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Development of operationalized intravenous to oral antibiotic switch criteria

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Objectives: Despite huge overlap in suggested criteria for a safe intravenous (iv)-to-oral antibiotic switch, there is considerable variation in their operationalization. The objective of this study was to develop a set of measurable conditions that should be met in adult hospitalized patients for a safe iv-to-oral switch.

Methods: A RAND-modified Delphi procedure was performed to develop a set of operationalized iv-to-oral switch criteria. Switch criteria and their accompanying suggested measurable conditions were extracted from the literature and appraised by a multidisciplinary expert panel during two questionnaire rounds with a face-to-face meeting between these two rounds. In a final step, the experts could approve the set of developed operationalized switch criteria.

Results: Seven switch criteria and 41 accompanying measurable conditions extracted from the literature were appraised. Sixteen measurable conditions that operationalize six switch criteria were selected: (i) stable systolic blood pressure; and the absence of (ii) fever, (iii) temperature $<36^{\circ}$C, (iv) malabsorption syndrome, (v) short bowel syndrome, (vi) severe gastroparesis, (vii) ileus, (viii) continuous nasogastric suction, (ix) vomiting, (x) (severe) sepsis, (xi) fasciitis necroticans, (xii) CNS infection, (xiii) *Staphylococcus aureus* bacteraemia, and (xiv) endovascular infection. In addition, (xv) the patient should be cooperative and (xvi) adequate antimicrobial concentration should be achievable at the site of infection by oral administration.

Conclusions: These operationalized criteria can be used in daily clinical practice. Future use of these criteria in audits and as rules in clinical decision support systems will facilitate the performance and evaluation of iv–oral switch programmes.

Introduction

To optimize clinical outcome while minimizing toxicity and to reduce costs and emergence of antimicrobial resistance, various stewardship interventions can be part of antimicrobial stewardship programmes (ASPs). The implementation of a programme for early switch from intravenous (iv) to oral antibiotic therapy is one of these interventions.[1–4]

Numerous studies have demonstrated the equal efficacy of an early iv-to-oral switch to a full course of iv therapy.[5,6] This early switch has many advantages, such as reduced incidence of catheter-related infections, a decreased hospital length of stay and significant decreases in costs.[4,7,8] The iv-to-oral switch criteria that can be found in the literature mostly overlap. However, there is considerable variation in their operationalization and they are often subjective.[9–11] Reaching consensus on the operationalization of the criteria for a safe switch to oral antibiotics is important for guiding physicians involved in antibiotic prescribing and achieving uniformity of switch practices in hospitals.

The aim of this study was to reach consensus on a set of iv-to-oral antibiotic switch criteria, and the measurable conditions that operationalize this set of switch criteria, that should be met in adult hospitalized patients for a safe switch after 48–72 h of iv therapy.

Methods

Study design

A RAND-modified Delphi procedure was used to reach consensus among an international, multidisciplinary expert panel (for its composition see the

Supplementary data available at *JAC* Online and the Acknowledgements section) on a set of iv-to-oral antibiotic switch criteria and the measurable conditions that operationalize these criteria.

Literature search and expert consultation

First, a systematic literature search was performed using the following databases: Embase, Medline, Web of Science, Scopus, Cochrane, PubMed and Google scholar. Only articles in the English language published after the year 2000 were included. For complete search strings see the Supplementary data available at *JAC* Online. Each article reporting on the development and appraisal of criteria for the iv-to-oral antibiotic switch published between January 2001 and September 2014 was individually evaluated by two reviewers. A list of unique iv-to-oral antibiotic switch criteria, with measurable conditions that operationalize these criteria, was extracted from the included studies. Before the Delphi procedure started the criteria were presented to the experts to check whether we grouped the criteria appropriately and whether they agreed with the formulation of the criteria.

RAND-modified Delphi procedure: brief description

Using the information from the literature search, the procedure included four steps. In Step 1, the measurable conditions that operationalize iv-to-oral antibiotic switch criteria were included in a questionnaire. Experts were asked to appraise the relevance and safety of these measurable conditions on a nine-point Likert scale. Measurable conditions with a median score of 7, 8 or 9 were accepted if there was agreement. Agreement was defined as >70% of the scores in this top tertile (7, 8 or 9). If the median score was <7 the measurable condition was rejected. The measurable conditions with a median score of 7, 8 or 9 and disagreement (i.e. ≤70% of the scores in the top tertile) were discussed during the face-to-face meeting. During Step 2 the identified areas of disagreement were discussed at a face-to-face meeting. After reaching agreement on the measurable conditions, Step 3 followed to appraise the relevance of the iv-to-oral switch criteria using a questionnaire. The same consensus rules as described above were applied. In Step 4 the experts were asked to approve the final set of switch criteria and the measurable conditions that operationalize them (Figure 1). A complete description of the procedure can be found in the Supplementary data available at *JAC* Online.

