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Evaluation of Empiric Management of Pediatric Community-Acquired Pneumonia

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Abstract

Objective: To assess if there was overuse of broad-spectrum antibiotics in the management of childhood community-acquired pneumonia (CAP). If evident, we sought to determine if proactive dissemination of the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America (PIDS-IDSA) guidelines by utilizing a Computer Physician Order Entry (CPOE) order set would increase adherence to the guidelines.

Design: Retrospective cohort study.

Setting: 100-bed tertiary academic children's hospital.

Patients: Hospitalized children with a discharge diagnosis of pneumonia, pleural effusion, and/or empyema.

Interventions: Identification of overuse of broad-spectrum antibiotics. A CPOE order set was designed based on the PIDS-IDSA guidelines with ampicillin as the preferred antibiotic in a fully immunized infant or child. Post-implementation of the CPOE order set, a 2-month analysis was conducted to assess effectiveness.

Results: Of the 231 charts eligible for review, 88 met inclusion criteria. 36 (40.9%) patients were not treated according to the guidelines, 39 (44.3%) patients were treated according to the guidelines and for 13 (14.8%) patients adherence to the guidelines was indeterminable due to lack of immunization documentation. Prior to hospital guideline dissemination, ceftriaxone (broad-spectrum antibiotic) was used as empiric therapy in 67% (60/88) of children. Implementation of the CPOE order set resulted in a 32% improvement in adherence to the national guideline recommendations ($p = 0.005$).

Conclusions: 48% of patients were not treated according to the PIDS-IDSA guidelines, after statistical adjustment for the indeterminable group (14.8%), indicating overuse of broad-spectrum antibiotics. Education and implementation of the CPOE order set resulted in improved adherence to the guidelines.

Keywords

Community acquired pneumonia, Pediatrics, Antimicrobial stewardship

Introduction

The 2011 Pediatric Infectious Diseases Society and the Infectious Diseases Society of America (PIDS-IDSA) clinical practice guidelines for the management of community-acquired pneumonia (CAP) recommends narrow-spectrum antimicrobial therapy for otherwise

healthy, fully-immunized children hospitalized with CAP. While assisting practitioners in the management of CAP, the goal of these guidelines is to decrease morbidity and mortality rates. In addition, the guidelines recommend minimization of antimicrobial resistance by limiting exposure to any antibiotic when possible, properly dosing antibiotics, and treating for the shortest effective duration. Ampicillin or penicillin is the narrow-spectrum inpatient antimicrobial therapy of choice for otherwise healthy fully-immunized patients [1].

Prior to this study, the empiric treatment of childhood CAP at our children's hospital was not standardized with lack of a formal pediatric antimicrobial stewardship program (ASP). We hypothesized that there was overuse of broad-spectrum antibiotics in the management of CAP, due to the observance of high volume of ceftriaxone orders. We sought to determine whether this use was appropriate, by defining appropriate therapy ordered in accordance with the PIDS-IDSA guidelines. Previous studies concluded that internal guidelines and education have an impact on antimicrobial use in the pediatric setting [2,3].

Previous studies have shown that approximately 3-10% of children receive narrow-spectrum antimicrobials as empiric CAP therapy [2-4]. If overuse of broad-spectrum antibiotics was evident at our hospital, the implementation of a Computer Physician Order Entry (CPOE) order set would be necessary to enforce compliance with the PIDS-IDSA guidelines. CPOE order sets guide prescribers when choosing therapy and dosages for specific indications. Previous studies have concluded that programs promoting guideline implementation are needed to optimize management of pediatric CAP [2,3].

We sought to determine the rate of adherence to the PIDS-IDSA guidelines at our institution, to analyze patient outcomes and to determine if the implementation of a CPOE order set was warranted. Adherence to the guidelines was low (less than 50% of the time) and we therefore implemented a CPOE order set to improve our antibiotic use to be in accordance with the PIDS-IDSA guidelines. Education was conducted and post-implementation of the order set data was collected over a two-month period.

