Vaccine xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Chronically ill adolescents are also incompletely vaccinated: A cross-sectional study in France

Christèle Gras-Le Guen [a,b,*], Arnaud Legrand [b], Marylène Caquard [a], Xavier Micaelli [a], Georges Picherot [a], Sylvie Lacroix [a], Christelle Volteau [c], Elise Launay [a,b]

[a] Department of Pediatrics, University of Nantes, Nantes, France
[b] National Institutes of Health and Medical Research, CIC 1413, University Hospital of Nantes, Nantes, France
[c] Plateforme de Biométrie, University Hospital of Nantes, Nantes, France

ARTICLE INFO

Article history:
Received 6 March 2017
Received in revised form 6 July 2017
Accepted 13 July 2017
Available online xxxx

Keywords:
Adolescent immunization
Chronic disease
Vulnerable population
France

ABSTRACT

Background: Adolescent vaccination coverage tends to be suboptimal, leading to resurgent infectious pathologies and vulnerability to various pathogens. The low frequency of medical consultations and missed opportunities for vaccination are often used to explain the low rate of vaccination. The aim of this study was to assess if the vaccination coverage rate is higher in chronically ill adolescents (CIA) who require a close pediatric specialized follow-up versus the rate in healthy adolescents (HA).
Methods: A monocentric cross-sectional study was conducted in the Nantes University Hospital. We included 114 CIA and 266 HA. The vaccination coverage rate and the up-to-date immunization status were compared between ill versus healthy adolescents for each of the following vaccines: diphtheria, tetanus, acellular pertussis, inactivated poliovirus (DTaP/IPV), measles-mumps-rubella (MMR), hepatitis B (HepB), meningococcal C conjugate (MnC), human papillomavirus (HPV) and composite combinations (e.g. DTaP/IPV-MMR-HepB-MnC).
Results: The overall immunization rate for DTaP/IPV-MMR-HepB-MnC was very low, with no significant difference between CIA and HA (9.6% versus 13.5%; p = 0.28). Most of the investigated vaccines exhibited similar immunization patterns for the two groups: DTaP/IPV (77.2 vs. 76.7%; p = 0.97), MMR (92.1 vs. 95.9%; p = 0.14), HepB (51.8 vs. 48.5%; p = 0.51) with the exception of the MnC (18.4 vs. 27.8%; p = 0.05) and HPV (28.6 vs. 16.1%; p = 0.04).
Conclusion: Despite undergoing specialized and close medical follow-up, we found that the vaccination coverage rate for the CIA remained suboptimal. This indicates that pediatricians need to check the vaccination status and, when required, ensure that the vaccination schedules for these fragile patients are up-to-date.

1. Introduction

Whereas the vaccination coverage of infants and pre-school children is considered to be high and to conform with the relevant national guidelines in France, adolescents remain largely incompletely vaccinated, and public awareness about adolescent vaccines is more limited [1,2]. In 2012, the vaccination coverage rate in a cohort of 750 15-year-old adolescents in France was 86% for the series of six diphtheria-tetanus-inactivated poliovirus vaccine (DT/IPV) doses, 77% for five acellular pertussis (aP) doses, 34% for two or three hepatitis B (HepB) doses, and 89% for two measles-mumps-rubella (MMR) doses [2]. In France, as in the United States (US), the level of vaccination coverage among adolescents is below the official target of 90%, and none of the official national vaccination targets were reached in 2012 [2,3].

Although it is a time when they may be exposed to serious yet preventable infectious diseases, immunization rates for adolescents in France are especially low for HepB virus and human papillomavirus (HPV); two of the most common sexually transmitted infections with potentially severe morbi-mortality [4]. Various barriers to provide immunizations to adolescents have been proposed [5]. Among the recurrent challenges are the decreased frequency of medical consultations by a healthy young population that rarely visits primary care physicians, and missed opportunities for vaccination. The latter were reported by Lee et al. in 2008 to be as high as 84% among the 103,739 visits for which the adolescents

* Corresponding author at: Department of Pediatrics, University of Nantes, Nantes, France.
E-mail address: christele.grasleguen@chu-nantes.fr (C. Gras-Le Guen).

http://dx.doi.org/10.1016/j.vaccine.2017.07.042
0264-410X/

in question were eligible for DT immunization at the time of their visit (e.g. preventive care, hospitalization, etc.) in the US [6].

In this context, we focused on the vaccination status of chronically ill adolescents (CIA) who were being monitored by highly-specialized pediatric hospital teams and we hypothesized that their close follow-up with repeated specialized consultations and hospitalizations should preclude the incomplete immunization that is often seen with healthy individuals in this age group. We conducted a cross-sectional study of the CIA, and we compared their immunization schedules to those of healthy adolescents (HA). The aim of our study was to assess if the vaccination coverage rate in CIA requiring close pediatric specialized follow-up is higher than that for HA.

