

The Experiences of A University Hospital Medication Preparation Unit in COVID19-pandemic

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COVID-19 pandemic is a major public health issue that has influenced the world globally. Since dealing with coronavirus is a highly complicated process in itself, the pharmacy-based medication preparation process has gained much more importance in this extraordinary situation. Despite several guidelines that have released how to reconstitute COVID-19 specific medications (1,2,3), the hospitals are faced to set their own medication management process due to the lack of reliable drug and disease-specific knowledge. In terms of medication and patient safety, to establish a safe non-cytotoxic medication preparation process, to ensure continuity of well-educated and motivated pharmacy staff are the key elements of pharmacy-based medication preparation units. This work aimed to share our experiences about how to be challenged with the risk in the drug preparation process during the pandemic as a university hospital pharmacy centered non-cytotoxic medication preparation unit

THE GENERAL PRECAUTIONS

- ❖ Domestic and international travel restrictions have been conducted, and hospital staff has undergone 14-day self-isolation after returning from abroad to prevent the Covid-19 disease outbreak.
- ❖ The number of staff had decreased according to their working shifts. To prevent possible coronavirus exposure and burnout syndrome, the number of employees during these days has been reduced by 40 % - 45 % compared to normal working shifts. Although there is no illegal obstacle to their working conditions, disabled pharmacy staff were allowed to work at home in for their health safety
- ❖ Up-to-date announcements and rules followed which has released from the Hospital Infection Control Committee
- ❖ Use of paper, files, and stationary materials in the unit were limited
- ❖ Transferring the drug by a medication preparation unit staff, instead of sending them by drug delivery tubes
- ❖ Daily changing of the uniforms of the staff
- ❖ Weekly supply of the necessary personal protective equipment
- ❖ Alternative transportation organizations provided by the management for staff who had difficulties with the public transportation system while they were commuting from their home to work. Additionally, alternative accommodation opportunities had set for staff who were reluctant to stay with their home regarding coronavirus spread since they live with their children and senior family members

THE ROLE OF NON-CYTOTOXIC MEDICATION PREPARATION DEPARTMENT IN THE PRECAUTIONS THAT WERE TAKEN IN COMMON AREAS OF THE HOSPITAL DURING COVID-19 PANDEMIC

A. Social Distance

- ❖ Shift order was changed to minimize the presence of the staff at the same time period at the same unit
- ❖ By minimizing the number of personnel at a specific time period, the physical condition of the drug preparation room has been adjusted
- ❖ Sitting side by side of the two personnel at the laminar airflow cabinet has been prevented
- ❖ IV antibiotics were prepared in a sterile cabin whereas PCA, potassium chloride containing liquids were prepared in a hepa-filtered clean room in the aseptic drug preparation area to eliminate possible contamination risks

B. The Ventilation and Air Conditioning System

- ❖ No further adaptation was required as the drug preparation room has already air-conditioned by a hepa-filtered ventilation system
- ❖ The temperature and the humidity of the room were regularly monitored by an automated thermostat

C. The Cleaning, Disinfection processes, and the wastes in the drug preparation area

- ❖ Cleaning/disinfection processes were carried out by the characteristics of the drug preparation areas, using appropriate cleaning materials, besides, extra attention was paid especially to frequently touched areas
- ❖ Cleaning was done starting from the clean area towards the dirty area
- ❖ 1/10 diluted chlorine tablet was used to clean floor and surface disinfection and the contaminated areas
- ❖ Hand sanitizer suitable for desktop use with a push-button head was placed in the door entrances
- ❖ Hand hygiene was ensured by washing hands with soap and water for at least 20 seconds at every entrance to the room, before and after each operation or immediately after contact with the dirty area
- ❖ The entrance of the drug preparation unit of the personnel working at different departments was restricted
- ❖ The processes such as cabin cleaning and medicine filling, which were carried out by porters before the pandemic, were started to be carried out by the drug preparation staff
- ❖ Every material or medicine boxes and ampoules that entered the drug preparation unit were cleaned with Klercide 70/30 PA and placed in clear bags in front of the door by the porters. These materials were then taken from the door by the drug preparation staff and placed on their shelves in the drug preparation area
- ❖ The gloves, gowns, and medical masks used were thrown into the hospital pharmaceutical waste bin whereas the glasses were disinfected with 70% alcohol

