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VIEWPOINT

Protecting children from iatrogenic harm during COVID19 pandemic

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Critical care management of patients with COVID-19 has been influenced by a mixture of public, media and societal pressure, as well as clinical and anecdotal observations from many prominent researchers and key opinion leaders. These factors may have affected the principles of evidence-based medicine and encouraged the widespread use of non-tested pharmacological and aggressive respiratory support therapies, even in intensive care units (ICUs). The COVID-19 pandemic has predominantly affected adult populations, while children appear to be relatively spared of severe disease. Notwithstanding, paediatric intensive care (PICU) clinicians may already have been influenced by changes in practices of adult ICUs, and these changes may pose unintended consequences to the vulnerable population in the PICU. In this article, we analyse several potential iatrogenic causes of the detrimental effects of the current pandemic to children and highlight the risks underlying a sudden change of clinical practice.

Key words: coronavirus; Covid-19; paediatric intensive care; paediatrics; therapy.

"Fear of disease killed more men than disease itself."

—Mahatma Gandhi

In a few months, the COVID-19 pandemic has rapidly spread from China, and as it moved west, health-care systems worldwide have been strained facing the worst health crisis of the century. COVID-19 has made our ground tremble. Entire populations are living under unprecedented lockdowns and uncertainty. At the frontline, health-care professionals are exposed not only to the challenge of managing the surge of critically ill patients but also to growing societal pressure from the public and from the media to cure this new viral disease as cases mount. The mixture of these factors, coupled with economic and political factors, puts at risk the fundamental principle of medicine built on science for patient well-being, and the loss of this may increase the risk of harm to our patients. This is particularly true in countries where social pressures may be acute.

Eminence-Based Medicine and Unintended Consequences

We doctors are humans and, as such, are influenced by our environment (what we hear, read or feel). As infections grew dramatically in western countries in early March 2020, some key opinion leaders and prominent researchers developed a series of observations and recommendations that significantly influenced clinicians taking care of the first COVID-19 cases.[1] Although, to date, no drug has shown to be beneficial for COVID-19 in randomised trials, many advocated for the off-label prescription of many pharmacological treatments, mostly based on anecdotes, small observational studies and biological plausibility: a 'this makes sense' or 'my way to do it' approach.

This sudden change of practice may have had unintended consequences. When a critically ill patient is admitted to an intensive care unit (ICU), the resulting outcome when discharged is the result of a complex interplay between the insult, the host and us – the physicians. Every medical intervention carries the risk of iatrogenic consequences, and they must always be balanced to give our patient a clear benefit. In the first weeks of the SARS-CoV-2 outbreak in Europe and the western world, we did not always adhere to these principles. Non-tested therapies are harmful until proven otherwise. The risk application of the particular therapy is uncertain, so we are essentially forced to gamble on the balance between harm and benefit. Phrases like '*intubation must be prioritized*' or '*patients should be left quiet*',[1,2] added to the fear of aerosolisation and of non-invasive respiratory support, may have contributed to the crumble of critical care response capacity of many countries and the shortage of mechanical ventilators, beds and common medications. The tendency towards more aggressive ICU management was mainly based on weak or absent supportive data, fuelled by *a secondary pandemic* of webinars, press coverage and social media spread of potential golden bullets to treat this new disease. The early approach to severe COVID-19 was in clear dissonance with the paradigm shift towards evidence-based ICU care over the last decade, with a 'less is more' approach for ventilatory management, resuscitation fluids, transfusions and other interventions.[3]

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An example is the intubation of hypoxaemic patients. Anecdotal reports suggesting a more favourable outcome with 'early' intubation in COVID-19 led to recommendations to avoid commonly used non-invasive treatments such as continuous positive airway pressure (CPAP), high-flow nasal cannula (HFNC) or non-invasive ventilation (NIV). Not surprisingly the first figures showed that NIV was used only in 1 of 10 patients with confirmed COVID-19 infection.[4] Early intubation of a patient with known or suspected COVID-19 with respiratory distress likely resulted in intubating patients who would have otherwise improved on CPAP or NIV. In addition, early intubation may also have denied life-saving treatment for other patients, especially in resource-limited settings. The iatrogenic costs, including ventilator associated pneumonia (VAP), ventilator-induced lung injury (VILI), hemodynamic disturbances, as well as the adverse effects of sedation and immobilisation, could have been avoided in some cases.

The walk away from evidence-based medicine is not novel. In medicine, particularly critical care, history has taught us that many initially promising hypotheses, plausible mechanisms and observations failed to pass the test of randomised trials and were found to be no better than prior standards of care.[5] During the first 2 months of the COVID-19 pandemic, emotions and anecdotes prevailed over science, and eminence prevailed over evidence-based medicine.[6] In these early days of the pandemic, scarcity of data and provocative claims of benefit led to a significant change in practice. This quickly changed the entire playbook of modern critical care medicine.

Avoiding Iatrogenic Pandemic for Children

Paediatric critical care may be particularly susceptible to threats against evidence-based medicine. There are few randomised trials in critically ill children, and as a result, many of the therapies provided in a paediatric intensive care unit (PICU) are based on extrapolation from adult studies or observational clinical trials. As these changes in practice came under scrutiny,[7] paediatricians in PICUs began to ask themselves how they would prepare for critically ill children. Should we change our proven, established current practices to mimic (yet) unproven adults' perspectives?