2. Methods

2.1. Population and data collection

A cross-sectional study was conducted, from May 2012 to May 2013, that included CIA born between 1995 and 1999 (i.e. who were 13–18 years of age), who were being monitored (e.g. for diabetes mellitus, anorexia nervosa, or cystic fibrosis) at one of the pediatric clinics of the Nantes University Hospital. HA were recruited as direct siblings from 9 to 20 years of age (thereby providing adjustment for their the socio-economic environment) and healthy volunteer school-age adolescents from 13 to 18 years of age, from three representative campuses of the Nantes agglomeration (i.e. a socio-economic panel involving rural to inner city schools for optimal representativity with the CIA). CIA and their siblings were included during a consultation at the University Hospital of Nantes from May 2012 to May 2013. HA from campuses were recruited from March to May 2013, directly on the campuses. CIA were eligible if they were 13–18 years of age and were being monitored at the clinics of Nantes University Hospital for diabetes mellitus, anorexia nervosa, or cystic fibrosis. Siblings were eligible if they were 9–20 years of age and if they did not have a chronic disease. HA from campuses were eligible if they were 13–18 years of age and if they did not have a chronic disease. Adolescents were included if they and their caregivers agreed to participate in the study and if they brought along their health booklet. Adolescents were excluded if the health-booklet was not legible and if the vaccinations were not administered in France. The data collection concerning the immunization schedule was performed once during the study period during a medical consultation for the CIA and their siblings, and during a school visit for the HA. The data collected was in regard to the vaccination schedule, age, and gender for all of the adolescents, as well as the socio demographics and clinical data (e.g. the number of consultations and hospitalizations, family history of chronic disease, etc.) for the CIA. For the HA, the data collected were only those available in the health booklet; i.e., the vaccination status, any periods of hospitalization, and the date and reason for their most recent medical consultation. The vaccination status was recorded in the health booklets. In France, health legislation specifies that all vaccinations should be noted in this booklet with the date of their administration, the batch number, and the physician's signature. The CIA and their parents were also asked if they thought that their vaccination schedule was up-to-date so as to evaluate their knowledge about their own or their adolescent's vaccination status.

Parents and adolescents were individually informed by the medical doctor and the teaching staff, and written consent was obtained prior to them undergoing an anonymized health booklet examination (the health booklets were photographed and directly anonymized by a Clinical Research Technician before being analyzed for the study). The protocol was approved by the Ethics Committee of the institution (GNEDS) on the 16th of April 2012.

The primary outcome was in regard to the overall up-to-date vaccination status for the DTaP/IPV, MMR, HepB and meningococcal C conjugate vaccine (MnC). Secondary outcomes were up-to-date immunization rates for each vaccine specifically, among all groups, as well as determinants of vaccination status for the CIA. According to the French guidelines, adolescents were considered to be up-to-date with their vaccinations if they had received six or more doses of DTaP/IPV, two (if 20 μg formulations) or more HepB doses, two or more MMR doses, one to three HPV doses, and one MnC dose [7]. If the adolescent was not vaccinated on time in accordance to vaccination schedule but secondarily caught up, their status was considered to be "up-to-date". We only considered vaccinations adapted to the age of the adolescent at time of the study. If an adolescent was too young to be targeted by a specific vaccination, their vaccination status was classified as "up-to-date".

2.2. Statistical analyses

In 2010, Gaudelus et al. reported that 17% of French adolescents were up-to-date with their overall vaccination schedules [8]. For the CIA, we expected to see at least an 80% increase in the prevalence of vaccination coverage. Thus, we speculated that the prevalence would increase from 17% to 30%. In a bilateral approach, with a target power of 80%, 5% alpha risk, and a CIA/HA ratio of 1/2, 339 adolescents (113 CIA / 226 HA) would be required for this evaluation.

Statistical analyses were conducted using SAS 9.3® software. Quantitative variables are presented as the means or medians depending on the distribution, and standard deviations or interquartile range (IQR). Qualitative variables are presented as the frequency of each modality with 95% confidence interval (95% CI). Chi-square and MacNemar's tests were performed to compare frequencies between chronically ill vs. healthy adolescents. Lastly, univariate and multivariate log-binomial regressions were performed to explore determinants of the vaccination status with prevalence ratios (PR) for the most controversial vaccines in French adolescents (i.e. HepB, MnC, and HPV). The candidate variables for the study of determinants were the age, single parent family, place of residency (e.g. rural vs. urban), the level of education of both of the parents, employment status of both of the parents, family history of chronic disease, and family income for the adolescents. Variables that were associated with vaccine coverage with a p-value less than 0.2 in the univariate analysis were selected in the multivariate model. A p-value less than 0.05 was considered significant.

3. Results

3.1. Study population

Of the 164 eligible adolescents from 13 to 18 years of age with a chronic disease and who were seen at the hospital clinics from May 2012 to May 2013, 49 were not included as they declined to participate in the study, so that ultimately 114 were included (70% of the eligible CIA). The vaccination statuses of these CIA were compared to those of 266 HA of whom 208 were adolescents from campuses out of a total of 336 who were solicited (from four classrooms at three campuses; 62% recruitment rate); and 58 among siblings (100% recruitment rate) for a cohort comprising a total of 380 adolescents (Fig. 1). Median ages were 16.1 years [IQR 15.3–16.9], 14.5 years [IQR 14–15], and 14.8 years [IQR 14.1–16.1] for the CIA, the HA, and sibling adolescents, respectively ($p < 0.001$). The

Please cite this article in press as: Gras-Le Guen C et al. Chronically ill adolescents are also incompletely vaccinated: A cross-sectional study in France. Vaccine (2017), http://dx.doi.org/10.1016/j.vaccine.2017.07.042