Experiences of dental clinical trials management under COVID-19 in China

Zheng Wang,[1,2] Ruiqi Chen,[1,2] Zhihong Liu[1,2] and Jinjun Liu*[3]

Key points

Dental hospitals are under strict nosocomial infection control during COVID-19 waves.

Execution of clinical trials in dental hospitals are encountering heightened difficulties.

This paper shows management measures of clinical trials in dental hospitals when under COVID-19 waves.

Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is responsible for the ongoing coronavirus disease 2019 (COVID-19) pandemic. Despite progress in pandemic prevention and control, it has always been a difficult task for China to pursue a 'zero COVID-19' strategy. Given the aerosol transmission of COVID-19 and the strict nosocomial infection control in dental hospitals, the execution of clinical trials in oral, dental and craniofacial research have encountered heightened difficulties. During this wave of the pandemic, the Institute of Clinical Trials in our hospital has continuously organised experts to discuss how to improve the management of clinical trials and we have made improvements in their management with the following principles: subject protection being our priority, humanised service being our pursuit and the quality of clinical trials being the cornerstone. Here, we share our experiences and current practices in clinical trial management with our peers worldwide, aiming to promote the management of clinical trials and contribute to the development of stomatology under the constraints of COVID-19 waves.

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a β-type coronavirus, which is responsible for the ongoing coronavirus disease 2019 (COVID-19) pandemic. The main modes of COVID-19 transmission are via droplets and direct contact with infected symptomatic patients or asymptomatic individuals.[1,2] With the delta variant, the Omicron-driven flare-up and the summer months, the status of pandemic prevention and control is complex and becoming grimmer.[3] As of April 2022, over 500 million confirmed cases and over six million deaths have been reported globally. China is still the only country holding fast to its goal of eliminating COVID-19. Despite that, the number of new COVID-19 cases and deaths have continued to decline. The policy of China remains challenging, even with the precise prevention and control which has already been implemented efficiently.[4,5]

A dental hospital is an institution that integrates examination, diagnosis and treatment. Owing to the use of ultrasonic and other specialised equipment used to treat dental patients, their saliva, blood and other body fluids can be distributed in the form of small diameter aerosol particles. These particles could be suspended in the air for an extended period of time. The inhalation of these particles induces cross-infection. Therefore, the task and pressure of nosocomial infection control are much more difficult in dental hospitals than in general hospitals.[6] In the early stages of the COVID-19 pandemic in China, outpatient services were closed and only the emergency departments were open in all types of dental hospitals.[6,7] Currently, the medical routine in China's dental hospitals has become more normal. However, dental hospitals have been kept under the harsh state of strict nosocomial infection control due to the successive waves of COVID-19.

During the pandemic worldwide, clinical trials suffered from long interruptions. Given this historical background, the performance and management of clinical trials in dental hospitals has become more difficult than ever before. It remains a neglected field. What is the status of clinical trials regarding dental and oral health in China? How can we ensure safe, efficient and smooth execution of clinical trials?

As the staff of the State Institute of Drug Clinical Trials, Hospital of Stomatology, Xi'an Jiaotong University, one leading tertiary dental hospital in Northwestern China, we would like to share our experiences and current practices regarding the management of clinical trials.

This article will primarily outline how we protect the interests of enrolled subjects, enhance the efficiency of ongoing trials and provide humanised service to clinical trial sponsors and clinical research associates (CRAs) in the context of the COVID-19 pandemic. Our aim is to promote the management of clinical trials and contribute to the development of stomatology.

[1]Key Laboratory of Shaanxi Province for Craniofacial Precision Medicine Research, College of Stomatology, Xi'an Jiaotong University, China; [2]State Institute of Drug Clinical Trial, Hospital of Stomatology, Xi'an Jiaotong University, China; [3]Department of Physiology and Pathophysiology, School of Basic Medical Sciences, Xi'an Jiaotong University, China.
*Correspondence to: Jinjun Liu
Email address: jupet.1128@mail.xjtu.edu.cn

Refereed Paper.
Submitted 30 January 2022
Revised 26 April 2022
Accepted 6 May 2022
https://doi.org/10.1038/s41415-022-5205-7

Experiences and current practices

Principle

Our measures (Fig. 1) comply with the direction of the Central Committee of the Chinese Communist Party and the Government. These measures follow the overall principles of the National Health and Health Commission's requirements for the prevention and control of major infectious diseases. These measures observe the directives of *Good clinical practice (2020)*,[8] *Good clinical practice for medical devices*,[9] *Consensus on clinical trial management under level 1 significant public health emergency response (infectious disease)*[10] and the Declaration of Helsinki.[11]