D. The control of healthcare employees' and other personnel's health

- ❖ Fever, cough, cold, body aches, diarrhea, weakness, travel history, and COVID-19 patient contact were questioned daily, and the employee who observed or declared any symptoms was immediately referred to the occupational physician
- ❖ If not required, the traveling of the drug preparation unit staff was restricted
- ❖ All personnel in the unit were subjected to antibody tests twice by the hospital

E. Organizing Meeting / Training Activities

- ❖ Meetings with the managers, in-team meetings or trainings were provided with online the "Teams" application

THE ROLE OF NON-CYTOTOXIC MEDICATION PREPARATION TEAM IN THE TREATMENT PROTOCOL FOR THE PATIENTS DIAGNOSED WITH COVID19

- ❖ Crushed & divided medications, concentrated electrolytes, heparin solutions, PCA solutions, port, and arterial wash solutions, parenteral drug doses of pediatric patients, and contemporaneous drugs continued to be prepared in the ready to administration team of our pharmacy. The preparation of solid oral dosages, which should be administered to intubated Covid-19 patients through a nasogastric tube or PEG, was prepared by the ready to administration team of our pharmacy.
- ❖ There is no evidence-based data on the bioavailability of these enteric-coated tablets after being crushed and administered to these vulnerable patients. The biggest challenge was lack of the reliable medication information sources. Before starting the Covid-19 medications preparation process, possible risks that could arise if crushed administration of these drugs were evaluated with a multidisciplinary team.
- ❖ Strict measures were taken to control the number of patient-specific medicines provided by the district health directorate according to epicrisis of the patients and the doctor directives
- ❖ If a dose adjustment is necessary, or if there are tablets to be pulverized, a follow-up card was issued for these patients according to instructions
- ❖ The patient's name, protocol number, and the name of the drug physically taken were noted, photographed and shared within a social messaging group that includes not only the drug preparation unit staff but also the managers. In addition, separate drug delivery forms were kept for these drugs
- ❖ For prepared-sent drugs, the date, patient information (the floor where the patient stays, the name and the dose of the drug, and the time for the drug to be administered), and the name of the porter who carried the drug were noted on the delivery form.

THE DRUGS INCLUDED IN THE PROTOCOL AND PREPARED IN THE DRUG PREPARATION

A. Preparation of Lopinavir/Ritonavir (®Kaletra 200 mg / 50 mg film coated tablet)

In line with the statement published by the General Directorate of Public Hospitals, Hospital Pharmacy Management in March-2020 (4); Kaletra should be swallowed whole by the patient and not be chewed, broken or crushed. For patients who cannot be applied Kaletra 200 Mg / 50 Mg Film-Coated Tablets orally for various reasons, these tablets should be prepared to be administered in liquid form in the medicine preparation areas with personal protective equipment.

Recommended Kaletra preparation protocol

- ❖ Tablets are grinded in a mortar to pulverize, the dose is weighed and poured into a syringe(A) following the removal of the plunger of the syringe
- ❖ The plunger is put back in place and pushed to the last point without squeezing the pulverized drug
- ❖ The luer-lock cap is attached to the syringe tip and the syringe is labelled
- ❖ 20ml of the dispersion solution containing 1% carboxymethylcellulose or equivalent was drawn into another syringe(B) and a luer-lock cap is attached
- ❖ Syringe A and syringe B were then connected to each other using a female-female luer-lock connection C
- ❖ The content in in syringe B is transferred into syringe A pushing forward and backward of the plungers of the syringes for several times until the pulverized drug is completely dissolved
- ❖ If any residual dust particles in the syringe is observed, it is washed with the glucose solution to be administered to the patient (Figure 1)



Figure 1. Recommended preparation method with a female-female connection

The protocol we have used to prepare Kaletra

- ❖ Tablets were pulverized by a sterile hood in the drug grinding machine
- ❖ The pulverized tablets were then poured into a **lavage syringe*** following the removal of the plunger of the syringe
- ❖ In a **perfuser syringe**, approximately 10-12ml of 20% **dextrose** ‡ was drawn and and two syringe tips were connected to each other using a **3 way infusion manifold**^
- ❖ The contents were mixed pushing plungers forward and backward till the pulverized drug was completely dissolved
- ❖ The final mixture was adjusted to 20% dextrose/20ml in the **lavage syringe** and the lavage syringe cap was attached to the tip of the syringe

‡ As Kaletra suspension supplied from abroad contains dextrose, we suspended the kaletra with dextrose during the preparation phase.

