

The Use of Oxygen in the Delivery Room

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We hope to base our practice on the best evidence available. The International Liaison Committee on Resuscitation (ILCOR) is committed to a transparent process that allows its guideline developers as well as the subsequent guideline users to understand how the evidence base was created and how the evidence is valued.

In 2015, the ILCOR adopted a process that would enable a near continuous review of resuscitation science by evaluating high-priority population, intervention, comparator, and outcome (PICO) questions.¹ The process is ambitious. Knowledge synthesis units with expertise in searching scientific databases and performing systematic reviews and meta-analysis address broad PICO questions (questions that may be large and complicated or topics covering several PICO questions that can be grouped together and explored by using sensitivity or subgroup analyses). Potentially, such a systematic review will lead to a meta-analysis and a broader understanding of the available evidence.

Importantly, the ILCOR has endorsed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.^{2,3} By using GRADE, the quality of the evidence supporting the effect of an intervention on a specific outcome of interest is rated. Randomized controlled trials (RCTs) start as high-quality evidence, and observational studies start as low-quality evidence. Five factors may lead to downgrading the quality of the evidence. For RCTs, the 5 critical domains that could

downgrade the evidence are the risk of bias, imprecision, generalizability, inconsistency, and publication bias.

Two examples of this process related to neonatal interventions are reported in this issue of *Pediatrics*.^{4,5} A general PICO question was created, leading to 2 separate systematic reviews of initial oxygen use in the resuscitation of preterm and term infants. A detailed, complete, and methodologically sound analysis is presented. In term infants, the authors report on 10 studies (5 RCTs and 5 quasi RCTs). For term infants, the initial use of room air compared with 100% oxygen in resuscitation was associated with a benefit in short-term mortality (typical relative risk: 0.73; 95% confidence interval [CI]: 0.57–0.94; 7 studies [1469 infants]). Hypoxic-ischemic encephalopathy was not reduced in this analysis (typical relative risk: 0.89; 95% CI: 0.68–1.18; 5 studies [1315 infants]). Fewer studies reported on developmental follow-up, and no differences were noted (typical relative risk: 1.41; 95% CI: 0.77–2.60; 2 studies [360 infants]).

For preterm infants, the results are less clear. The authors identified 10 RCTs and 4 observational studies. There were no statistically significant benefits or harms from starting with a lower compared with a higher fraction of inspired oxygen. No difference in the risk of short-term mortality is reported (typical relative risk: 0.83; 95% CI: 0.50–1.37; 10 studies [968 infants]).

Importantly, the authors report on the GRADE assessment of the quality of the evidence. The terminology for GRADE recommendations has evolved

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in recent years. Originally, terms such as “low-quality evidence” or “high-quality evidence” were used in GRADE. More recently, the term “certainty of evidence” has become the preferred term.⁶ When seen in this light, the next steps of creating recommendations on the basis of this evidence become more problematic. Marginal effects or no effects are noted from the intervention. In addition, the estimates are imprecise, and the inherent bias of trials that are difficult to blind comes into play. In both analyses, short-term outcomes, such as mortality, are judged as low certainty, and longer-term neurodevelopmental outcomes are judged as very low certainty. Even if one had faith in the evidence, how we would apply the intervention? What are the targets? How long should we take to achieve the desired target?

That is why the next steps are so hard. Guideline developers must not only grapple with the quality or certainty of the evidence but also account for individual and societal values and preferences, resource implications, and feasibility.⁷

As these reviews move toward recommendations, the fact is that we will begin our resuscitation with some oxygen (as low as 21% or as

high as 100%). Ultimately, a decision will have to be made regarding how much oxygen with which we start. Yet, given the paucity of evidence, the single greatest point we can take from these analyses is that we are uncertain. Although we must act, our obligation is not simply to conduct the well-thought-out recommendations that will evolve from this process but to acknowledge the huge gaps in knowledge that exist and commit to further research on the subject.

ABBREVIATIONS

CI: confidence interval

GRADE: Grading of
Recommendations
Assessment,
Development and
Evaluation

ILCOR: International Liaison
Committee on
Resuscitation

PICO: population, intervention,
comparator, and outcome

RCT: randomized controlled trial

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