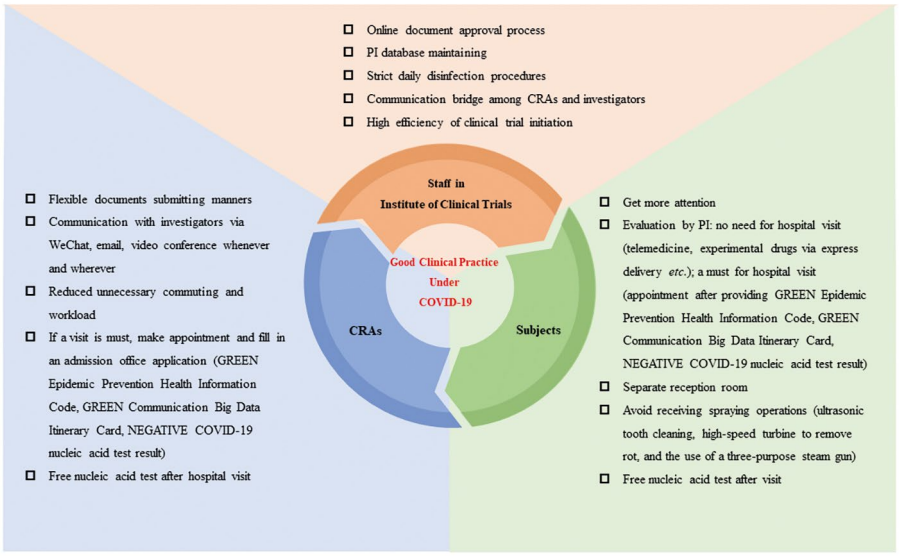

Fig. 1 Our experiences and current practices in clinical trial management under the COVID-19 pandemic. During the pandemic worldwide, clinical trials suffered from long interruptions. As the staff of the Institute of Clinical Trials of one leading tertiary dental hospital in Northwestern China, we would like to share our experiences and current practices regarding the management of clinical trials: subject protection is our priority, humanised service is our pursue and quality of clinical trials is our cornerstone

Subject protection is our priority

Currently, the pandemic risk level for each city or district (as a unit) has been constantly assessed by the Chinese Government. This is based on the Government's corresponding demographic and epidemiological evaluation regarding the aim of precise infection control and prevention. Nevertheless, partial lockdowns and restrictions on citizen movement exert negative effects on clinical trials. This is especially true for patient visits.

In our hospital these days, all enrolled patients receive more attention than usual because of the COVID-19 pandemic. The dental hospital is a relatively high-risk place of cross infection due to COVID-19. As a person's visit approaches, the principal investigator (PI) or subordinate investigator (Sub-I) will contact the subject and evaluate the necessity of a hospital visit. If the subject is enrolled in a clinical trial whose focus is oral fungal infection, recurrent aphthous ulcer, oral anti-anaerobic bacteria infection etc, a hospital visit is not necessary. The investigators will provide the subject with telemedicine and mail the experimental drugs according to the requirements of the clinical trial protocol. When this is complete, the investigators will record the visit in detail and save the document in the subject's case report form. Doing so can avoid the subject visiting the dental hospital. This can minimise the infection risk of enrolled subjects.

If the subject is enrolled in a clinical trial that must be performed in a hospital or the experimental drugs cannot be used outside the hospital, such as injections, the PI or Sub-I will assess the location and health status of the subject. They will decide if the subject can come to the hospital. First, the subject must provide their pandemic prevention health information code (Fig. 2a) and communication big data itinerary card (Fig. 2b), which are developed by the Chinese Government and built in WeChat, Alipay and other widely used apps in China. These e-card and e-codes can help determine the subject's exposure risk, travel history, relationship to carriers and duration of time in high-risk areas. If the code or card of the subject is yellow or even red, they not only cannot participate in clinical visits, but also need to go through at least 14 day of medical quarantine before they get 'green'. Only if the subject's code and card are green will the PI or Sub-I then arrange a specific time for the subject to visit the hospital. When the 'green' subject comes to our hospital at the appointed time, they must provide the negative result of a COVID-19 nucleic acid test which was performed within the last 48 hours. The person must also accept a temperature check before receiving medical treatment. To ensure the safety of all enrolled subjects, separate reception rooms are prepared in all departments to ensure that subjects complete the visit in a neutral diagnostic location during the pandemic period (Fig. 2c).

Moreover, if not a must, the use of aerosol generating procedures will be suspended during medical treatment, even when required by clinical trial protocols. If these treatments are a must, the subject will be asked to gargle with povidone iodine or cetylpyridinium chloride before the aforementioned procedures. Investigators will also wear high-grade protective clothing and protective masks (Fig. 3). After treatment, investigators will record the visit in detail.