Methods

Data source and patient population

This was a retrospective, single-center study, conducted at a 100-bed tertiary care academic children's hospital. This was an Institutional Review Board (IRB) approved study. Written informed consent of included patients was not required by the IRB. Children aged 3 months through 21 years were eligible if they were discharged from the general and intensive care pediatric units with an International Classification of Diseases, Ninth Revision (ICD-9) billing code discharge diagnosis of pneumonia, pleural effusion or empyema from September 17, 2013 through September 17, 2014. Children were excluded if they had an immunodeficiency, resided in a long-term care facility, or had at least one chronic medical condition, with the exception of asthma or reactive airway disease (RAD). Data extraction was attained using appropriate discharge diagnostic codes. Data were collected on standard case report forms. Chest radiographs were classified as bacterial, atypical bacterial, viral, or a combination. A chest radiograph finding of increased perihilar markings/bronchitis/bronchiolitis was defined as a viral etiologic pathogen. Atypical bacteria were read as multifocal/hazy or patchy infiltrate/streaky opacity/bibiasilar infiltrate and bacterial pathogen read as bilateral lobar pneumonia/infiltrate/focal opacity/multifocal/hazy or patchy infiltrate/streaky opacity/bibasilar infiltrates.

Adherence to national guidelines

An assessment of the empiric treatment of childhood CAP over a one-year time period was conducted. Empiric antibiotics were defined as the initial antibiotics administered to a patient upon suspicion of CAP, regardless of which unit the child was admitted to at the time of antibiotic order. The PIDS-IDSA guidelines state that fully immunized patients and in regions with minimal pneumococcal penicillin resistance, recommended therapy is narrow-spectrum ampicillin or penicillin. Amoxicillin was also considered appropriate therapy, as it is the first line outpatient treatment. Broad-spectrum antibiotics were considered any antibiotic besides penicillin, ampicillin or amoxicillin and defined as non-compliant with the guidelines unless given appropriately based on immunization status as noted below. Local epidemiologic data was evaluated to assess the rate of penicillin resistance for *Streptococcus pneumoniae*; our 2014 antibiogram stated 100% susceptibility to parenteral penicillin G at the non-meningitis breakpoint.

Fully immunized patients were defined as patients up to date on their *Haemophilus influenzae type b (Hib)* and *Streptococcus pneumoniae (S. pneumoniae)* immuniza-

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tions. Children's immunization status was based on actual immunization records or physician documentation, usually reported by the child's parents. According to the national guidelines, if a child is up to date on his/her immunizations, first line therapy is narrow-spectrum antimicrobials; broad-spectrum antimicrobials were appropriate and in accordance with the guidelines if a child were not up to date. Broad-spectrum antimicrobials were also appropriate when patients who previously failed beta-lactam outpatient therapy or who were exposed to a beta-lactam antibiotic for greater than 48 hours, both within the previous 30 days. Failure of outpatient therapy was based on the provider's decision, typically if the child received antibiotics for a minimum of 48 hours.

If overuse of broad-spectrum antibiotics was evident, implementation of a CPOE order set based on a hospital-wide guideline for the empiric management of CAP was deemed appropriate. Based on our preliminary results, a pediatric pneumonia CPOE order set (Table 1) was developed and initiated in March 2015. Prior to the initiation, education was conducted to the nursing staff, pediatric physician residents and attending pediatric physicians. The pharmacy resident, pediatric clinical pharmacist and infectious disease pediatric specialist provided education with a verbal 10-minute explanation and a paper handout of the new hospital guideline and the existence of the CPOE order set. To ensure adequate education and to assess effectiveness, one month after implementation, a two-month analysis using the same criteria pre CPOE order set was to be conducted. This analysis would assess if the dissemination of the hospital-wide guidelines with the CPOE order set as a tool to aid in the adherence to the hospital guideline would improve adherence to the PIDS-IDSA guidelines.

Outcomes

The main outcome measure was overuse of broad-spectrum antibiotics in the empiric management of childhood CAP at a tertiary care academic hospital. If overuse of broad-spectrum antibiotics was evident, the creation of a CPOE order set was warranted to aid in the enforcement of adherence to the PIDS-IDSA guidelines. Secondary outcome measures include antibiotics upon discharge, length of stay, and development of pneumonia-associated complications. Outcomes were analyzed to determine if the choice of antimicrobial therapy had an impact. Descriptive statistics, including frequency distributions and cross-tab tables were used to describe available study data using statistics data editor SPSS version 21.

