status, raw shellfish consumption, travels to highly endemic areas for hepatitis A virus infection, etc.). All data were reported on the personal form shown in Fig. 1.

The statistical analysis for association between qualitative variables was performed using the chi-square or the Fisher's exact test, as appropriate. Analysis of variance followed by multiple comparison test (Scheffé test) was used to compare mean ages of different groups.

The dependence of anti-HAV reactivity from predictive variables was tested by univariate and multivariate logistic regression. Differences were considered significant when P values were lower than 0.05. All elaborations were performed with the Stata Statistical Software, release 6.0 (StataCorp., College Station, TX, USA).

3. Results

Subjects of the study group (sewage workers) and of the control group (other workers) were preliminarily analyzed for the most important potentially confounding variables considered in the study.

The two groups almost overlapped with regard to number of household members and number of travels abroad. Differences existed in the composition of the two groups with regard to sex, since occupation in sewage plants was almost exclusive for males (only 6% of the study group consisted of females), while in the control group, 69% of subjects were males and 31% females.

Slight differences were detected in the variables 'educational level' (only 2% had a university degree among sewage workers vs. 11% in the controls); family income (slightly higher in the study group) and raw shellfish consumption (more frequent in the study group: 58% — than in the control group: 26%).

Prevalence of anti-HAV positivity in workers of the sewage plant was 33/65 (50.7%). In the control group, antibodies to hepatitis A virus were detected in 70/160 subjects (43.7%). The difference was not statistically

Table 1
Demographic characteristics, and frequency distribution of antibody to Hepatitis A virus, in sewage workers and control group

Demographic characteristic	Sewage workers ($n = 65$)		Control group ($n = 160$)		Statistical significance
	Anti-HAV positive	Anti-HAV negative	Anti-HAV positive	Anti-HAV negative	
Total	33	32	70	90	ns[a]
Age (years)					
≤30	2	4	0	18	ns
31/40	6	12	13	29	ns
41/50	14	10	22	32	ns
51/60	10	6	24	10	ns
>60	1	0	11	1	
Place of birth					
North-centre	22	31	59	86	ns
South	11	1	11	4	ns
Educational level					
Primary school	5	3	23	7	ns
Lower secondary school	20	12	22	31	ns
Higher secondary school	7	15	19	40	ns
University degree	0	1	6	11	ns
No answer	1	1	0	1	
Family income (million It Liras)					
20/30	1	1	8	15	ns
31/40	3	6	8	10	ns
41/50	11	6	25	14	ns
51/70	10	11	19	34	ns
71/100	7	7	4	9	ns
>100	0	1	4	6	ns
No answer	1	0	2	2	
Number of family members					
1	0	1	3	2	ns
2	3	6	8	7	ns
3	10	10	24	30	ns
4	15	7	22	29	ns
5	3	7	9	11	ns
6	1	1	1	9	ns
7	1	0	1	1	ns
No answer	0	0	2	1	
Travels abroad					
Never	10	8	29	23	ns
Africa/Asia	7	6	11	17	ns
Europe	16	16	24	41	ns
North America	0	1	3	1	ns
South America	0	1	2	7	
No answer	0	0	1	1	
Raw shellfish consumption					
Yes	20	18	18	24	ns
No	13	14	50	65	ns
No answer	0	0	2	1	

[a] ns = non significant.

significant ($\chi^2 = 0.917$; $P = 0.338$). In the group of sewage plant workers, the mean duration of exposure was 11.9 years (S.D. = 6.1 years) among anti-HAV positive subjects, and 10.4 years (S.D. = 6.3 years) among seronegative subjects ($P = 0.104$; non-significant). We also calculated mean ages of anti-HAV positive and anti-HAV negative subjects among sewage plant workers and control population. Among sewage workers, anti-HAV negative subjects had a mean age of 38.7 years (S.D. = 8.4 years), and anti-HAV positive individuals had a mean age of 43.8 years (S.D. = 9.1 years). In the control group, the mean age of anti-HAV negative subjects was 37.8 years (S.D. = 8.7 years), while that of anti-HAV positive subjects was 47.7 years

(S.D. = 8.9 years). The analysis of variance showed an overall significant difference among mean ages of the four groups. The difference of mean age between anti-HAV positive and negative sewage plant workers was less than 5 years. However, the Scheffé test was not significant ($P = 0.135$) also due to the relatively small size of the two groups. The difference between anti-HAV positive and negative other workers was statistically significant (9.9 years; $P < 0.001$).

