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Survey of Inpatient Clinical Providers' Antibiotic Prescribing Knowledge

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Abstract

Background—Inpatient providers have varying levels of knowledge in managing patients with drug and/or penicillin (PCN) allergy.

Objectives—Our objectives were: 1) to survey inpatient providers to ascertain their baseline drug allergy knowledge and preparedness in caring for patients with PCN allergy and 2) to assess the impact of an educational program paired with the implementation of a hospital-based clinical guideline.

Methods—We electronically surveyed 521 inpatient providers at a tertiary care medical center at baseline and again six weeks after an educational initiative paired with clinical guideline implementation. The guideline informed providers on drug allergy history taking and antibiotic prescribing for inpatients with PCN or cephalosporin allergy.

Results—Of 323 unique responders, 42% [95% CI 3748%] reported no prior education in drug allergy. Considering those who responded to both surveys (N=213), we observed a significant increase in knowledge about PCN skin testing (35% vs. 54%, $p<0.001$) and loss of PCN allergy over time (54% vs. 80%, $p<0.0001$). Among those who reported attending an educational session (N=62), preparedness to determine if an allergy was severe significantly improved (77% vs. 92%, $p=0.03$). Other areas, including understanding absolute contraindications to receiving a drug again and PCN cross-reactivity with other antimicrobials, did not improve significantly.

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Conclusion—Inpatient providers have drug allergy knowledge deficits but are interested in tools to help them care for inpatients with drug allergies. Our educational initiative and hospital guideline implementation were associated with increased PCN allergy knowledge in several crucial areas. To improve care of drug-allergic inpatients, more research is needed to evaluate hospital policies and sustainable educational tools.

Keywords

Drug; Antibiotic; Penicillin; Cephalosporin; Inpatient; Allergy; Hypersensitivity; Anaphylaxis; Immune-mediated; IgE Mediated; Drug Allergy; Antibiotic Allergy

Introduction

Approximately half of all patients admitted to the hospital receive antibiotics, and 25% of inpatients who require antibiotics have at least one antimicrobial drug allergy.[1] Penicillin (PCN) allergy is reported in up to 10% of the general population and up to 20% of inpatients.[1–6] Patients with reported PCN allergies receive more costly and broad-spectrum antibiotics than patients without these reported allergies.[1–6] Furthermore, many patients with reported PCN allergy are not receiving drugs that are safely tolerated despite a PCN allergy, such as later generation cephalosporins and carbapenems.[1,5,7–13] Reported allergies to PCN, however, do not equate with true IgE-mediated allergy. After formal allergy evaluation, including skin testing, up to 99% of patients with reported PCN allergy are found not be allergic.[2–5,14,15]

Inpatient providers have limited knowledge about drug allergy, PCN cross reactivity with other antibiotics, and the utility of PCN skin testing.[13,16,17] Despite these knowledge deficits, it is these providers who are evaluating and prescribing antibiotics to inpatients with drug allergy. Prior efforts to survey providers on this topic have been limited by low or unreported response rates, or lack of detail.[13,16–18] Past surveys have not assessed the impact of interventions targeted at improving provider management of patients with drug and PCN allergy.

This study sought to identify gaps in PCN and drug allergy knowledge among inpatient providers at a single tertiary care center and to assess the impact of a targeted educational program paired with the implementation of a hospital-based clinical guideline.

Methods

In anticipation of an educational initiative and implementation of a hospital-wide clinical guideline, we electronically surveyed inpatient providers at the Massachusetts General Hospital (MGH), a 947-bed tertiary care facility in Boston, Massachusetts. Providers included house staff from neurology, pediatrics, internal medicine, orthopedic surgery, and general surgery as well as attending hospitalist physicians and nurse practitioners (NPs). Participants received a link to a web-based survey one week prior to implementation of the clinical guideline and six weeks after implementation of the clinical guideline. The survey was voluntary and anonymous. The research protocol was approved by the Partners Human Research Committee. The survey was conducted and data maintained using Research

Electronic Data Capture (REDCap) hosted at Partners Healthcare.[19] Through the REDCap interface, survey responses between identical responders can be paired though modules for tracking responders and viewing data are separate.