We also instituted a green channel for nucleic acid testing for clinical trials by coordinating with other departments, such as the clinical laboratory and security department. All subjects, sponsors, CRAs, or anyone who is engaged in a clinical trial in our hospital, can take a free nucleic acid testing (Fig. 2d). This green channel is very convenient for individuals travelling to and from home, from other cities or maintaining their busy work schedules.

Humanised service is our pursuit

To initiate a new clinical trial, the sponsors and CRAs must often rush between the company's headquarters and the hospital for hospital selection. For ongoing clinical trials, CRAs often work in multiple hospitals in multiple cities to increase recruitment speed and enhance the quality of clinical trials. In this unique COVID-19 pandemic period, the characteristic of their work presents great risks to the prevention and control of nosocomial infections. To minimise the

Fig. 2 Strengthened protection for an enrolled subject. a) Pandemic prevention health information code. b) Communication big data itinerary card. c) Separate reception room for subjects enrolled in clinical trials. d) Tickets for free nucleic acid testing

hidden dangers of nosocomial infections and provide convenience to sponsors and CRAs, several measures have been taken.

First, the online document approval process was implemented in our hospital. In the past, CRAs sent paper documents to the Institute of Clinical Trials when there were revisions in informed consent, protocol deviation, or the appearance of severe adverse effects. Now, these documents can be submitted in a more flexible manner, which includes email and express delivery. When we receive the documents, we approve, reject, or ask for revisions immediately. In addition, during the pandemic period, several specially assigned staff are responsible to receive mailed drugs, instruments, documents and conduct strict disinfection procedures in accordance with the pandemic prevention regulations. This action ensures that no pandemic prevention mistakes occur and all ongoing clinical trials are conducted smoothly.

Second, WeChat chatting groups have been established. These groups enable the sponsor and CRAs to communicate with the staff in our hospital whenever and wherever necessary. This greatly facilitates the daily workload and reduces unnecessary commuting.

Third, we collected the curriculum vitae of PIs and established a 'PI database' in our hospital. After the sponsors or CRAs contact the Institute of Clinical Trials to indicate their intention to initiate research, our staff select the most appropriate PI from the database. The selection is based on the characteristics of the clinical trial and the PI is then recommended to sponsors and CRAs. Next, we help both parties communicate and reach their research intention through new media, such as WeChat, email, video conference etc. The establishment of the PI database establishes a bridge for rapid, non-physical communication among investigators, sponsors and CRAs and greatly reduces the inter-city travel of the sponsors and CRAs. It contributes to the implementation of the 'zero tolerance' COVID-19 prevention and control strategy in China.

If the sponsors or CRAs must come to our hospital for a visit, they are required to make an appointment with our staff and complete an admission office application form. This form contains the items they must manage, the status of their health code, the status of their itinerary code and the expected visit time, among others. According to the pandemic prevention policy of our province, these individuals must show nucleic acid test results sampled within 48 hours of their visit. After the visit, we can provide a free nucleic acid test for them so that they can return to a company in another city more conveniently.

Quality of clinical trials is our cornerstone

Electronic examinations and approvals were carried out in our hospital during the pandemic. This measure is conducive to the prevention and control of the pandemic and helps to reduce the travel burden for the sponsors and CRAs. However, there is often a time lag in the express delivery of paper-based documents. This causes difficulties in daily document management. The quality of clinical trials was the most important

Fig. 3 Enrolled subject under medical treatment. Doctor and nurse are in protective clothing and protective masks

factor. For this reason, our staff make efforts to overcome the heavy daily workload, strengthen the frequency of document self-examination of the agency and ethics office and ensure both pandemic prevention and the efficient process of clinical trials.

Conclusions

The pandemic is an ordeal; however, it is also a valuable opportunity. During this wave of the pandemic, the Institute of Clinical Trials in our hospital has continuously organised experts to discuss how to improve the management of clinical trials. Finally, we have made improvements to the following three aspects of clinical trials: subject protection being our priority; humanised service being our pursuit; and the quality of clinical trials being the cornerstone. We took this opportunity to significantly shorten the average duration of project approval, improve the efficiency of clinical trial project approval and strengthen the management of clinical trials. This not only ensures the smooth conduct of clinical trials and improves their management, but it also contributes to the cultivation of a rigorous, scientific and standardised medical team in our hospital.

Ethics declaration

The authors declare no conflicts of interest.

Written consent to publish was obtained for Figure 3.

Funding information

This work was supported by National Natural Science Foundation of China 82071670 and 81771616 (to Jinjun Liu).

Author contributions

Zheng Wang led on the first draft. Zheng Wang, Ruiqi Chen, Zhihong Liu and Jinjun Liu contributed to the high-efficient management of clinical trials during COVID-19, participated in the editing process and approved the final version.

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