The demographic characteristics and frequency distribution of antibodies to the hepatitis A virus in sewage workers and in the control group are reported in Table 1. Since differences in the overall prevalence of anti-HAV between sewage workers and controls were not significant, we also performed univariate analysis on all subjects considered as a single group. The results of univariate analysis of seroprevalence of antibodies to HAV in sewage workers and control population are shown in Table 2.

Logistic regression was performed on the study and on the control group separately for all variables collected in the data collection form. Only the influence of sex was not investigated in the study group due to the low number of females. Occupation in sewage plants was not significantly associated with higher risk of anti-HAV positivity even in logistic regression analysis (odds ratio = 0.91; 95% C.I. 0.40–2.08; P = n.s.). No statistically significant association was found between different investigated factors and anti-HAV reactivity in the group of sewage workers. However, P values for

Table 2
Seroprevalence of antibody to hepatitis A virus in sewage workers and control population considered as a single group: univariate analysis

Demographic characteristic	Anti-HAV+(103), No. (%)	Anti-HAV−(122), No. (%)	OR[a] (95% CI)[b]	P-value
Age (years)				
≤30	2 (8.3)	22 (91.7)	1[c]	
31/40	19 (31.7)	41 (68.3)	5.225 (1.11–24.54)	0.036
41/50	36 (46.)	42 (53.8)	9.16 (2.01–41.72)	0.004
51/60	34 (68)	16 (32)	23.37 (4.88–111.76)	0.000
>60	12 (92.3)	1 (7.7)	71.5 (8.96–570.27)	0.000
Place of birth				
North-centre	81 (40.9)	117 (59.1)	1[c]	
South	22 (81.5)	5 (18.5)	4.37 (1.67–11.41)	0.003
Educational level				
Primary school	28 (73.7)	10 (26.3)	1[c]	
Lower secondary school	42 (49.4)	43 (50.6)	0.34 (0.15–0.80)	0.014
Higher secondary school	26 (32.1)	55 (67.9)	0.16 (0.07–0.39)	0.000
University degree	6 (33.4)	12 (66.6)	0.17 (0.05–0.60)	0.006
No answer	1	1		
Family income (million It Liras)				
20–30	9 (36)	16 (64)	1[c]	
31–40	11 (40.7)	16 (59.3)	0.95 (0.30–2.92)	ns
41–50	36 (64.3)	20 (35.7)	2.8 (1.03–7.61)	ns
51–70	29 (39.2)	45 (60.8)	1.00 (0.38–2.61)	ns
71–100	11 (40.7)	16 (59.3)	1.06 (0.34–3.33)	ns
>100	4 (36.4)	7 (63.6)	0.88 (0.20–3.93)	ns
No answer	1	0		
Number of family members				
1 or 2	14 (47)	16 (53)	1[c]	
>2	87 (45.3)	105 (54.7)	0.91 (0.71–1.16)	ns
No answer	2	1		
Travels abroad				
Never	39 (55.7)	31 (44.3)	1[c]	
Africa/Asia	18 (43.9)	23 (56.1)	0.64 (0.29–1.39)	ns
Europe	40 (41.2)	57 (58.8)	0.58 (0.31–1.08)	ns
North America	3 (60)	2 (40)	0.54 (0.08–3.47)	ns
South America	2 (20)	8 (80)	0.35 (0.08–1.47)	ns
Raw shellfish consumption				
Yes	38 (47.5)	42 (52.5)	1[c]	
No	63 (44.4)	79 (55.6)	1.18 (0.68–2.04)	ns

[a] Univariate odds ratio.
[b] Confidence intervals.
[c] Reference group.

Table 3
Sewage workers and control population considered as a single group: variables significantly and independently associated with the presence of antibody to HAV

Variable	Adjusted odds ratio	(95% CI)	*P* value
Age (years)			
≤30	1[a]		
31–40	5.41	1.10–26.63	0.038
41–50	9.95	2.08–47.52	0.004
51–60	26.50	5.27–133.23	0.000
>60	87.75	10.55–729.78	0.000
Place of birth			
North-centre	1[a]		
South	5.74	1.99–16.51	0.001
Educational level			
Primary school	1[a]		
Lower secondary school	0.34	0.15–0.80	0.014
Higher secondary school	0.16	0.07–0.39	0.000
University degree	0.17	0.05–0.6	0.006

[a] Reference group.

age and place of birth were 0.054 and 0.058, respectively.

In the control group, older age and place of birth in the south of the country were significantly associated with positivity ($P < 0.001$ and $P = 0.019$, respectively).

Univariate analysis and multivariate analysis were subsequently performed on the overall sample under study irrespective of occupation in sewage plants. The results are reported in Table 3.

