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CURRENT EVENTS

The role of the critical care pharmacist during the COVID-19 pandemic

Les missions du pharmacien clinicien en soins critiques pendant la pandémie COVID-19

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HIGHLIGHTS

- The COPIL allowed the restructuring of the ICU in record time to double its capacity.
- The CCP, integrated in the COPIL and already a member of the ICU team for a few years, provided an essential link between the ICU and the pharmacy during the COVID-19 pandemic.
- The CCP implemented actions to avoid health products shortages, to secure practices and played a key role in the critical analysis of emerging published data in COVID-19 potential treatments.

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Summary On January 4 2020, the World Health Organization (WHO) reported the emergence of a cluster of pneumonia cases in Wuhan, China due to a new coronavirus, the SARS-CoV-2. A few weeks later, hospitals had to put in place a series of drastic measures to deal with the massive influx of suspected COVID-19 (COronaroVIrus Disease) patients while securing regular patient care, in particular in the intensive care units (ICU). Since March 12th, 77 of the 685 COVID-19 patients admitted to our hospital required hospitalization in the ICU. What are the roles and the added-value of the critical care pharmacist during this period? His missions have evolved although they have remained focused on providing health services for the patients. Indeed, integrated into a steering committee created to organize the crisis in the intensive care units, the role of the clinical pharmacist was focused on the organization and coordination between ICU and the pharmacy, the implementation of actions to secure practices, to train new professionals and the adaptation of therapeutic strategies. He participated to literature monitoring and increased his involvement in the clinical research team. He provided a link between the ICU and the pharmacy thanks to his knowledges of practices and needs.

MOTS CLÉS
Pharmacie clinique ;
Pharmacien clinicien en soin critique ;
Pandémie COVID-19 ;
SARS-CoV2 ;
Réanimation

Résumé Le 4 janvier 2020, l'Organisation mondiale de la santé (OMS) a signalé l'émergence d'un cluster de cas de pneumonie à Wuhan, en Chine, due à un nouveau coronavirus, le SRAS-CoV-2. Quelques semaines plus tard, les hôpitaux ont dû mettre en place une série de mesures drastiques pour faire face à un afflux massif de patients suspects COVID-19 (COronaroVIrus Disease) tout en sécurisant les prises en charge, en particulier dans les unités de soin critique. Depuis le 12 mars, 77 des 685 patients COVID-19 admis dans notre hôpital, ont relevé d'une prise en charge spécialisée en soins critiques. Quels sont les rôles et les valeurs ajoutées du pharmacien clinicien en réanimation pendant cette période ? Ses missions ont évolué même si elles sont restées axées sur la promotion des services de santé aux patients. En effet, intégré au sein d'un comité de pilotage créé pour organiser la crise au niveau des unités de soin critique, le rôle du pharmacien clinicien était axé sur l'organisation et la coordination entre ces unités et le service pharmacie, la mise en œuvre d'actions visant à sécuriser les pratiques et former de nouveaux professionnels et l'adaptation des stratégies thérapeutiques. Il a participé à la veille bibliographique et renforcé son implication dans l'équipe de recherche clinique. Le pharmacien clinicien permet de faire le lien entre les unités de soin critique et la pharmacie dont il connaît les pratiques et besoins.