Results

Expert panel

The experts ($n = 19$) were clinical microbiologists ($n = 6$), infectious disease consultants ($n = 7$) and clinical pharmacists ($n = 6$) from the Netherlands, Belgium, the USA and the UK.

Literature search and expert consultation

Our literature search resulted in 1568 articles, of which 86 contained potential iv-to-oral antibiotic switch criteria (Figure S1). A list of eight unique iv-to-oral switch criteria was extracted from the included studies, with 41 measurable conditions. The experts suggested rephrasing the switch criterion 'an oral variant of the antibiotic has to exist' to 'an oral variant of the antibiotic with good bioavailability has to exist'. Furthermore, the switch criteria 'clinical improvement should be observed' and 'signs and symptoms related to the infection have to be resolved or improved' were merged, because these criteria were believed to be similar, resulting in a final set of seven switch criteria (Table S1).

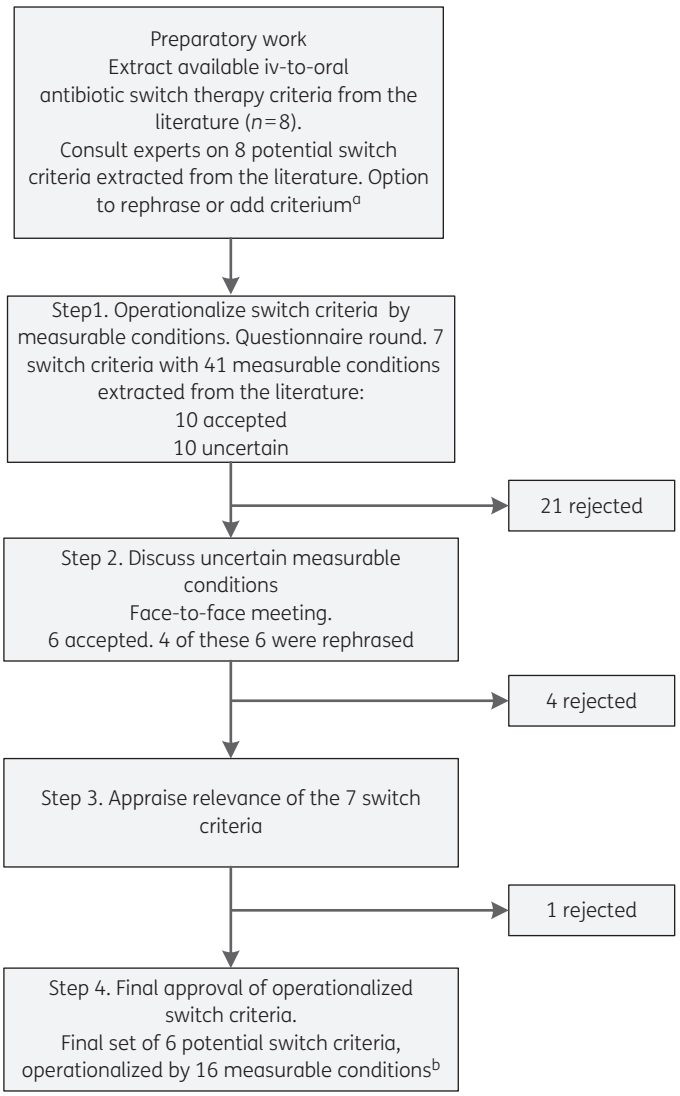

Figure 1. Steps in the RAND Delphi procedure. [a]Two criteria were rephrased, one duplicate criterion was removed, no criteria were added. [b]One of the switch criteria is not operationalized, because no operationalization is found in the literature.

RAND-modified Delphi procedure (Figure 1)

Step 1, Questionnaire 1

Eighteen experts completed and returned the questionnaire (response rate 94.7%). Ten of the 41 measurable conditions were accepted and 21 were rejected. The experts achieved no agreement on 10 potential measurable conditions, which operationalize six different iv-to-oral antibiotic switch criteria. No new measurable conditions were suggested.

Step 2, Face-to-face meeting

Nine experts attended the meeting. Four measurable conditions were rejected during this meeting and six measurable conditions were accepted, of which four were accepted after rephrasing (Table S1).