Viral illnesses are common in PICUs; paediatric intensivists have learned hard lessons from managing critically ill children with viral

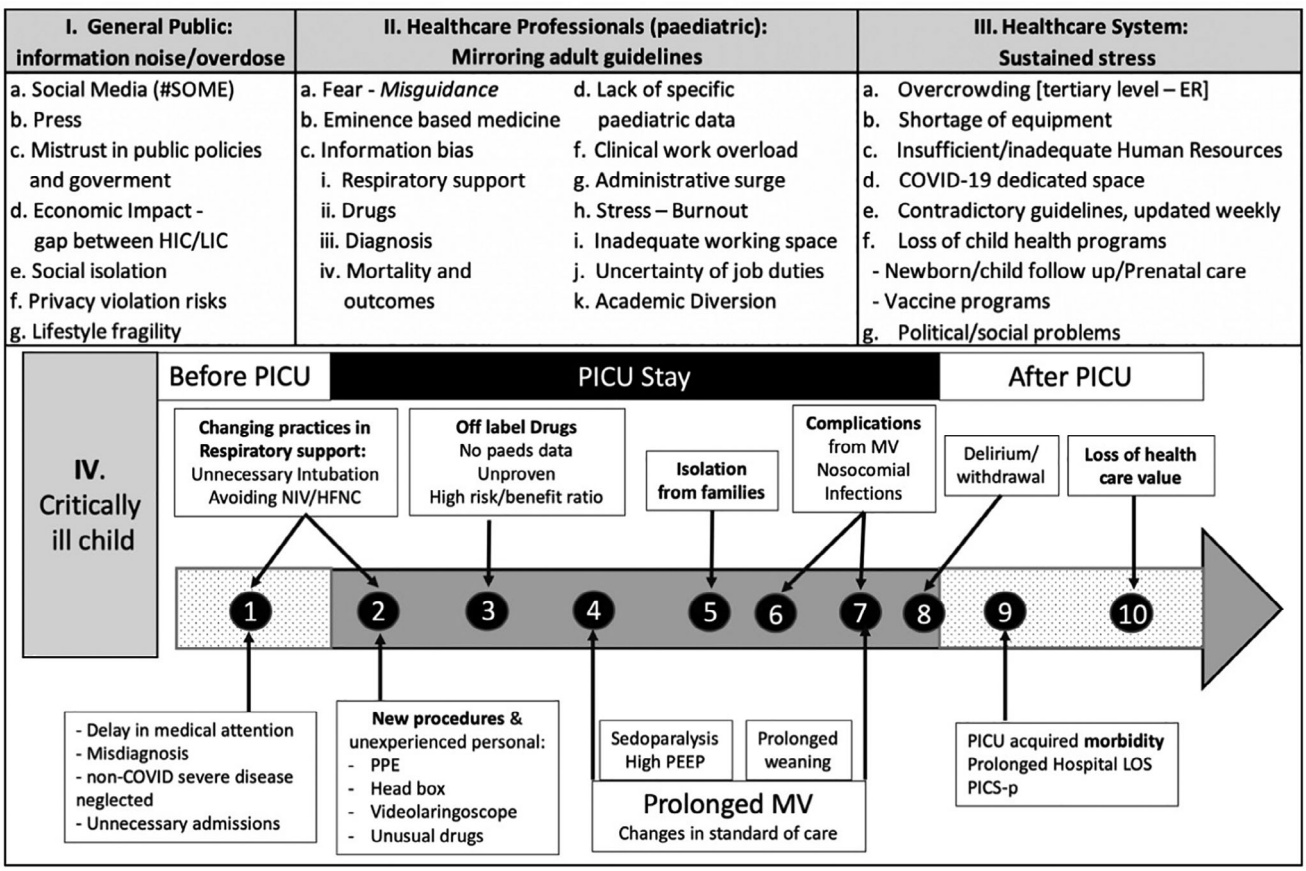

Fig. 1 Key factors that may affect optimal care of critically ill children. The figure specifically shows the multi-level involvement: general public information overload (Box I), paediatric health-care professionals' uncertainty (Box II) and sustained stress of health-care system (Box III). In addition, we added a detailed timeline of critically ill children with crucial steps and issues that can affect their clinical course (Box IV). (ER, emergency room; HFNC, high-flow nasal cannula; HIC, high-income countries; LIC, low-income countries; LOS, length of stay; MV, mechanical ventilation; NIV, non-invasive ventilation; PICS-p, post-intensive care syndrome in paediatrics; PICU, paediatric intensive care unit; PEEP, positive end expiratory pressure; PPE, personal protective equipment).

disease. Just a couple of decades ago, the standard treatment for respiratory failure was widespread, almost routine, intubation and mechanical ventilation. Currently, the extended use of NIV has reduced the need for intubation, decreasing complications, nosocomial infections, residual morbidity and length of PICU stay.[8]

It is dangerous to divert from well-established and proven therapies during this time of crisis. Avoiding NIV and applying COVID-19 guidelines to COVID-19 and non-COVID-19 children out of fear is not what is right for our patients and is not consistent with medical evidence. Rather, we should continue to provide care as we did before the pandemic outbreak by being *aggressively gentle*: a 'Stick with what we know that works' approach. Deviating from core therapies and using unproven therapies 'just to try' could harm children. We have identified several potential causes of the detrimental effects of current pandemic to children (Fig. 1), which include both medical and non-medical issues, such as isolation from families.

We are aware that it is in our medical nature to prefer intervention to inaction. During these challenging times, it is tempting to abandon routine care in favour of newer and more exciting therapies and clinical approaches. However, we must remember that there must always be sufficient justification to administer a medication to a critically ill patient and that this justification must not be anecdotal because the first duty of medicine is 'do no harm'. Even in times of crisis, *Primum non nocere* should prevail.

Authors contributions

AC, SG and FD designed and drafted the manuscript. CLC participated in the editing of the manuscript and made substantial contributions to the final version. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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