Editorial

COVID 19: Effect on Clinical Research

Pallavi Ahluwalia
Professor, Department of Anesthesiology
Teerthanker Mahaveer Medical College and Research Centre,
Uttar Pradesh 244001

Various factors have imposed tremendous impact on research during COVID 19 epidemic and clinical trials have taken a back foot. Clinical research was always challenging but conducting clinical trials during pandemic is particularly difficult especially when we are dealing with a novel virus. There is very little information about the disease and there is no reliable therapeutic information available. We're learning new things about it every day. There is an urgent desire to try or experiment new treatment regimens with or without their proven benefit. But trying an empirical therapy might not be the best approach. Therapeutic agents must be analyzed carefully in terms oftheir clinical outcomes and risk reward ratio. The current situation necessitates the critical need for therapeutic COVID 19 treatment along with clinical research to establish its safety in various groups like pregnant females, geriatric age group and children. Various ongoing research projects are also presently constrained because of redirection of resources and limitations in terms of in-person visits. So we need to look at the issues that arise during clinical trials in a pandemic. How they are tackled and how various other aspects like patient safety and ethics are dealt with?

We have seen an increased workload during the pandemic in terms of a large number of patients being diagnosed and admitted in hospital or Intensive Care Units (ICU). ICU's are currently running at expanded capacity. Several new ICU's are created to cater to increased patient input. Frontline Health care workers are working under the constant stress of getting exposed to the virus and fears regarding infection transmission to fellow staff, facing issues like fatigue and burnout. Some healthcare workers providing bedside care feel that it is impossible to deliver optimal patient care and do meaningful research simultaneously. The major challenge is maintaining standards of clinical care in current scenario. Developing a vaccine or selecting newer drugs rapidly in mid-outbreak isethically tricky and difficult. On the other hand, there is a concern aboutthe delay in the implementation of effective therapies if we await the results of Randomized Control Trials."We can expect dramatic effects on clinical trials (on going or new) during pandemic because of various factors such as travel limitations, active quarantine of patient and staff members, study closures because of redirection of resources and interruptions in the supply of products required for investigations".[1]

Other challenges include precise recording of the detailed impact of drug on the patient, detailed information about patient outcomes and adverse effects during pandemic. The clinicians are already overwhelmed because of increased number of patients getting infected daily. The patient variables needs to be recorded in an organized and methodicalway such as presence or absence of the virus, viral titres, antigen tests, haematological investigations, oxygen level measurement, requirement of oxygen or non-invasive ventilation/ventilator use etc. Randomisation may not be possible. Also it is ethically not possible to have a placebo group. At present various clinical trials are being conducted to measure therapeutic outcomes. Information about therapeutic benefits can be gained very rapidly owing to large number of patients affected with COVID 19. As a measure to overcome challenges and regional variations, World Health Organization (WHO) launched an international clinical trial called Solidarity, so that various clinical centres from different countries could participate. The main aim was to find an effective treatment for COVID 19. Trial compares options against standard of care, to assess their relative effectiveness. Several regimens: like the antimalarial drug such as Hydroxychloroquine; an antiviral drug example Remdesivir; and anti-HIV drugs, Lopinavir, Ritonavir, with or without the immune-system modulator interferon-beta-1a were part of trial.[2] WHO has cautioned physicians and medical associations against recommending or administering these unproven treatments until there is sufficient evidence?

'US Food and Drug Administration also have given recommendations for conducting clinical trials. The top most priority is participant's safety. It is essential to maintain compliance with good clinical practice, andminimize the anticipated risks that jeopardise trial integrity during the COVID-19 pandemic.'[3] One way to achieve this is by identifying the activities that place study participants at increased risk of COVID-19 due to study specific procedures. Trials should achieve timely recruitment, proper adherence to protocol-specified procedures along with ensuring participant's safety, high retention of participants, and proper statistical analyses to avoid undue loss of statistical power and increased risk of bias due to missing data.[3]

Various factors influence clinical trials. Patient-related issues include compliance with an intense study protocols and limitations of frequent visits to hospital because of lockdown in certain areas or movement restrictions to contain epidemic. Well organised infrastructure and management is required if there is involvement of multiple departments in clinical trial (i.e. need for radiological images and biopsy reports). Rapid administrative response, reorganisation of hospital management, and medical spaces and staff is required to prioritize COVID-19–infected patients. Cooperation and interdependence among various specialities is required to follow protocol procedures. There are increased safety concerns for participants in case they require some protocol-specific procedures for studies without violatingthe study protocol. Since this is a novel virus, more refinement of staff roles and study specific training of investigators may be required in clinical trials.[4]

The need of the hour is to develop new approaches like telehealth, home based testing. Innovating new ideas like courier pickup and delivery of samples. Participants can be followed up telephonically or by email or by requesting them to update data on electronic health portals.

Clinically, daily we are updating information about patient management and prognostic factors to recognize and treat high risk patients early in the course of the disease. Frontline workers are working hard to treat patients, identify certain markers that will help us improve clinical outcomes and educating and spreading knowledge. Hopefully very soon, various therapeutic trials will get completed and we get results about clinically effective therapeutic agents. As investigators and clinicians, there is an innate desire to find a cure that is effective in saving millions of patients and brings this pandemic to an end. We have learnt many lessons from past epidemics and we are utilising our previous knowledge to control COVID 19. Various measures like hand hygiene, social distancing and wearing a mask, temperature screening etc. have helped us slow down the spread of virus. With mutual support and encouragement we can move forward and focus on our goals to make clinical research better. The bright side is that we are evolving and making new innovations to advance our clinical research.

References

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