Table 1. Switch criteria, and operationalized criteria, that should all be met in adult hospitalized patients for a safe iv-to-oral switch

A. Vital signs should be good or improving
Systolic blood pressure should be stable without inotropics or fluid resuscitation
B. Signs and symptoms related to the infection have to be resolved or improved
Temperature should be <38.3°C[a] without antipyretics
Temperature should be >36 °C
C. The gastrointestinal tract (GIT) has to be intact and functioning
Absence of the following conditions
malabsorption syndrome
short bowel syndrome
severe gastroparesis
ileus
continuous nasogastric suction
D. The oral route should not be compromised
No vomiting
Patient should be cooperative
E. Absence of contraindicated infections
Adequate antimicrobial concentrations are not achievable at the site of infection by oral administration
Absence of the following infections
(severe) sepsis
fasciitis necroticans
CNS infection
S. aureus bacteraemia
endovascular infection (e.g. endocarditis)
F. An oral variant[b] of the antibiotic with good[c] bioavailability has to exist

[a]Chosen by the experts.
[b]Oral variant can be another antibiotic with appropriate microbiological profile.
[c]60%–90%, in accordance with the literature.

Step 3, Questionnaire 2

Eighteen experts completed and returned the questionnaire (response rate 94.7%). Six of the seven iv-to-oral antibiotic switch criteria were accepted. No additional criteria were suggested.

Step 4, Final approval

All experts ($n = 19$) returned the document and approved the set of operationalized switch criteria (Table 1). The final set consisted of 16 measurable conditions: (i) stable systolic blood pressure; and the absence of (ii) fever, (iii) temperature <36°C, (iv) malabsorption syndrome, (v) short bowel syndrome, (vi) severe gastroparesis, (vii) ileus, (viii) continuous nasogastric suction, (ix) vomiting, (x) (severe) sepsis, (xi) fasciitis necroticans, (xii) CNS infection, (xiii) *Staphylococcus aureus* bacteraemia, and (xiv) endovascular infection. In addition, (xv) the patient should be cooperative and (xvi) adequate antimicrobial concentration should be achievable at the site of infection by oral administration.

Discussion

With this study, using a RAND-modified Delphi procedure, we developed a set of operationalized iv-to-oral antibiotic switch criteria that all have to be met in adult hospitalized patients for a safe switch after 48–72 h of iv therapy. These operationalized criteria can be used in daily clinical practice, by antibiotic stewardship teams and by attending physicians. Additionally, they may facilitate auditing iv-to-oral antibiotic switch practices on a specific ward or hospital, and enable comparisons between hospitals or regions.

Since iv-to-oral switch is one of the most cost-effective stewardship interventions, several iv-to-oral antibiotic switch programmes are being used and implemented in hospitals.[9] In addition, the switch from iv to oral is one of the recently developed structure and process indicators that characterize ASPs among different countries and healthcare systems.[12] However, although early iv-to-oral switch has been advocated for many years, uptake has been difficult at both the national and the individual level.[13] A recommendation for national uptake is that a consensus document with switch criteria should be developed with involvement of stakeholders.[14] Our criteria were defined by national and international experts from involved medical disciplines, which are the key stakeholders for such a consensus.

The present study has several strengths. First, a RAND-modified Delphi procedure was used, in which a systematic literature search and input from an international multidisciplinary expert panel were combined.[15] This study design enabled us to include experts from different regions and areas of expertise semi-anonymously, so that domination by powerful individuals was avoided in the questionnaire rounds. Clinical microbiologists, infectious diseases consultants and clinical pharmacists from both teaching and non-teaching hospitals participated in the study. Given the high response rate in all study rounds, we were able to include various relevant perspectives, which we believe strengthened the results of our study.

Our study also has limitations that should be mentioned. Not all experts could attend the face-to-face meeting and all experts who joined this meeting were from the Netherlands. However, all disciplines and hospital types were represented during this meeting. We also asked all experts for approval of the final set of operationalized switch criteria and for any final remarks. Considering the 100% response and approval rate, we believe that the fact that not all experts could attend the face-to-face meeting did not influence the validity or reliability of our study results.

The developed measurable conditions are a first step towards standardized iv-to-oral switch criteria. However, to improve antibiotic use in an effective and sustainable manner, more is needed than only guidelines and instructions.[16] Electronic reminders generated by a clinical decision support system (CDSS) are believed to have a great potential to facilitate a timely iv-to-oral switch.[3,17–19] The specific and generally applicable criteria we developed offer the opportunity to develop a generally applicable CDSS to remind physicians about switching from iv to oral therapy.

In conclusion, with a RAND-modified Delphi procedure we developed a set of six iv-to-oral antibiotic switch criteria operationalized by 16 measurable conditions. All of these operationalized criteria have to be met in adult hospitalized patients for a safe switch after 48–72 h of iv therapy.

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Transparency declarations

None to declare.

Supplementary data

Supplementary data, including Figure S1 and Table S1, are available at *JAC* Online (http://jac.oxfordjournals.org/).

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