The survey questions were created by specialists from Allergy/Immunology (AI), Infectious Diseases (ID) and two survey research experts. While no validated survey instrument on PCN allergy existed, two questions from a previously published instrument were adapted for use.[16] The survey instrument was tested and revised through detailed interviews with five MGH clinical fellows. Survey questions covered three areas: respondent characteristics, preparedness/comfort, and knowledge (Table E1).

After the initial survey was conducted, we implemented a hospital-based clinical guideline to help providers in drug allergy history taking and antibiotic prescribing for inpatients with PCN or cephalosporin allergy. The guideline includes a standardized method for primary teams to perform test doses to β-lactam antibiotics, and institution-specific information regarding inpatient skin testing and desensitization, antimicrobial resistance patterns, and pharmacy formulary considerations (Online Repository text).

Coincident with guideline implementation, 10-minute educational presentations were offered to fifteen different groups of providers throughout the hospital from April 3, 2013 through May 15, 2013. The presentation's goal was to introduce the clinical guideline and show providers how navigate to the guideline electronically. The educational initiative also relayed antibiotic stewardship goals and key concepts about PCN allergy, including: (1) patients with reported PCN allergy may not be truly allergic (IgE-mediated allergy); (2) the evaluation of PCN allergy begins with a drug allergy history; (3) even those who are truly PCN-allergic may have lost their allergy over time; (4) skin testing for IgE-mediated PCN allergy is a valid tool that is available; (5) many cephalosporins, especially in the later generations, can be safely tolerated despite true PCN allergy; and (6) severe cutaneous reactions and hypersensitivity reactions (HSRs) with organ involvement preclude future use of that drug. After providing brief evidence supporting these concepts, providers were presented with three clinical vignettes highlighting the inpatient relevance of the guideline. The educational initiative did not review any answers to the survey instrument questions. After each presentation, cards with figures from the clinical guideline were distributed and posted in hospital workrooms. The full guideline was available electronically to all staff.

Analysis and Statistical Methods

For preparedness questions, Likert responses were dichotomized into "prepared" (providers who responded very prepared or somewhat prepared) or "unprepared" (providers who responded very unprepared or somewhat unprepared). For knowledge questions, answers were scored as incorrect or correct for single item questions. For the multi-item questions, frequencies and scores were calculated using the number each provider got correct out of the 13 possible correct for the question on cross reactivity and out of 5 possible correct for the question on absolute contraindications to receiving a drug again. For those ordinal scores, medians and quartiles were reported.

Statistical methods to assess the education and guideline impact included nonparametric tests, such as Wilcoxon signed rank test for paired continuous and rank data and the McNemar test for paired binary data. An analysis of providers whose answers changed from the pre to post survey was conducted and assessed by a one-sample test of proportions. The providers who reported they had attended one of the educational sessions or used the clinical guideline were compared with those who did not using a nonparametric test for trend. Responses of NPs were compared with those of medical doctors (MDs) using Fisher's Exact test or Wilcoxon rank sum test. Post survey responses of 38 people who did not take the first test were compared with those of 285 people who did take the first test using Wilcoxon rank sum test. All statistical analyses were conducted in SAS version 9.3 (SAS Institute Inc., Cary, NC, USA).

Results

Sixty-two percent of providers (323 of 521) responded to at least one of the two surveys. Two hundred and eighty five providers (55%) responded to the pre survey, and 250 (48%) responded to the post survey. Two hundred and thirteen inpatient providers (41%) completed both surveys. Of MD respondents to both surveys, more were from non-surgical specialties than surgical specialties (43% vs 29%, $p<0.01$)(Table E2). Of all respondents, 82% (N=265) were physician trainees (residents or fellows), 8% (N=27) were attending hospitalist physicians, and 8% (N=26) were NPs (Table I). One hundred and thirty six (42%) of respondents reported no prior drug allergy education. Fewer NPs reported receiving drug allergy education than MDs (36% vs 53%, $p=0.18$).

