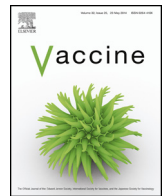




Contents lists available at ScienceDirect

Vaccine

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



Active opioid use does not attenuate the humoral responses to inactivated influenza vaccine

Ekaterina Moroz^{a,1}, Randy A. Albrecht^{b,c}, Brandon Aden^a, Ann Bordwine Beeder^a, Jianda Yuan^d, Adolfo García-Sastre^{b,c,e}, Brian R. Edlin^{a,f}, Mirella Salvatore^{a,*}

^a Department of Medicine, Weill Cornell Medical College, US

^b Department of Microbiology, Icahn School of Medicine at Mount Sinai, US

^c Global Health and Emerging Pathogens Institute, Icahn School of Medicine Mount Sinai, US

^d Immune Monitoring Facility, Ludwig Center for Center Immunotherapy, Memorial Sloan Kettering Cancer Center, New York, NY, US

^e Department of Medicine, Division of Infectious Diseases, Icahn School of Medicine at Mount Sinai, US

^f Institute for Infectious Disease Research, National Development and Research Institutes, New York, NY, US

ARTICLE INFO

Article history:

Received 7 November 2015
Received in revised form 18 January 2016
Accepted 25 January 2016
Available online xxx

Keywords:

Influenza vaccination
Hemagglutination inhibition
Microneutralization
Heroin
Methadone
Opioid users

ABSTRACT

Background: Influenza vaccination is recommended for vulnerable individuals, including active drug users, to prevent influenza complications and decrease influenza spread. Recent studies suggest that opioids negatively regulate immune responses in experimental models, but the extent to which opioid use will affect the humoral responses to influenza vaccine in humans is unknown. This information is critical in maximizing vaccination efforts.

Objective: To determine whether there is a difference in antibody response after influenza vaccination in heroin or methadone users compared to control subjects.

Methods: We studied active heroin users, subjects on methadone maintenance treatment (MMT) and subjects that did not use any drugs before and 1 and 4 weeks after vaccination with trivalent influenza vaccine (TIV). We measured hemagglutination inhibition and microneutralization titers, and we compared geometric mean titers (GMT), and rates of seroprotection and seroconversion for each of the vaccine strains among the 3 groups of subjects.

Results: Heroin users, subjects on MMT and non-user controls mount a similarly robust serologic response to TIV. GMT and rates of seroprotection and seroconversion were not significantly different among groups.

Conclusion: Our results suggest that opioid use do not significantly alter antibody responses to influenza vaccine supporting the vaccination effort in these populations.

© 2016 Elsevier Ltd. All rights reserved.

1. Background

Vaccination is the most widely used strategy to prevent influenza infection and is especially recommended for high-risk groups, such as opioid users. The US Public Health Service has identified heroin users as a population in whom influenza transmission during a pandemic is likely to be especially problematic [1]. In addition to requiring culturally competent outreach efforts and often having poor access to adequate housing and hygiene, opioid

use itself may place this population at increased risk for contracting (and transmitting) influenza. Furthermore, opioid users may have more severe influenza complications, as suggested by experimental studies showing that morphine-treated rats had reduced inflammatory lung responses and decreased viral clearance after influenza infection [2,3]. Epidemiological data also show that individuals using opioids have an increased incidence of pneumonia [4]. Recent studies, in fact, suggest that the immune response to infection or vaccination can be modulated by opioids, either by direct binding to the μ -opioid receptors (MOR) present on the leukocytes, or indirectly [5–7]. In animals models, heroin and its metabolite, morphine, negatively affect innate immunity [8–11], and antibody production [12]. In addition, opioid administration increases the susceptibility and severity of bacterial and viral infections [13–15].

Studies in humans also support the role of opioids in the regulation of both innate and acquired immunity [5,15–19], it is unclear, however, whether all opioids share the same immunosuppressive

* Corresponding author at: Department of Medicine, Weill Cornell Medical College, 1300 York Avenue, LA-249, Box 125, New York, NY 10065, US.
Tel: +1 646 318 8506; fax +1 212 746 8675.

E-mail address: mis2053@med.cornell.edu (M. Salvatore).

¹ Present affiliation: Memorial Sloan Kettering Cancer Center, New York, NY, United States.

Table 1
Baseline characteristics of the study subjects.

