

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Pediatrics

ESPS manuscript NO: 25246

Title: An Evidence-Based Approach to Transitioning Antimicrobials from Intravenous to Oral in Pediatric Patients with Acute Uncomplicated Osteomyelitis

Reviewer's code: 01202121

Reviewer's country: 0

Science editor: Fang-Fang Ji

Date sent for review: 2016-03-01 10:04

Date reviewed: 2016-03-05 04:38

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

COMMENTS TO AUTHORS

No mention is made of the role of surgery, and if the antibiotics in the studies looked at were pre or post-operative. A review article should include a critical appraisal of the papers involved. This would greatly enhance the quality of the review.

Response:

1. Role of surgery

- An introduction to the role of surgery can be found on page 4-5 and is highlighted. We also went through the literature and included a sentence or two about the role of surgery in each trial if anything was mentioned.

2. Critical appraisal of the papers

- Throughout the literature evaluation, we added a brief appraisal of each of the papers regarding strengths and limitations of the studies.

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Title: An Evidence-Based Approach to Transitioning Antimicrobials from Intravenous to Oral in Pediatric Patients with Acute Uncomplicated Osteomyelitis

Reviewer's code: 00186496

Reviewer's country: China

Science editor: Fang-Fang Ji

Date sent for review: 2016-03-01 10:04

Date reviewed: 2016-03-10 15:35

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

COMMENTS TO AUTHORS

The article systematically reviewed published literatures regarding the transition of antibiotics from IV to oral for uncomplicated acute osteomyelitis in the pediatric population. Additionally, the authors presented proposed algorithm of the transition to oral antibiotics from intravenous therapy for pediatric patients with acute uncomplicated osteomyelitis. The topic is important. However, the systematical review should include the procedures of literature retrieval, including and excluding standards of these literatures, as well as the quality control. We suggested the authors use the following paper as reference. Optimization of sympathectomy to treat palmar hyperhidrosis: the systematic review and meta-analysis of studies published during the past decade. Surg Endosc. 2011 Jun;25(6):1893-901

Response:

- a. A highlighted paragraph consisting of how our literature retrieval was done is now on page 4 of the manuscript. It entails what was included and excluded in regards to the literature search.

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Name of journal: World Journal of Clinical Pediatrics

ESPS manuscript NO: 25246

Title: An Evidence-Based Approach to Transitioning Antimicrobials from Intravenous to Oral in Pediatric Patients with Acute Uncomplicated Osteomyelitis

Reviewer's code: 00506500

Reviewer's country: Israel

Science editor: Fang-Fang Ji

Date sent for review: 2016-03-01 10:04

Date reviewed: 2016-03-17 14:43

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Y] Accept
<input checked="" type="checkbox"/> Y] Grade B: Very good	<input checked="" type="checkbox"/> Y] Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

COMMENTS TO AUTHORS

Comprehensive, well-written and balanced review of the current recommendations for managing acute pediatric osteomyelitis. I included my minor remarks in the following file: Abstract Background: Osteomyelitis is a bacterial bone infection that generally requires prolonged antibiotic treatment and potential surgical intervention. If left untreated, acute osteomyelitis can lead to chronic osteomyelitis and overwhelming sepsis. Focal complications from osteomyelitis in pediatric patients include bone growth disturbances, limb-length discrepancies, abnormal gait, arthritis, and fractures. Early treatment is necessary to prevent these complications, and with improvements in disease management and antibiotic therapy, the standard of care is progressing to a shorter duration of intravenous antibiotics and transitioning to oral therapy for the rest of the treatment course. Methods: We systematically reviewed the current literature on pediatric patients with acute osteomyelitis to determine when and how to transition to oral antibiotics from a short course of IV therapy. Discussion: When is an appropriate time to switch to oral antibiotics is a challenging question surrounding the treatment of acute osteomyelitis in pediatrics. Studies have shown that switching to

oral therapy after a short course (i.e. 3-7 days) of intravenous therapy has similar cure rates to continuing long-term intravenous therapy. Studies have also shown an increased risk of complications with prolonged intravenous use. Parameters that help guide clinicians on making the switch to oral therapy include a downward trend in fever, improvement in local tenderness, and a normalization in C-reactive protein concentration. Conclusion: Based on the available literature, we recommend transitioning antibiotics to oral after three to seven days of intravenous therapy for pediatric patients (except neonates) with acute uncomplicated osteomyelitis if there are signs of clinical improvement, and such regimen should be continued for a total antibiotic duration of four to six weeks. Keywords: Antimicrobials, C-reactive protein, intravenous, oral, osteomyelitis, pediatrics Core tip: When is an appropriate time to switch to oral antibiotics is a challenging question surrounding the treatment of acute uncomplicated osteomyelitis in pediatrics. With improvements in disease management and antibiotic therapy, the standard of care is progressing to a shorter duration of intravenous antibiotics and transitioning to oral therapy for the rest of the treatment course. This review aims to evaluate the current literature in order to help clinicians make sound decisions on when and how to transition from IV antibiotics to oral therapy in pediatric patients with acute uncomplicated osteomyelitis.

INTRODUCTION Osteomyelitis is an infection of the bone. These infections can spread to the bone numerous ways including trauma, cellulitis, septic arthritis, or bacteremia. Acute osteomyelitis in children is most commonly hematogenous in origin.¹ In high-income countries, acute osteomyelitis occurs in about 8 of 100,000 children per year, but it is considerably more common in low-income countries.² Boys are two times more prone to acute osteomyelitis than girls.² While *Kingella kingae* is by far the most common causative organism of acute osteomyelitis below the age of 4 years [Chometon S, Benito Y, Chaker M, Boisset S, Ploton C, Bérard J, Vandenesch F, Freydière AM. 2007. Specific real-time polymerase chain reaction places *Kingella kingae* as the most common cause of osteoarticular infections in young children. *Pediatr. Infect. Dis. J.* 26:377-381.], *Staphylococcus aureus* (*Staph. aureus*) is the predominant pathogen in older children, followed by respiratory pathogens such as *Streptococcus pyogenes* and *Streptococcus pneumoniae*.³ Osteomyelitis can be classified into three separate categories: acute, subacute, and chronic. Osteomyelitis is considered as acute if the

Response:

- a. We have made all the changes that were recommended by this reviewer and are highlighted in the main manuscript.