Critical care pharmacist in routine practice

The ICU is an unusual environment to practice pharmacy at the patient's bedside: prescriptions are complex; many patients have multiple organ failures, are in unstable and critical conditions and require specialized expertise. Polypharmacy is common, causing frequent drug interactions and side effects. The added-value of a critical care pharmacist (CCP), a practice which remains rare in France, has been described as: decreasing the rate of medication errors (66%), reducing costs, and decreasing the length of hospital stay and mortality [1—5]. In our center, seven fulltime equivalent (FTE) pharmacists work as clinical pharmacists in a healthcare service including 1,5 CCP FTEs (one FTE in ICU and 0.5 FTE in critical care research). The CCP takes part in medical visits and analyzes prescriptions suggests drug forms, infusion modifications, dosing adjustments, pharmacokinetic optimization and advises on drug incompatibilities [6]. He ensures the safety of computerized prescriptions, develops protocols and audits, teaches health professionals, contributes to improve practices, and performs medico-economic evaluations [7]. He also plays an active role in the clinical research team and manages the ICU drug supply chain. A pharmacy technician, from the hospital pharmacy, manages every day the drugs (Pyxis Medstation ES® secure cupboard), medical devices, intravenous fluids, dialysis solutions and nutrition storage. This organization ensures streamlined practices, secures the drug supply chain and allows nurses to spend more time on patient bedside care. The CCP regularly reassesses the supply chain, trains newcomers and intervenes on request in case of lack of supply or traceability. A multidisciplinary approach is crucial to provide optimal care in ICUs and physicians have reported

that involvement of a CCP increases their pharmaceutical knowledges [8—10].

Critical care pharmacist role during the COVID-19 pandemic

Integration in a steering committee

At the beginning of the pandemic, the emergency and intensive care departments set up a steering committee (COmité de PILotage: COPIL), a multidisciplinary working group involving intensivists, anesthetists, paramedical staff, an administrative manager and a CCP as recommended in a recent French paper [11]. COPIL met twice a day and made decisions based on patient flows and availability of human and material resources. Some points raised during the COPIL were transmitted to the institutional crisis unit for further discussion and decisions at a hospital level. The CCP participated in each COPIL and gave advice on health product management between the ICU and the pharmacy.

Critical care pharmacist as a health product coordinator

Of the original 20 ICU beds before the crisis, nine were retained for routine non-COVID patients and we added a further 21 beds for COVID patients giving a total capacity of 41 beds: 32 COVID and nine non-COVID. The storage sites were shared between the two units. The CCP played a key role in coordinating health product supply as reported by the pharmacy staff and the needs of the ICU teams in terms of therapeutic provision or ergonomic storage. He was responsible for checking that the beds complied with ICU requirements, organizing the pharmacy and hygiene teams, ensuring clear and safe access to drugs and medical devices, and prevention of cross-contamination. The addition of any new drug (e.g., albumin or some antibiotics) or stock modifications (of opioids, neuromuscular blocking agents, hypnotics, vasopressors, nitric oxide) and supply chain were evaluated by a pharmacist/CCP binomial. The CCP, expert on ICU practices, advised the pharmacist in his purchase orders in relation to unusual posology for certain therapeutics (sedation, neuromuscular blocking agents, heparin) and to the ICU-beds occupancy. All the processes were approved by the ICU managers.

Critical care pharmacist as a central actor of health product strategies

A major challenge during COVID-19 was to ensure availability of ''equipment'' to provide optimal and safe patient care:

- the CCP partnered with the sterilization department to carry out numerous tests to evaluate the feasibility of single-use equipment sterilization (personal protective equipment or exhalation valves in mechanical ventilators);
- in parallel, the pharmacy control laboratory introduced control parameters for expired masks by equipping them with a particle counting device;
- alternative administration methods for anti-infectives were considered without active systems [12];
- the CCP participated in management of sterile medical devices and strategies, in particular for closed-system endotracheal suctioning and hydrophilic/hydrophobic filters, not only to ensure optimal ''intra-muros'' stocks but also to support other hospitals in need.

The CCP also led a project to adapt therapeutic strategies after an alert concerning the storage of sedatives and neuromuscular blocking agents, by tracking consumption with data extraction software thereby defining the minimum and maximum storage thresholds (+25% at the height of the crisis). The dosages of all neuromuscular blocking agents and their position in the ICU strategy were studied with the anesthetists and entered into a computer-based patient record called Cerner®. To avoid shortages of critical drugs, the anesthetists drastically reduced their use of propofol which they replaced with loco-regional anesthesia and other anesthetic drugs such as ketamine. For the same reason, rocuronium was preferred over cisatracurium besilate (usually used in ICUs). On the other hand, the pharmacy provided pre-prepared syringes of cisatracurium besilate with the regular doses based on data software extraction, to avoid preparation errors and again to reduce the nurses' workload. To reduce the number of times the nurses had to enter patients' rooms to top up the electronic syringe pumps and to avoid the shortage of propofol, it was replaced by a sufentanil/midazolam mixture at double concentration (10 μg/mL, 2 mg/mL, respectively). Likewise, the AnaConDa® system—an innovative technique for non-intravenous analgesia used in ICUs by a few experienced teams—was implemented to deliver halogenated gases into the respiratory system [13]. This latter project was funded by the Fondation de France following a response to a call for projects.