Results

Pre-Order set implementation

Study population: The discharge diagnosis code data extraction resulted in 231 patient charts. After the exclusion criteria was applied, 88 charts were eligible for re-

Table 1: The CPOE order set.

Fully immunized patients*	Ampicillin 50 mg/kg/dose Q6H
Not fully immunized patients*	Third-generation parenteral cephalosporin (Ceftriaxone) 75 mg/kg/dose Q24H
Penicillin allergy	Clindamycin 5 mg/kg/dose Q8H
Presumed atypical pneumonia	Add azithromycin 10 mg/kg/dose x1, then 5 mg/kg/dose Q24H x4 days
Presumed atypical pneumonia in patients allergic to macrolides	Levofloxacin 6 months to < 5 years: 10 mg/kg/dose Q12H >= 5 years-16 years: 10 mg/kg/dose Q24H
***S. aureus* (MRSA) suspected**	Add vancomycin 15 mg/kg/dose Q6H
Influenza suspected	Diagnose and treat influenza infection as appropriate
*Fully immunized: Received 3 primary doses of *Hib* and *S. pneumoniae*	

Table 2: Patient characteristics.

	Pre-order set	**Post-order set**
Age (years)	Mode: 1	Mode: 2
	Range: 0-19	Range: 0-18
	≤ 5 years of age: 87.5%	≤ 5 years of age: 65%
Direct ICU admission	21.60%	20%
Season of admission	Winter-Fall	Spring
Beta-lactam antibiotic use within previous 30 days	19/88 (21.5%)	6/25 (24%)
Up to date on immunizations	62/88 (70.5%)	25/25 (100%)
Lack of immunization documentation	18/88 (20.5%)	0/25 (0%)
Penicillin allergy	8/88 (9.1%)	2/25 (8%)
Asthma/RAD	22/88 (25%)	8/25 (32%)

view. Sixty-two percent of children had chronic medical conditions and thus excluded. Children evaluated were between 4 months and 19 years of age, with 92% being 6 years of age or younger. The majority of children included were admitted to the general pediatric unit (78.4%), with the remainder admitted to the pediatric intensive care unit (PICU). Admissions peaked in the fall and winter (56.8%). 9.1% (8/88) of our patients had a documented penicillin allergy. One quarter of our studied population had documented asthma or RAD. See Table 2.

A major determining factor of defining the overuse of broad-spectrum antimicrobials was the child's *Hib* and *S. pneumoniae* immunization status. 70.5% (62/88) of our patients were up to date on the *Hib* and *S. pneumoniae* immunizations, 9.1% (8/88) of our patients were not up to date, and 20.5% (18/88) were not recorded. Therefore, we were unable to determine if 20.5% (18/88) of our patients were inappropriately exposed to broad-spectrum antibiotics.

21.6% (19/88) of our patients were recently exposed to a beta-lactam antibiotic, within the previous 30 days, with a minimum of 48 hours of therapy, including failure of therapy of current pneumonia diagnosis. Therefore, a broad-spectrum antibiotic was appropriate for their empiric therapy.

Antibiotic prescribing pre-order set

Overuse of broad-spectrum antibiotics was evident in 40.9% (36/88) of our children and after statistical adjustment for the indeterminable group, 48% of children were not treated in accordance with the PIDS-IDSA guidelines. Overuse of broad-spectrum antibiotics was indeterminable in 14.8% (13/88) of children. While we did not have documentation of 20.5% (18/88) of children's immunization status, 5.6% (1/18) of these children had recent exposure to a beta-lactam antibiotic, thus a broad-spectrum antibiotic was used appropriately. 75% (66/88) of our patients received broad-spectrum beta-lactams (ceftriaxone, amoxicillin/clavulanate, and cefpodoxime) and 21.8% (19/88) of patients were treated with amoxicillin or ampicillin. 12.5% (11/88) of children were treated with azithromycin in addition to a beta-lactam and 1.1% (1/88) of the patients treated with azithromycin as the sole empiric treatment.

A sub-group analysis was conducted in the 25% (22/88) of patients who had a diagnosis of asthma/RAD at the time of empiric treatment of pneumonia to assess if they were treated differently. 59.1% (13/22) of the RAD/asthmatic patients were treated with ceftriaxone, 27.3% (6/22) were treated with amoxicillin, 9.1% (2/22) were treated with amoxicillin/clavulanate, and 4.5% (1/22) were treated with azithromycin alone. Therefore, patients with this comorbidity were not treated differently than patients without RAD/asthma.