In the pre-intervention survey (N=285), 193(68%) providers reported that they were very prepared or somewhat prepared to prescribe antibiotics to patients with PCN allergy (Table II). More providers felt prepared to determine if a hypersensitivity reaction was severe or life-threatening, with 236 (83%) reporting that they were very or somewhat prepared. Baseline knowledge about PCN skin testing was poor, with only 103 (36%) of providers knowing that skin testing is valid tool for assessing PCN allergy. Over half of respondents (163, 57%) reported that a PCN allergy was permanent. Respondents had a median score of 85% [IQR 77–92%] when asked to identify antibiotics that could be safely prescribed in patients with PCN allergy. Considering β-lactam antibiotics, 95 respondents (33%) would not prescribe meropenem; 153 respondents (54%) would not prescribe cefepime; and 179 respondents (63%) would not prescribe ceftriaxone to a patient with PCN allergy. Conversely, 42 respondents (15%) would give piperacillin-tazobactam (an anti-pseudomonal penicillin); 39 respondents (14%) would give cephalexin (a 2nd generation cephalosporin); and 7 respondents (2.5%) would give amoxicillin (an amino penicillin) to a patient with PCN allergy. Respondents had a median score of 60% [60–80%] when asked to identify conditions that are absolute contraindications to receiving the culprit drug again. Symptoms consistent with Stevens-Johnson Syndrome (SJS)/Toxic Epidermal Necrolysis (TEN) and Drug Rash Eosinophilia and Systemic Symptoms (DRESS) Syndrome were not recognized as absolute contraindications to receiving that drug again by 85 (30%) and 96 (34%), respectively.

A subgroup analysis of NPs in the pre-intervention survey (N=22) found they had a significantly lower score for knowing which antibiotics can be safely prescribed for patients with a history of penicillin allergy than MDs (73% vs 83%, p<0.001). Knowledge about PCN skin testing and allergy being permanent was only slightly lower for NPs than MDs (27.3% vs 37.2%, p=0.49 and 45.5% vs 58.2%, p=0.27 respectively).

In the post-intervention survey, an overwhelming majority of respondents (244/250, 98%) indicated that they were interested in using a clinical guideline to help with drug allergy history taking and antibiotic prescribing in patients with PCN or cephalosporin allergies. Of the 247 responders175 (71%) reported being aware of the clinical guideline, 75 (30%) reported being present at an educational session, and 43 (17%) reported they had used the clinical guideline in their inpatient care. Post-intervention survey responses showed no significant knowledge difference between those providers who took the first survey and those who did not.

Considering responders to both surveys (N=213), changes from the pre-intervention to post-intervention showed a significant increase in knowledge of PCN skin testing from 35% to 54% (p <0.001) (Figure 1). Likewise, knowledge about allergy not being permanent improved from 54% to 80% (p<0.001). Knowledge of cross reactivity and absolute contraindications to giving a drug did not change significantly between the two surveys (Figure 2). Changes from the pre-intervention to post-intervention survey showed small increases in preparedness to prescribe antibiotics to patients with PCN allergy, from 82% (N=172) to 85% (N=179) of respondents indicating that they were prepared (p= 0.66). The number of respondents who felt prepared to determine if an allergy was severe showed a small change that was not statistically significant.

Among those who reported attending an educational session (N=62), preparedness to determine if allergy was severe significantly improved from 77% to 92% (p= 0.03) and preparedness to prescribe antibiotics to patients with PCN allergy showed a small improvement from 66% to 76% that was not statistically significant (p=0.13). Among those who reported attending an educational session or using the clinical guideline (N=84) and whose answers changed between surveys, preparedness to prescribe antibiotics in patients with PCN allergy and to determine if allergy was severe both showed a significant change in providers becoming prepared (p=0.03 and p=.018, respectively).

Discussion

This is the first report of a successful drug allergy educational initiative for general inpatient providers. The survey results highlight that although inpatient providers have limited prior education about drug allergy and have deficits in knowledge and comfort regarding drug and PCN allergy, they are interested in tools to help them care for drug-allergic patients, and significant improvements can be seen with brief education sessions and adoption of clinical guidelines. In areas crucial to the judicious and appropriate use of antibiotics among patients with reported PCN-allergy, our educational initiative and integration of a clinical guideline was associated with significant knowledge improvements. However, in areas critical to safe antibiotic prescribing for drug-allergic patients, such as β-lactam cross reactivity and

determining absolute contraindication to drug use, we were unable to demonstrate an impact of our educational initiative and guideline.

