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Original Article

Increased defibrillator therapies during influenza season in patients without influenza vaccines

Sheldon M. Singh, MD[a,*], Russell J. de Souza, ScD, RD[b,c], Ramanan Kumareswaran, MD[a]

[a] Schulich Heart Program, Sunnybrook Health Sciences Center, Faculty of Medicine, University of Toronto, Toronto, ON, Canada
[b] Department of Clinical Epidemiology and Biostatistics, Faculty of Health Sciences, McMaster University, Hamilton, Ontario, Canada
[c] Clinical Nutrition and Risk Factor Modification Center, St. Michael's Hospital, Toronto, Ontario, Canada

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ABSTRACT

Background: The association between influenza vaccination and implantable cardiac defibrillator (ICD) therapies during influenza season is not known and is described in this study. Understanding this association is important since reduction in ICD therapies during influenza season via use of influenza vaccination would benefit patients physically and psychologically.

Methods: Patients presenting to the Sunnybrook Health Sciences Center ICD clinic between September 1st, 2011 and November 31st, 2011 were asked to complete a survey evaluating their use of the influenza vaccine. The number of patients with any ICD therapy and the total number of ICD therapies in the six months before and the three months during the 2010–2011 influenza season were determined. Poisson regression analysis was employed to assess differences in the average number of ICD therapies received during the influenza season based on vaccine status (vaccinated vs. unvaccinated). The analysis was repeated after limiting the cohort to patients with a left ventricular ejection fraction $\leq 35\%$.

Results: A total of 229 patients completed the survey, 78% of whom received the influenza vaccine. Four patients had more than one ICD shock during the study period. Electrical storm was rare ($n=2$). A trend toward more ICD therapies (unadjusted incident rate ratio (IRR)=3.2; $P=0.07$) and appropriate ICD shocks (unadjusted IRR=9.0; $P=0.17$) was noted for unvaccinated compared to vaccinated patients. This association persisted when analysis was limited to patients with a left ventricular ejection fraction $\leq 35\%$ (all ICD therapies: unadjusted IRR=5.8; $P=0.045$; adjusted IRR=2.6; $P=0.33$). No patient who received the influenza vaccine, and had a reduced ejection fraction, received an approprite ICD shock during influenza season (unadjusted $P<0.002$).

Conclusion: A trend toward more ICD therapies during influenza season was observed in patients who did not receive the influenza vaccine compared to those who did. The association was stronger in patients who received appropriate ICD shocks and in patients with left ventricular systolic dysfunction. Further work to confirm these findings is recommended.

1. Introduction

The association between influenza-like illness and adverse cardiac events has been reported in several observational studies [1,2], prompting the American Heart Association and Canadian Cardiovascular Society to recommend annual influenza vaccination for patients with cardiac disease [3,4]. However, there has been no study on the association between influenza vaccination and cardiac arrhythmia, an underappreciated contributor of cardiac morbidity and mortality. In this exploratory retrospective study of 229 patients, we assessed the association between influenza vaccination and implantable cardioverter defibrillator (ICD) therapies in the six months before and the three months during the 2010–2011 influenza season.

2. Materials and methods

All patients with an ICD presenting for routine follow up at the Sunnybrook Health Sciences Center ICD clinic, Toronto, Canada between September 1st and November 30th, 2011 were asked to participate in a survey assessing their use of the influenza vaccination in the previous influenza season.

* Correspondence to: Schulich Heart Program, A222, Sunnybrook Health Sciences Center, 2075 Bayview Avenue, Toronto, Ontario, Canada M3A 1T4.
Tel.: +1 416 480 6100x83659; fax: +1 416 480 6913.
E-mail address: sheldon.singh@sunnybrook.ca (S.M. Singh).

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Patient demographics, co-morbidities, and medication use were ascertained from responses to survey questions and a review of each patient's hospital chart. Each patient's ICD chart was reviewed to confirm the incidence of any ICD therapy (appropriate and inappropriate shock or antitachycardia pacing) for an arrhythmic event between June 1st, 2010 and March 1st, 2011. Inappropriate ICD therapies secondary to lead or device malfunctions were excluded, as they do not reflect arrhythmic events. The type of each ICD therapy was adjudicated by two individuals (R.K. and S.M.S.). December 1st, 2010–March 1st, 2011 was considered influenza season, consistent with the peak of influenza season in Canada [5], whereas June 1st, 2010–November 30th, 2010 was deemed "pre"-influenza season. Of note, a good match between the influenza vaccine and globally circulating influenza strains was noted during this influenza season [6].

Patients were divided into two groups: those that received the influenza vaccine and those that did not. Patient characteristics for each group were reported as proportions, mean ± standard deviation or median with range where appropriate. Student's *t*-, Fisher's exact, and Wilcoxon Rank-Sum tests were used to assess differences between the two groups.