Respiratory Viral Panel (RVP) results

Out of the 56 children who had PCR testing for respiratory viruses, 60.7% (34/56) children tested positive for a virus. The most common viral pathogen was respiratory syncytial virus (RSV). We analyzed discharge antibiotics based on respiratory viral panel (RVP) results. Of the children who tested positive for a respiratory virus, 70.6% (24/34) of patients were discharged with antibiotics. However, only 11.8% (4/34) patients who were positive for RVP had a chest radiograph reading consistent with solely viral pneumonia (increased perihilar markings/bronchitis/bronchiolitis). Including atypical bacteria, 73.5% (25/34) of patients with a positive RVP had a chest radiograph reading consistent with bacterial pneumonia based on our categorization of radiograph findings.

Length of treatment course

The most frequent length of treatment course was 10 days (33.3%) with 90.8% of patients treated for 11 days or less. 10.3% (9/88) of the patients were treated for one day. Length of treatment course was statistically similar regardless of therapy ($p = 0.839$).

Complications and 30-day re-admissions

4.4% (4/88) of the children developed a pneumonia-associated complication. Complications were empyema/pleural effusion, acute respiratory failure, empyema and necrotizing pneumonia, and pericarditis. 75% (3/4) of children who developed a complication were not treated according to the PIDS-IDSA guidelines. However, data is lacking if these children were treated with broad-spectrum or narrow spectrum-antibiotics. Additionally, these numbers are too small for statistical significance.

5.7% (5/88) of children were readmitted within 30 days. Four of these children were inappropriately treated and for 1 child it was indeterminable due to lack of immunization documentation. 94.3% of children had a length of hospital stay less than or equal to 5 days. Length of stay was statistically similar regardless of therapy, ($p = 0.835$).

Post-Order set implementation

Prior to the implementation of the order set, over a one-year time period, our institution lacked adherence to the guidelines regarding antibiotic use 48% of the time, after adjustment for the unknown vaccination status group. One month after implementation of the order set, adherence was assessed over a two-month period, see Table 3. The patient characteristics of the two groups are indicated in Table 2. Implementation of the order set decreased non-adherence to the guidelines to 16% ($p =$

0.005) using the Pearson chi-square test. In comparison to the pre-order set cohort, length of stay was statistically similar regardless of therapy (p = 0.637). However, 12% (3/25) of children developed a complication post-order set compared to 4.4% (4/88) who developed a complication pre-order set. In the post-order set implementation, 2 of the patients developed a pleural effusion; 1 patient was treated with ceftriaxone and the other with ampicillin. The third patient developed respiratory failure and septic shock with Methicillin-resistant *Staphylococcus aureus* growth in the pleural fluid. This patient was empirically treated with ampicillin and was the only patient post implementation with a complication admitted to the PICU.

Discussion

Brogan, et al. published a multicenter study of children hospitalized for CAP showed that cephalosporins accounted for 45% of empiric therapy with penicillins

Table 3: Results.