Baseline knowledge was most deficient in understanding the usefulness of PCN skin testing, and was worse than previously described. In one prior survey, 65% of internists knew about the validity of PCN skin testing.[16] While it is unclear why more of our surveyed providers did not know about the validity of PCN skin testing, this difference may be due to the recent variability in the availability of reagents for PCN skin testing. Although skin testing to PCN has been used since the 1960s, from September 2000 through November 2001 and from September 2004 through September 2009, the essential reagent for PCN skin testing (penicilloyl-poly-lysine) was commercially unavailable. The surveyed providers were mostly house staff, which suggests they received their initial medical training during or immediately after this period where skin testing was not available. Furthermore, despite the current availability of this reagent, only about 600 hospitals have penicilloyl-poly-lysine (Pre-Pen) on formulary.[20] Our educational initiative and clinical guideline resulted in a 1.5-fold increase in providers' knowledge of the validity PCN skin testing. This change is important since inpatient use of PCN skin testing has been shown to be associated with decreased costs and broad spectrum antibiotics use in some settings.[2,3,15,21]

Understanding that a drug allergy is not a permanent, lifelong condition was lacking and similar to prior data.[16] While approximately half of our responders understood that PCN allergy was not permanent at baseline, after our intervention, the majority (80%) answered correctly. Penicillins and early generation cephalosporins remain first-line antimicrobial management for many inpatient infections, including common infections with methicillin-sensitive staphylococcus, streptococcus, and enterococcus and rare infections such as peptostreptococcus, actinomyces, propionibacterium, and listeria.[22–27] With the knowledge that PCN allergy wanes over time, providers may increasingly consider further PCN allergy evaluation for optimal treatment of these and other infections.

These survey results raise significant concerns regarding patient safety. Approximately 30% of providers did not recognize symptoms of HSRs that are absolute contraindications to receiving a drug again, and this deficit in knowledge was unchanged by our intervention. This finding was important since over 90% of respondents were MDs. Learning the classification and pathophysiology of HSRs is part of preclinical medical education and has been recommended as clinical medical education for medical students by the American College of Allergy, Asthma and Immunology.[28] This study indicates that inpatient providers need more education on the different types of HSRs, including those that should be considered absolute contraindications such as SJS/TEN and DRESS Syndrome.

Understanding cross reactivity between PCN and other β-lactam antibiotics is challenging, even for allergists.[4,13,29] Although the allergic determinants of cephalosporins in later ($3^{rd}/4^{th}$) generation are most commonly derived from the side chain (R-group) rather than the β-lactam ring,[7–9,11] providers did not know if they could prescribe later generation cephalosporins to patients with PCN allergy Improved education for inpatient providers about how to give PCN-allergic patients cephalosporins must be clearly communicated for improved stewardship and patient safety.

Our intervention did not significantly improve providers' reported preparedness to prescribe antibiotics or to determine if an allergy was severe. One explanation for not seeing a significant improvement is survey timing. We distributed our post-intervention survey only 6 weeks after the educational initiative and guideline implementation, so providers may not have yet encountered a patient for whom this guideline would be relevant. Indeed, only 17% of providers had used the clinical guideline at the time of this second survey. This hypothesis is further supported by the significant improvement in preparedness seen by the subgroup of providers who were directly present at an educational initiative or used the guideline in practice.

NPs trended towards having less drug allergy education and knowledge than MDs. This is a crucial area of future study because NPs, as well as physician assistants, are increasingly providing front-line inpatient care, a trend that is likely to continue due to shortages of physicians, efforts to reduce healthcare costs, decreasing funding for graduate medical education, and limitations in house staff work hours. If NPs have low knowledge of PCN or drug allergy, we should not only investigate their current education and training modules, but also create appropriate in service education to ensure that their education is commensurate with their inpatient expectations for taking a drug allergy history and safely and appropriately ordering antibiotics for patients with drug allergies.