Among 225 total studied subjects, data regarding all variables were available for 217 individuals.

Three variables were significantly associated with anti-HAV positivity: increasing age ($P < 0.001$); birth in the south of the country ($P < 0.01$) and lower school education ($P < 0.001$). These statistically significant differences persisted after removing all other possibly related variables in a step-wise logistic regression.

4. Discussion

Sewage plant workers are at theoretical risk of HAV infection, since the virus is frequently isolated from waste waters. In a recently published article, hepatitis A virus was detected in as many as 80% of raw sewage samples concentrated by ultrafiltration. Also the final effluent was occasionally shown to be contaminated, thus indicating the possibility for HAV to cross the wastewater treatment plant [2].

Occupational exposure might occur either directly via splashes or aerosol of contaminated water, or indirectly due to lack of compliance to standard operating procedures (i.e. food consumption or smoking in the workplace).

No previous study published in the international literature showed a dramatic increase of risk in sewage workers compared with other unexposed workers. However, several authors report a slightly higher prevalence of anti-HAV in subjects employed in the treatment of waste waters. Among employees of the municipality of Copenhagen, sewer workers showed a prevalence of anti-HAV of 80%, versus 60% in gardeners and 48% in clerks. The prevalence was correlated with age rather than duration of employment [3]. In Singapore, the seroprevalence of anti-HAV positive sewage workers was 2.2 times higher than that of another non-occupationally exposed group. It must be noted that seroprevalence was correlated with age and educational levels, the association being independent of the occupational association [4].

An article on workers of the Parisian area in France shows an adjusted odds ratio for anti-HAV 2.15 times higher in sewage workers compared to those not occupationally exposed, although the overall rate of reactivity was not statistically different in the two groups [5].

In our study, we selected the control group among workers in the same municipality where the sewage plant was located, but with no potential occupational exposure to contaminated fluids, and we matched sewage workers and controls for age and place of birth (north or south of the country); this should have prevented any selection bias in the control group.

The results show that the only variables significantly associated with anti-HAV reactivity both in univariate and in multivariate analysis were increasing age, place of birth in the south of the country and lower educational level. Treatment of sewage as an occupation did not turn out to be related to a higher prevalence of antibodies to the hepatitis A virus. This could be explained by different considerations. First, the relative risk of HAV infection in sewage workers versus the general population does not seem to be very high according to the data reported in the international literature [3–5]. For this reason, it is hard to reach a definitive demonstration of increased probability of infection, also due to the relatively low number of subjects working in sewage plants. Moreover, the prevalence of HAV infection in the general population of Italy has been historically higher than in Central and Northern European countries. Only in recent decades has the circulation of the virus dramatically decreased; thus increasing the number of susceptible subjects in the younger age groups [6]. Therefore, the change in the epidemiological patterns of HAV infection in Italy could be too recent to allow for detection of a significant difference of risk between exposed and unexposed individuals.

In this view, the results of our study should not be interpreted as contradictory with the importance of

vaccinating sewage workers. The progressive decline of the previously described cohort effect could put into evidence an occupational risk of HAV infection.

The changing epidemiology of HAV infection in Italy with increasing numbers of susceptibles in adults and the potential occupational risk suggest that the present indication to immunize sewage plant workers against hepatitis A should be maintained.

References

[1] Malfait P, Lopalco PL, Salmaso S, et al. An outbreak of hepatitis A in Puglia, Italy, 1996. Eurosurveillance 1996;1:33–5.

[2] Divizia M, Ruscio V, Degener AM, Panà A. Hepatitis A virus detection in wastewater by PCR and hybridization. New Microbiol 1998;21:161–7.

[3] Skinoj P, Hollinger FB, Hovind-Hougen K, et al. Infectious liver diseases in three groups of Copenhagen workers: correlation of hepatitis A infection to sewage exposure. Arch Environ Health 1981;36:139–43.

[4] Heng BT, Goh KT, Doraisingham S, Quek GH. Prevalence of Hepatitis A virus infection among sewage workers in Singapore. Epidemiol Infect 1994;17:162–6.

[5] Cadilhac P, Roudot-Thorval F. Seroprevalence of hepatitis A virus infection among sewage workers in the Parisian area, France. Eur J Epidemiol 1996;12:237–40.

[6] Bonanni P, Colombai R, Franchi G, Lo Nostro A, Comodo N, Tiscione E. Experience of hepatitis A vaccination during an outbreak in a nursery school of Tuscany, Italy. Epidemiol Infect 1988;121:377–80.