	Pre-order set	**Post-order set**
Empiric therapy: Adherence to guidelines	52%*	84% (21/25)
Empiric Antibiotic	Amoxicillin/clavulanate + azithromycin: 1/88 (1.1%)	Amoxicillin/clavulanate: 1/25 (4%)
	Amoxicillin/clavulanate: 3/88 (3.4%)	Amoxicillin: 6/25 (24%)
	Amoxicillin: 15/88 (17.2%)	Azithromycin + Ceftriaxone: 1/25 (4%)
	Ampicillin: 3/88 (3.4%)	Azithromycin: 3/25 (12%)
	Azithromycin + Ceftriaxone: 9/88 (10.3%)	Cefpodoxime + azithromycin: 1/25 (4%)
	Azithromycin: 1/88 (1.1%)	Ceftriaxone: 6/25 (24%)
	Cefpodoxime + Azithromycin: 1/88 (1.1%)	Clindamycin: 1/25 (4%)
	Ceftriaxone: 49/88 (56.3%)	
	Clindamycin: 1/88 (1.1%)	
	Levofloxacin: 1/88 (1.1%)	(The 2 patients with penicillin allergy: 1 patient treated with ceftriaxone and one with clindamycin)
	Vancomycin + Ceftriaxone: 1/88 (1.1%)	
Antimicrobial therapy duration (days)	Mode: 10	Mode: 10
	Mean: 8.34	Mean: 8.4
Chest radiograph results	Atelectasis: 2.3%	Atelectasis: 0%
	Atypical + Other*: 4.4%	Atypical + Other*: 16%
	Atypical Pneumonia: 20.7%	Atypical Pneumonia: 12%
	Bacterial Pneumonia: 54%	Bacterial Pneumonia: 20%
	Effusions/Empyema: 1.1%	Effusions/Empyema: 12%
	No pneumonia: 2.3%	No pneumonia: 8%
	Radiograph not documented: 5%	Radiograph not documented: 4%
	Viral Pneumonia: 10.3%	Viral Pneumonia: 24%
		Bacterial + Atypical: 4%
Respiratory Viral Panel (RVP) conducted	57/88 (64.8%)	15/25 (60%)
Positive RVP	34/57 (59.7%)	9/15 (60%)
RVP results	Adenovirus: 1/34 (2.9%)	Corona 229E + Parainfluenza 1: 1/9 (11.1%)
	Coronavirus: 1/34 (2.9%)	Influenza B: 1/9 (11.1%)
	Influenza A: 3/34 (8.8%)	Metapneumovirus: 3/9 (33.3%)
	Metapneumovirus: 4/34 (11.8%)	Parainfluenza 3: 1/9 (11.1%)
	Parainfluenza 1: 1/34 (2.9%)	Rhino/enterovirus: 2/9 (22.2%)
	Parainfluenza 3: 4/34 (11.8%)	RSV: 1/9 (11.1%)
	Rhino/enterovirus: 6/34 (17.7%)	
	RSV: 14/34 (41.2%)	
Blood cultures	37/88 drawn (42%)	9/25 drawn (36%)
	36 no growth	0 no growth
Length of stay (days)	Mode: 1	Mode: 2
	Range: < 1-15	Range: < 1-5
	Mean: 2.6	Mean: 2.2
Readmissions	5/88 (5.7%)	1/25 (4%)
Development of pneumonia-associated complications	4/88 (4.4%)	3/25 (12%)

Discharge antibiotics	No antibiotics: 15/88 (17%)	No antibiotics: 2/25 (8.3%)
	Amoxicillin: 24/88 (27.3%)	Amoxicillin: 12/25 (50%)
	Amoxicillin/clavulanate: 16/88 (18.2%)	Amoxicillin/clavulanate: 2/25 (8.3%)
	Amoxicillin + azithromycin: 3/88 (3.4%)	Cefdinir + azithromycin: 1/25 (4.2%)
	Augmentin + azithromycin: 2/88 (2.3%)	Cefdinir: 2/25 (8.3%)
	Cefdinir + Azithromycin: 1/88 (1.1%)	Azithromycin: 4/25 (16.7%)
	Cefacolor: 1/88 (1.1%)	Clindamycin: 1/25 (4.2%)
	2nd or 3rd generation cephalosporin: 17/88 (19.3%)	
	Azithromycin: 6/88 (6.8%)	
	Levofloxacin: 2/88 (2.3%)	
	Piperacillin/tazobactam: 1/88 (1.1%)	
	Clindamycin: 1/88 (1.1%)	
	*: Statistically adjusted for indeterminable adherence therapy due to lack of immunization documentation	*: Other: Bacterial, effusions/ empyemas, or atelectasis

and aminopenicillins rarely used [4]. Our study showed that cephalosporins accounted for empiric therapy 70% of the time (majority ceftriaxone, 67% (59/88)), with 25% (22/88) of our patients treated with penicillins, including amoxicillin and amoxicillin/clavulanate. However, only 2.3% (3/88) of those patients were treated with aminopenicillins or penicillins. This raised the question of the appropriateness to use amoxicillin as inpatient therapy in a child that can tolerate medication by mouth. In our study, we concluded that it is appropriate, and in accordance with the PIDS-IDSA guidelines. However, the guidelines state that if a child warrants hospitalization, parenteral therapy should be used.