Strengths of this study include the pairing of individual provider data, anonymous survey design, strong response rate, and rigorous guideline implementation. We were able to use survey responders as their own controls, therefore increasing internal validity. By keeping the survey anonymous, we likely had lower reporter bias. Our overall survey response rate was consistent with previously published data surveying physicians and was as high or higher than previous surveys on drug allergy.[16,17,30,31] Based on prior data showing that successful guideline implementation is dependent on multiple implementation strategies,[32–35] we paired our guideline implementation with educational outreach.

Potential limitations to our study include a paired provider response rate of just over 40%, lack of long-term follow up, and assessment of only a single institution. Because of limited collected demographic information, we were only able to assess whether responders to our survey differed from nonresponders in limited ways, raising the possibility of selection bias. However, because we surveyed only inpatient providers at a single institution and response rate by role and specialty was in proportion to those invited to complete the survey, it is likely that responders and nonresponders had similar demographic characteristics. Because of house staff turnover July 2013, we could not administer additional surveys to assess whether the gains from our intervention were sustainable. Lastly, the educational program and the clinical guideline were implemented at a single institution, albeit an institution that is similar to many other tertiary care referral centers.

Our study expands on the previous limited data demonstrating knowledge deficiencies among inpatient providers in PCN and drug allergy, and expands on what is known to offer a potential solution. Despite the observed deficits, the educational needs of inpatient providers are not being routinely met. Few institutions have implemented guides for when to order PCN skin testing, or have used Allergists or Pharmacists to help inpatient providers

appropriately prescribe antibiotics in PCN-allergic patients.[2,3,5,21] Standardized guidelines for hospitals created with multidisciplinary support from AI, ID, and Pharmacy are needed. Inpatient providers will need additional education about PCN and drug allergy in this setting for safe and appropriate antibiotic use. Further research is needed to elucidate the most effective strategies for management of drug-allergic inpatients, and the optimal way to educate their inpatient providers.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

PCN	penicillin
MGH	Massachusetts General Hospital
NPs	nurse practioners
REDCap	Research Electronic Data Capture
AI	Allergy/Immunology
ID	Infectious Diseases
MDs	medical doctors
HSRs	Hypersensitivity Reactions
SJS/TEN	Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis
DRESS	Drug Rash Eosinophilia and Systemic Symptoms

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Highlights box

1. What is already known about this topic?

   Patients commonly report allergy to penicillin (PCN). Inpatient providers lack knowledge of PCN allergy evaluation. Allergy assessment of inpatients with reported PCN allergy is important for high quality patient care and appropriate utilization of antibiotics.

2. What does this article add to our knowledge?

   Providers lack formal education in drug allergy and express interest in tools to help them care for drug-allergic inpatients. A brief educational initiative, paired with a clinical guideline, was associated with improved drug allergy knowledge.

3. How does this study impact current management guidelines?

   Allergists can work effectively with colleagues from Infectious Diseases and Pharmacy to create guidelines that improve the care of drug-allergic inpatients. Inpatient providers will require additional education about drug allergy.

