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Research paper

Face and content validity of variables associated with the difficult-to-sedate child in the paediatric intensive care unit: A survey of paediatric critical care clinicians☆,☆☆

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ABSTRACT

Background: Clinicians recognise that some critically ill children are difficult-to-sedate. It may be possible to identify this clinical phenotype for sedation response using statistical modelling techniques adopted from machine learning. This requires identification of a finite number of variables to include in the statistical model.
Objective: To establish face and content validity for 17 candidate variables identified in the international literature as characteristic of the difficult-to-sedate child phenotype.
Methods: Paediatric critical care clinicians rated the relevance of 17 variables characterising the difficult-to-sedate child using a four-point scale ranging from not (1) to highly relevant (4). Face and content validity of these variables were assessed by calculating a mean score for each item and computing an item-level content validity index. Items with a mean score >1 were rated as having adequate face validity. An item-level content validity index ≥0.70 indicated good to excellent content validity.
Setting and participants: Web-based survey emailed to members of the Pediatric Acute Lung Injury and Sepsis Investigators Network or the Society of Critical Care Medicine Pediatric Sedation Study Group.
Results: Of 411 possible respondents, 121 useable surveys were returned for a response rate of 29%. All items had a mean score >1, indicating adequate face validity. Ten of 17 items scored an item-level content validity index ≥0.70. The highest scoring items were requiring three or more sedation classes simultaneously, daily modal sedation score indicating agitation, sedation score indicating agitation for 2 consecutive hours, receiving sedatives at a dose >90th percentile of the usual starting dose, and receiving intermittent paralytic doses for sedation.
Conclusions: Computation of an item-level content validity index validated variables to include in statistical modelling of the difficult-to-sedate phenotype. The results indicate consensus among paediatric critical care clinicians that the majority of candidate variables identified through literature review are characteristic of the difficult-to-sedate child.

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1. Introduction

Each year, more than 115,000 critically ill children receive sedation to help them tolerate intubation and mechanical ventilation.[1] A substantial number of these children do not respond as expected to appropriately dosed sedation and remain agitated for some period of time, leading to iatrogenic injury and increased stress.[2–5] These children who remain agitated despite receiving usual doses of sedation or are eventually adequately sedated but require much larger amounts of sedative drugs are described by the clinical team as treatment failures, suboptimally sedated, or difficult-to-sedate.[6–8] Little is known about the reasons contributing to this phenomenon in these children, preventing early identification of the child who will be difficult-to-sedate. The child is often identified as difficult-to-sedate at the time care providers are actively administering sedative drugs, resulting in a delay in the attainment of therapeutic concentrations and the desired clinical effect.[8–10] This experience causes excessive and potentially avoidable burden on the child and family and increases the chances that the child's safety has been compromised and injury may have occurred.[2–5] Developing a mechanism to identify the difficult-to-sedate child could allow for early identification and prepare the care provider with *a priori* knowledge that the child may require more than the typical sedation needs. However, the first step towards the goal of early identification is consensus on the characteristics defining the difficult-to-sedate child.

2. Background

Many factors hamper identification of the difficult-to-sedate child. Sedation in the paediatric intensive care unit (PICU) is a complex phenomenon, impacted by multiple variables. Easily implemented, valid, and reliable instruments that describe sedation levels in children have only become available and widely used in the last decade.[11,12] Patients cared for in the PICU vary widely in age and encompass enormous physiological and psychosocial differences.[7] Although well-studied in adults, there are limited data on the metabolism and elimination of drugs commonly used for sedation in critically ill children.[13,14] Organ maturation and critical illness affect the rate at which sedation medications are distributed, metabolised, and eliminated from the body.[7] The influence of psychosocial development in response to sedation is not thoroughly described. There may be a genetic basis for the difficult-to-sedate child because of polymorphisms in the genes that encode drug metabolising enzymes as well as pertinent receptors.[3,15] Finally, each PICU's individual sedation management plan dictates how and when sedation is delivered, the specific agents and doses used to provide sedation, and the definition of optimal levels of sedation.[7] These factors contribute to the challenge of studying sedation in critically ill children.

Defining sedation-related clinical phenotypes in critically ill children would facilitate better clinical management of these patients while decreasing potential harm. Specifically, insight into an individual child's response to sedation would allow the selection of personalised therapy and potentially contribute to improved clinical outcomes. Phenotype identification supports treatments geared to the needs of individual patients by considering each individual's unique genetic, biomarker, phenotypic, or psychosocial characteristics that distinguish them from other patients with similar presentations.[16] High doses of sedatives and the simultaneous use of multiple sedative agents, as typically occurs in the difficult-to-sedate child, generally result in adverse effects such as hypotension, bradycardia, propofol infusion syndrome, and iatrogenic withdrawal syndrome.[17] Based on recent evidence that prolonged or repeated use of sedative and anaesthetic drugs may negatively affect the developing brain by causing brain cell death, the United States Food and Drug Administration has required a warning be added to drug labels indicating that brain development in children aged 3 years and below may be affected by exposure to these drugs. Included in this group are some of the most commonly used paediatric sedation drugs including midazolam, lorazepam, pentobarbital, ketamine, and propofol.[18] Identifying and providing targeted sedation strategies most effective for the difficult-to-sedate child could minimise these effects.

An operational definition of the difficult-to-sedate child clinical phenotype does not exist. In other populations, advanced statistical methods including cluster, classification and regression tree, and latent class analysis have been used to analyse large data sets and create an operational definition of specific phenotypes within a disease process such as childhood asthma, paediatric sepsis, or acute respiratory distress syndrome.[19–21] These statistical methods require identification of candidate variables likely to be associated with the concept under investigation. In the case of intubated and sedated children, the difficult-to-sedate child clinical phenotype might include a combination of demographic, physiologic, genetic, and developmental factors.[22–24]

Using a three-step process, we sought to create an operational definition of the difficult-to-sedate clinical phenotype using a large data set from the Randomized Evaluation of Sedation Titration for Respiratory Failure (*RESTORE*) study (clinicaltrials.gov identifier: NCT00814099).[9] The *RESTORE* data set includes 2449 children with acute respiratory failure and contains hundreds of variables and thousands of data points, requiring a thoughtful approach to identifying candidate variables. Step one in identifying candidate variables from those available in the *RESTORE* database was the completion of a concept analysis using the methodology described by Walker and Avant.[25] The concept analysis was based on a review of the international literature related to sedation in paediatric critical care. Thirty-three studies (16 from Europe, 13 from the United States and Canada, and 4 from South America) were reviewed and are listed in Table 1.

The second step in creating our operational definition, described in this article, involved assessing face and content validity of the candidate variables identified in the concept analysis. We did this to substantiate their appropriateness and ensure all possible candidate variables were included in step three, a planned latent class analysis. Although face and content validity are generally used in instrument assessment, we used them here to obtain expert opinion on which of the variables identified through the literature review and concept analysis were consistent characteristics of the difficult-to-sedate child. Face validity assesses whether an instrument seems to measure what it purports to measure. It assesses the relevance of an item to a construct in the opinion of experts.[26] Content validity is generally used to assess whether the content of an instrument is inclusive and representative of the domain of interest, i.e., do the items completely measure the domain.[27–29] Polit and Beck[29] note that content validity assesses if the items in the tool, when considered as a group, provide a reasonably complete operational definition of the construct being measured. Although not intended to be a formal instrument for repeated use, our survey was constructed to include what we had identified as the characteristics of the difficult-to-sedate child phenotype and used to seek expert opinion as to their relevance and completeness. Here, we report on the face and content validity of candidate variables potentially

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