Characteristic	Heroin users	Methadone users	Control group	<i>p</i> value ^a	Opioid users (heroin + methadone)	<i>p</i> value ^{**}
N of subjects	10	11	20		21	
Age – years				<0.01 ^a		0.12
Mean ± SD	21.7 ± 2.3	29.5 ± 5.6	28.5 ± 5.0		25.8 ± 5.8	
Median	21.5	30	29		23	
Range	19–24	25–40	22–35		19–40	
Sex – no. (%)				0.02 ^b		<0.01
Male	9(90)	8(73)	8(40)		17(81)	
Female	1(10)	3(27)	12(60)		4(19)	
Race – no. (%)				0.11		0.04
White	10(100)	8(73)	9(45)		18(86)	
Black or African American	0	1(9)	6(30)		1(5)	
Asian	0	1(9)	4(20)		1(5)	
All other races	0	1(9)	1(5)		1(5)	
Ethnicity				0.99		0.96
Non-Hispanic/Latino	9(90)	10(91)	18(90)		19(90)	
Hispanic/Latino	1(10)	1(9)	2(10)		2(10)	
^d Prior influenza vaccination (ever) – no. (%)	6(60)	7(63.6)	11(61) ^e	0.98	13(62)	0.96
^d HCV infection	3(30) ^f	1(9)	0(0)	0.03 ^c	4(19)	0.04

^a Three-way comparison.^{**} Comparison of all opioid users vs controls.^a Age, pairwise comparisons: heroin users vs control group $p < 0.01$; methadone users vs control group $p = 0.60$; heroin users vs methadone users $p < 0.01$.^b Sex, pairwise comparisons: heroin users vs control group $p < 0.01$; methadone users vs control group $p = 0.08$; heroin users vs methadone users $p = 0.31$.^c HCV infection, pairwise comparisons: heroin users vs control group $p < 0.01$; methadone users vs control group $p = 0.17$; heroin users vs methadone users $p = 0.22$.^d By self report.^e Unknown for 2 patients in control group.^f One subject cleared the infection.

properties. In fact some study suggests that while heroin negatively affects both innate and acquired immunity, patients on long-term methadone treatment seem to have preserved immune functioning [20]. The clinical relevance of this immunomodulation remains uncertain [21].

Although some studies have shown decreased antibody responses among illicit drug users to some vaccines, there is a lack of definitive studies regarding the immunogenicity of vaccination strategies in people who inject drugs for diseases that are highly prevalent or difficult to control, such as influenza [22]. One study evaluated the response to influenza vaccine in former drug users who also have HIV, but not in active users [23]. Some studies found that people using heroin had decreased rates of seroconversion to hepatitis B vaccine compared to individuals who did not use opioids [24–26], although others suggested that the antibody responses were normal after boosting the vaccines with 3 doses [27–29]. Likewise, antibody responses of heroin users after a single dose of hepatitis A virus vaccine are low [30]. These studies have limitations because they used heterogeneous samples that include individuals of various ages with comorbid chronic infections, such as HIV, that can also affect the immune response, vaccines that require booster administrations to achieve protection, and used historic controls for comparing antibody responses.

The present study was designed to ascertain whether opioid use impairs the humoral response to a single dose of influenza vaccine and to determine whether the response to vaccine was different in subjects using heroin compared to those on methadone maintenance therapy (MMT). This information will be useful for the design and implementation of vaccination strategies for seasonal influenza and pandemic influenza preparedness for people who use heroin.

2. Methods

2.1. Participants and study design

We performed a prospective observational study during the influenza season 2010–2011, to compare antibody responses to influenza vaccination among healthy adults aged 18–40 years of any race or sex who used heroin or methadone and healthy adults

with the same characteristics but not using opioids. Active heroin users, defined as individuals using intravenous heroin at least once week for the previous 6 months or longer, were recruited from among participants of the Swan Project, a community-based study of young people who injected illicit drugs [31]. Subjects on MMT were recruited from the outpatient methadone program at New York Presbyterian Hospital and were defined as individuals on a stable dose of methadone receiving treatment in the clinic for at least 3 months. Healthy non-user controls were enrolled through flyers and magazine advertisement. Urine toxicology tests were performed at each visit for each subject to confirm patient drug use status. Exclusion criteria included obesity (body mass index > 40), history of acute hypersensitivity to eggs or egg products, acute illnesses at enrollment, history of Guillain-Barré syndrome, pregnancy, HIV infection, blood transfusion in the past 3 months, use of cytokine-based therapies or therapies causing immunosuppression, advanced liver or kidney disease and previous receipt of the influenza vaccine for the season. Information including demographic characteristics, medical history, use of medications, history of alcohol and drug use, history of influenza vaccination or disease were collected at enrollment. HCV status was obtained by self-report. Opioid users enrolled from Swan and MMT participants had been recently tested for HCV antibody and RNA and given their results. Venous blood and urine specimens were obtained from each subject prior to vaccination and at 1 and 4 weeks following vaccination for antibody titers and for toxicology screening respectively. Subjects were asked about symptoms that would be consistent with influenza or influenza-like infection at each visit. Subjects received an incentive of \$20 at each study visit to cover transportation and a snack. This study was performed in accordance with the human experimentation guidelines of the United States Department of Health and Human Services and was approved by the Institutional Review Board at Weill Cornell Medical College. Written informed consent was obtained from all study participants.

2.2. Vaccine

Subjects received a single intramuscular dose of the currently licensed inactivated trivalent vaccine (Fluzone, Sanofi) for the year

Download English Version:

<https://daneshyari.com/en/article/10963187>

Download Persian Version:

<https://daneshyari.com/article/10963187>

[Daneshyari.com](https://daneshyari.com)