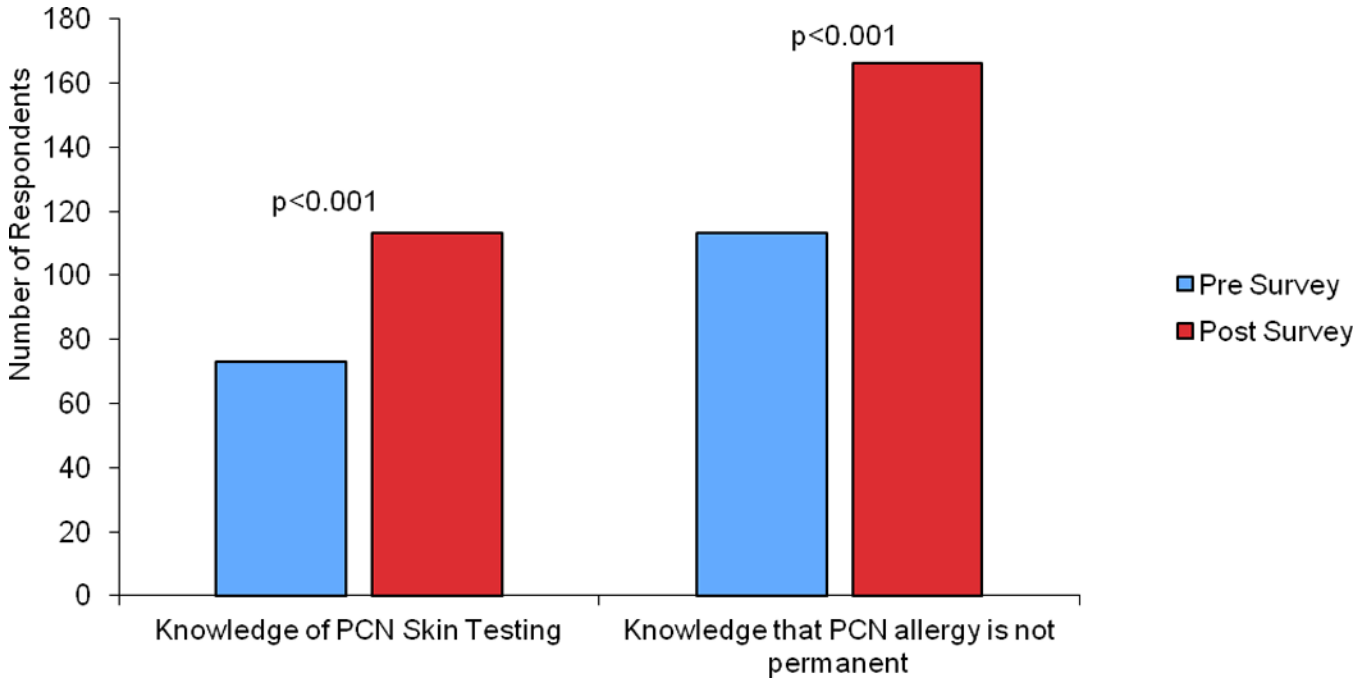

Figure 1.

Impact assessment of the educational initiative and implementation of a hospital-based clinical guideline on knowledge of PCN skin testing and loss of PCN allergy over time (N=213).

