ICU
MANAGEMENT & PRACTICE

The Landscape of COVID-19 Clinical Trials

Introduction

In an effort to gather evidence through scientifically rigorous trials to guide optimal management of COVID-19, researchers in the US have started multiple parallel clinical trials. In this systematic review, the researchers evaluate the characteristics and issues surrounding simultaneous trials being conducted.

Methods

This systematic review, conducted in June 2020, used publicly available data using PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) reporting guideline. The www.ClinicalTrials.gov registry was searched for all interventional trials related to COVID-19 and resulting data was analysed. Only one US-based registry was used that represents only a small fraction of trials going on around the world is a limiting factor.

Results /Characteristics

After careful screening of the trials and eliminating inactive trials, a total of 674 trials were selected. Of these 83% (562) were randomised multigroup studies and 71% had a valid control group. Only 36% (201) were multicenter trials and chloroquine was the most tested intervention 132/562. Most trials (85%) focused on assessment of treatment and only 15% focused on prevention.

The most common end points that were being assessed included

- Onset of symptoms to the time taken for resolution (212 trials- 37.3%)
- Mortality (180 trials- 32.0%)
- Clearance of virus (124 trials – 22.1%)
- Need for mechanical ventilation (57 trials -10.1%)

Discussion

In this systematic review, the researchers found that the trial multiplicity rate was really high. For example, chloroquine was tested in 143 trials. While this multiplicity may provide a higher degree of data validation, it has an equally high probability of having positive findings owing to chance alone. These chance positive findings can lead to a wide use of an intervention that may not be effective or even dangerous.

High trial multiplicity rate can also compromise trial accrual and statistical power by creating an unnecessary competition between study participants as has already been witnessed in China. For example, the planned participant accrual for US-only COVID-19 treatment trials is about 45942 of which 13542 are for chloroquine-specific trials alone which makes it next to impossible to meet the enrollment target.

Recommendations

The medical community, institutional review boards, and regulators such as the US Food and Drug Administration (FDA) must coordinate efforts and devise a collaboration mechanism. They must work to standardise and synchronise study end points. Study end points should be objective in nature and include outcomes such as all-cause mortality, rates of mechanical ventilation, admission to intensive care etc. Coordination of efforts will reduce initiation of several similar trials at the same time eliminating publication bias as well as issues of incomplete participant

accrual. Duplication can be reduced and participant accrual can be enhanced through the use of makeshift cooperative groups as well. Efforts should be made to facilitate pooled analyses across trials.

A concerted effort will pave the way for the generation of high-quality evidence that can be used to guide patient management with the potential to save millions of lives around the world.

Source: JAMA

Image Credit: iStock

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