The number of vaccinated or unvaccinated individuals receiving any ICD therapy (defined as appropriate shock or antitachycardia pacing for ventricular arrhythmias or inappropriate shock or antitachycardia pacing for supraventricular arrhythmias) or any appropriate ICD shock during the "pre"-influenza season (defined as the two 3 month periods preceding influenza season) and during the influenza season (3 month period) was determined. Any ICD therapy was considered to be reflective of the total arrhythmia burden, and appropriate ICD shock was considered to be reflective of the malignant ventricular arrhythmia burden.

Possible endpoints that may differ between vaccinated vs. unvaccinated individuals were considered to be a reduction in the number of vaccinated individuals receiving any ICD therapy compared to unvaccinated individuals or a reduction in the total number of arrhythmic events requiring ICD therapies in vaccinated individuals, the latter of which accounts for clustering of arrhythmia during the winter months [7]. A binomial test for proportions was performed to assess differences in the total number of ICD therapies between the groups during "pre"- and influenza season. The "pre"-influenza season was divided into two 3 month periods for comparison with the 3 month influenza period. Poisson regression analysis [8] was employed to assess differences between groups in the number of ICD therapies received during influenza season. The analysis was repeated for appropriate ICD shocks during influenza season. Results were reported as an incident rate ratio (IRR) comparing the incidence of ICD therapies in unvaccinated vs. vaccinated patients.

Since the patient cohort in this study was small, thereby impacting the validity of multivariate analysis, our primary evaluation of ICD therapy incidence was unadjusted for differences between the two study groups with regard to factors known to impact cardiac arrhythmia, such as patient age, co-morbidity, or history of ventricular arrhythmias. Secondary analyses adjusted for these factors. Finally, when comparing the number of ICD therapies during influenza season between patients who were or were not vaccinated, an adjustment was made for the number of ICD therapies received in the "pre"-influenza period. We repeated the above analysis after restricting the cohort to those with a left ventricular ejection fraction $\leq 35\%$ to understand the impact of influenza vaccination on all ICD therapies and appropriate ICD shocks in patients with left ventricular systolic dysfunction.

For all analyses, a P-value < 0.05 was considered statistically significant. Statistical analyses were carried out using SAS version 9.3 (SAS Institute, Cary, NC). Ethical approval for this study was obtained from the Sunnybrook Health Sciences Center Research Ethics Board (Date of approval August 26th, 2011; Approval number: 258-2011).

3. Results

A total of 229 patients completed the survey, representing 44% of all ICD patients presenting to the Sunnybrook Health Sciences Center ICD clinic during the study period, of which 78% reported receiving the influenza vaccine. Table 1 summarizes the characteristics of patients who did and did not receive the influenza vaccine. Unvaccinated individuals were younger, less likely to have had a family physician for at least 5 years, and more likely to have received a primary prevention ICD. No differences in co-morbidities, left ventricular systolic ejection fraction, use of anti-arrhythmic drugs, or median household income, a marker of socio-economic status [9], were noted between the two groups.

The retrospective nature of the study allowed for complete information on ICD therapies to be obtained for all patients during the study period. Overall, 17% of the 229 patients in our cohort received any ICD therapy during the 9-month study period. Two patients had electrical storm during the study period – one patient who received the influenza vaccine had electrical storm in the "pre"-influenza season (4 discrete ventricular tachycardia episodes in 24 h requiring antitachycardia pacing) and one unvaccinated patient had electrical storm during influenza season (4 discrete ventricular tachycardia episodes requiring 4 ICD shocks). Multiple ICD therapies (≥ 2 appropriate or inappropriate ICD shocks or antitachycardia pacing) were noted in 19 patients, including 4 unvaccinated patients. Multiple ICD shocks (≥ 2 appropriate or

Table 1
Patient characteristics.

	Influenza vaccination status		***P*-value**
	Vaccinated ($N=180$)	**Not vaccinated ($N=49$)**	
Age (SD)	71 (10)	65 (11)	< 0.005
Male %	87	79	0.3
Median neighborhood income CDN$ (interquartile range)	27,086 (22,982–32,004)	26,305 (22,012–32,606)	0.9
Maintain family physician > 5years %	85	71	0.03
Coronary artery disease %	67	67	1.0
Renal disease %	7	12	0.2
Diabetes %	33	31	0.7
Stroke %	16	6	0.1
Ejection fraction % (SD)	29 (10)	29 (10)	0.8
Primary prevention defibrillator use %	76	86	0.04
Use of anti-arrhythmic drugs %	73	72	0.6

SD = standard deviation; CDN$ = Canadian dollar.