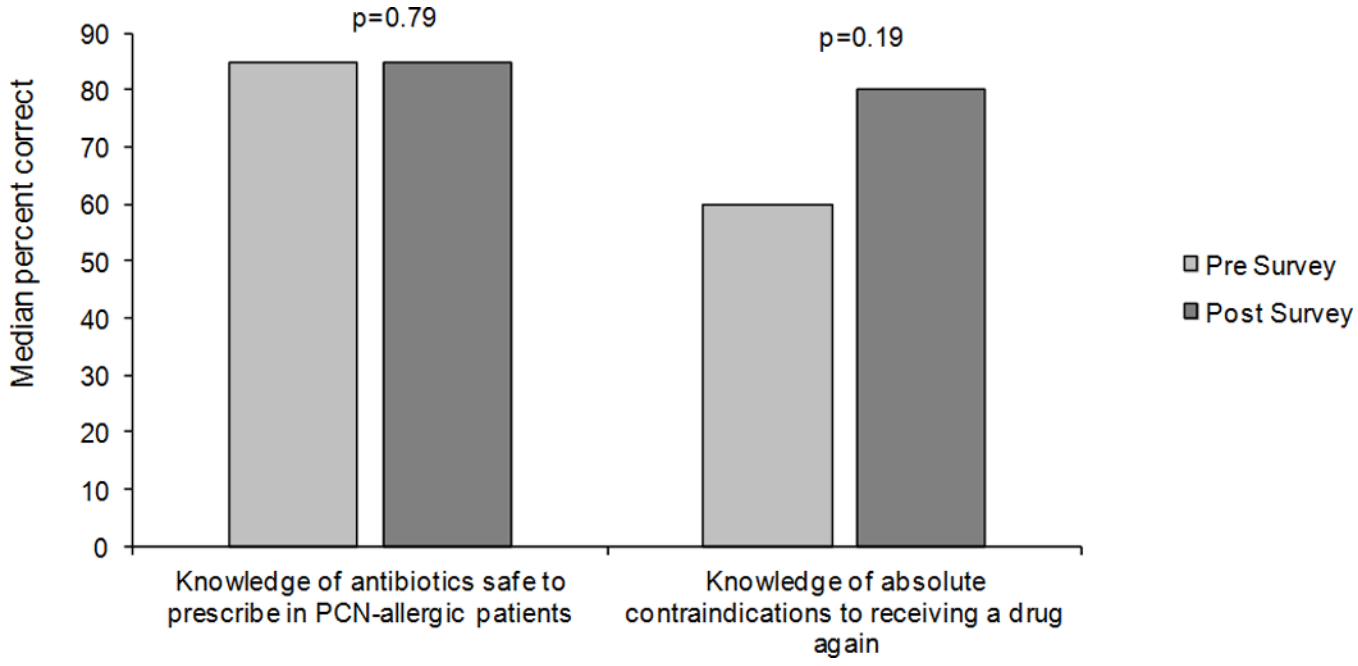

Figure 2.

Impact assessment of the educational initiative and implementation of a hospital-based clinical guideline on knowledge of PCN cross reactivity with other drugs and contraindications to receiving a drug again (N=213).

Table I

Characteristics of survey respondents and prior drug allergy education (N=323)

Respondent role	Number (%)	Number who reported no prior drug allergy education (%)
Physician Trainees	265 (82)	106(40)
Housestaff	263 (81)	106 (40.3)
PGY- 1	78 (29.6)	37 (47.4)
PGY- 2	75 (28.5)	27 (36)
PGY-3	73 (27.8)	28 (38.3)
PGY-4	25 (9.5)	10 (40)
PGY-5	11 (4.1)	4 (36.4)
PGY-6	1 (0.4)	0 (0)
Fellow	2 (0.6)	0 (0)
Attending Physician	27 (8.4)	15 (55.5)
Nurse Practitioner	26 (8.1)	14 (53.8)
Other or no response	5 (1.8)	1 (20)
Total	*323*	*136 (42)*

Table II

Responses to Pre Survey (N=285).

Text of Survey Question	**Result**	
Please describe the extent to which:	Very Prepared or Somewhat Prepared	
You feel prepared to prescribe antibiotics for the penicillin-allergic patient	193 (67.96)	
You feel prepared to determine if a patient has a history of an allergic reaction that was severe or life-threatening	236 (82.8)	
True/False:	Number correct (%)	Correct Answer
Skin testing is a valid tool for assessing whether a patient is penicillin-allergic	103 (36.1)	True
Once a patient develops an allergy to penicillin, they will always have this allergy	163 (57.2)	False
Check all that apply:	Number yes (%)	Correct answer
Which of the following may be safely prescribed in the penicillin-allergic patient:		
Meropenem	190 (66.7)	√
Amoxicillin	7 (2.5)	
Levofloxacin	275 (96.5)	√
Aztreonam	239 (83.9)	√
Cephalexin	39 (13.7)	
Sulfamethoxazole-Trimethoprim-	274 (96.1)	√
Doxycycline	260 (91.2)	√
Cefepime	132 (46.3)	√
Ceftriaxone	106 (37.2)	√
Vancomycin	273 (95.8)	√
Piperacillin-Tazobactam	42 (14.7)	
Metronidazole	279 (97.9)	√
Azithromycin	265 (93)	√
Which of the following reactions to penicillin are considered absolute contraindications to receiving the medication again, even by a process of desensitization:		
Hives	14 (4.9)	
Swelling of mouth and tongue (Angioedema)	122 (42.8)	
Fever with rash that involves ulceration of the buccal mucosa (SJS/TEN)	200 (70.2)	√
Kidney failure characterized by eosinophiliuria (AIN)	170 (59.7)	√
Rash, lymphadenopathy, fever, and increased liver function tests (DRESS)	189 (66.3)	√