Pre and post active dissemination of the guidelines, the duration of treatment was ten days for most patients, with a mean of eight days. The guidelines state that treatment courses of 10 days have been best studied. However, shorter courses may be just as effective. Further studies are needed to determine if a shorter duration would provide adequate treatment [1].

Based on the PIDS-IDSA guidelines, patients are treated based on their status of *Hib* and *S. pneumoniae* immunizations. Typically, the parent or caregiver verbally reported vaccination status, unless the patient was in our internal health system, where we had access of the direct immunization record. Physician documentation of immunization status in the patient charts lacked in 20.5% (18/88) of our population. The cohort of patients analyzed post-implementation of the CPOE order set had 100% documentation of the child's vaccination status. This may have been a result from the educational session where we addressed the importance of vaccination status and documentation when treating children with CAP. However, future efforts should include actual immunization record rather than parental report of vaccination.

The antibiogram used during this retrospective study was for the entire hospital, including adult and pediatric patients. A previous study concluded that pediatric care could be improved with use of a pediatric-specific antibiogram [5]. It would be beneficial to create a separate pediatric antibiogram for our children's hospital.

73.5% of patients with a positive RVP had a chest radiograph reading consistent with bacterial pneumonia. This finding may indicate that a superimposed bacterial infection often occurred as a result of a viral infection or may reflect how we categorized the chest radiograph findings but is difficult to standardize. However, our concern is the overuse of antibiotics for a viral infection. As noted, about 38% of the children had a positive RVP, with RSV the most common viral etiology. This finding is consistent with previous studies where RSV was the most common pathogen detected ranging from 28%-31% in pediatric patients with pneumonia [6,7].

A previous study assessed more than 15,000 hospitalized patients with CAP, determined costs for children hospitalized with CAP did not differ when treatment was narrow-or broad-spectrum antimicrobial therapy [8]. Therefore, this study did not aim at analyzing costs of therapy. However, from an antimicrobial stewardship perspective, narrow-spectrum antibiotic therapy is beneficial for other reasons including the prevention of antimicrobial resistance and risk for complications such as *Clostridium difficile*.

Continual education and reinforcement of the guidelines and the existence of the CPOE order set is an important factor to continue our currently improved adherence to the guidelines. As a teaching hospital, it will be important to continue education on the treatment of CAP to incoming residents.

Limitations

This study has several limitations. First, the data extraction did not account for all patients based on our inclusion criteria. Patient charts were extracted based on

discharge diagnoses, therefore only admitted patients, discharged with our selected ICD-9 codes were included in our analysis. Patients may have been empirically treated for the suspicion of CAP in the Emergency Department or treated as an admitted patient for suspicion of CAP, however those patients may not have had a final discharge diagnosis of CAP (or other included ICD-9 codes). Second, patients with a chronic disease were excluded from the review, with the exception of asthma/RAD patients. The guidelines exclude patients with chronic disease states, yet, at our institution we would consider treating a patient with RAD with narrow-spectrum antibiotics when CAP is suspected. Exclusion of these patients with these conditions would have decreased our studied population size by 25%. Third, adjustment for the unknown vaccination status group required us to statistically adjust the results. Excluding this group would have decreased our studied population size. Fourth, pre-implementation of the CPOE order set was during fall-winter and post-implementation was during spring. The difference in season of pre- and post-CPOE order set could affect the internal validity of our results. Overall, our study sample was limited, along with limitations of the retrospective nature and dependence on physician documentation which allows for bias.

Conclusions

In conclusion, nearly half of the children included in our study were not empirically treated according to the guidelines. After statistical adjustment for indeterminable appropriate use of antimicrobial therapy, use was inappropriate in 48% of patients. Adherence to the guidelines was poor, indicating overuse of broad-spectrum antibiotics for the empiric management of childhood CAP. A pneumonia CPOE order-set, along with education, was implemented resulting in a 32% improvement in adherence to the guidelines. Continued antibiotic stewardship would likely benefit from the implementation of other disease-specific physician order sets, along with education. In addition, a formal pediatric antimicrobial stewardship would be beneficial and is in the process of implementation.

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Conflict of interest

All authors report no conflicts of interest relevant to this article.

Manuscript preparation

Statistical and other analyses were done by statistics data editor IBM SPSS version 21.

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