* We preferred the lavage syringe not only for its compatibility with 3-way infusion manifold but also for IV administration risk elimination through ensuring patient and drug safety by preventing the risk of intravenous administration of the diluted suspended drug we have prepared. (Figure 2)

^ However, when we used a 3-way infusion manifold the strain during pushing and easy disconnection of the joints thus the risk of dose loss were the disadvantages. (Figure 2)

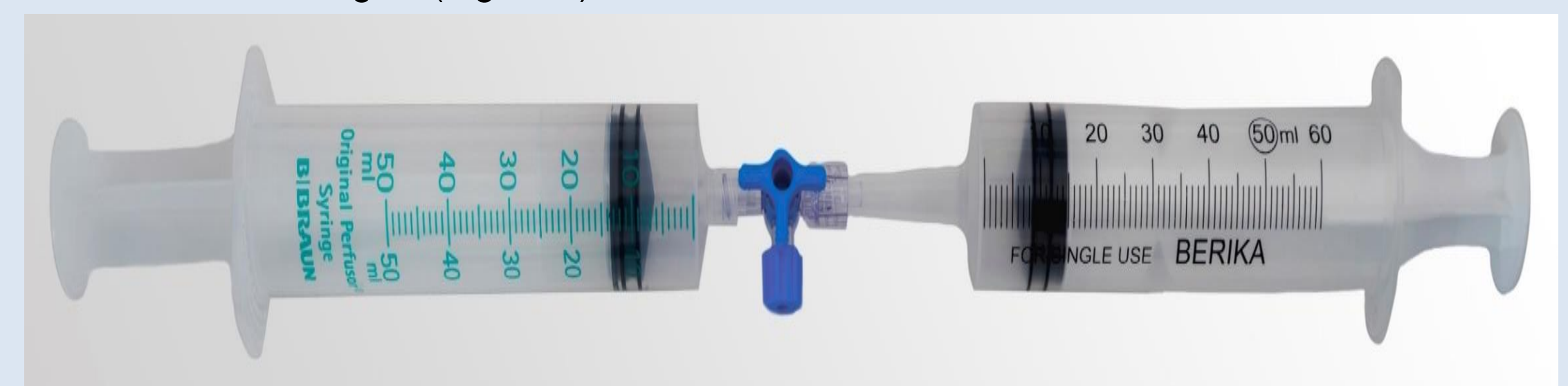


Figure 2. The applied preparation method with a 3 way infusion manifold

B. Preparation of Hydroxychloroquine sulfate (®Plaquenil), Favipiravir and Plaquenil + Simple Syrup Mixture

- ❖ In case of Plaquenil and Favipiravir preparation, the drug was pulverized with a sterile tablet grinding machine, labeled according to our hospital procedures and transferred to the floor where the patient stays
- ❖ Plaquenil suspension was prepared for our pediatric patients who cannot swallow tablets or who have difficulty in swallowing.
- ❖ The desired dose of medicine is pulverized and mixed with simple syrup as directed by the doctor.
- ❖ Before mixing with simple syrup, the pulverized tablet is homogenized with 2 ml of water for injection. It is labeled according to the procedures of our hospital and transferred to the floor.

C. Preparation of IV drugs- Tocilizumab (®Actemra)

- ❖ After the Actemra directive has been approved, the order was delivered to the drug preparation unit and each Actemra 400 mg / 20 ml vial of SF was prepared in 100 ml.
- ❖ Since Actemra is a new generation drug, no clear information was found about the use of protective equipment during the preparation process. For this reason, full equipment (sterile gowns, goggles, masks, caps, nitrile gloves) was worn.
- ❖ The drug was prepared with solid asepsis under the laminar airflow cabinet and delivered to the floor where the patient stay.

To sum up, the two pillars of dealing with the COVID-19 epidemic, which has affected the whole globally, are the proper preparation of the necessary medicines for treatment and the treatment itself. Drugs were prepared in line with the search for "a practical solution immediately" and the directives of the Ministry of Health and successfully administered to the patients. Our study is noteworthy as it shows that drugs can be prepared not only by the default ways but also by the different methods.

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