Critical care pharmacist as a health product expert focused on patient safety

Outside of a major health crisis, the risk of errors or incidents in the ICU concerns around 15% to 20% of patients and is mainly related to drug administration [14]. Some series report as many as two errors per patient per day, resulting in 45-92% of declared AEs and potentially life-threatening in 11% of cases [14—16]. AEs are common in the ICU due to the complexity of pathologies, the intensity of care provided, the vulnerability of patients and the number of drug treatments administered [17]. During the COVID-19 crisis, other factors were associated: extreme workload and probably less experienced teams coming from different services (voluntary anesthetists and paramedical teams from other departments or private establishments) [18]. The CCP played an important role to limit medication errors identifying high-risk drugs, securing delocalized drug storages, ensuring good use of health products and implementation of medication error analysis from experience feedback or electronic prescriptions. The following tasks were accomplished:

- the CCP created a folder of the protocols set up in the computer tool and recorded a computerized management documentary for each newcomer;

- nutrition, heparin or sedation protocols were distributed to each nurse as well as standard dilutions of drugs and main anti-infectives (beta-lactam antibiotics,...);
- ICU protocols were distributed to the anesthetists and explained by the CCP;
- a COVID-19 intubation protocol devised by an anesthetist was reviewed by the CCP to emphasize certain specificities related to COVID-19 (e.g., machine and patient filters [19]);
- an intubation kit was created in Pyxis® for nurses less accustomed to the Pyxis Medstation® ES;
- ''Missing'' protocols for standard ICU procedures were provided for mobilized nurses;
- the CCP provided advice to intensivists and anesthetists on specific requests (use of argatroban and neuroleptics, analysis of drug interactions ...).

Critical care pharmacist as an actor for literature monitoring and therapeutic strategy.

The CCP was involved in critical analysis of emerging published data of potential COVID-19 treatments. This crucial, time-consuming activity ensured that potential treatments were analyzed taking into account pharmacodynamics and pharmacokinetics, exploring optimal dosing regimens, considering risks and side effects (particularly important when drugs are used in an unusual context), and keeping in mind ethical principles. A multidisciplinary group, independent of the COPIL, including the CCP, was created to focus on COVID-19 therapeutic approaches and to work on institutional guidelines [20]. No consensus could be reached on therapeutic strategy whereas inclusion of patients into clinical trials was unanimous approved but hardly to access for non-university hospitals. Faced with an excessive number of critically ill patients, the COPIL, with the support of infectious disease specialists, decided to treat some critically ill patients with hydroxychloroquine after assessing their comorbidities and clinical aspects. The patients treated with hydroxychloroquine underwent strict continuous cardiac monitoring and repeated ECGs to detect any potential cardiac side effects. The cardiotoxic effects of hydroxychloroquine were known to be cumulatively dose dependent, typically occurring after a median of 7 years of treatment [21]. However, early cardiotoxicity was observed in this off-label use in a specific population in a context of emerging knowledge about SARS-CoV2 related cardiac disorders. These new data about pathophysiology, a lack of significant therapeutic effect, and pharmacovigilance issues raised by the CCP, led the COPIL to stop using hydroxychloroquine and to focus on immunomodulators based on data emerging from clinical research. Furthermore, a specific thromboprophylaxis protocol was implemented following a literature review by the CCP [22].

Overall, the CCP played an essential role in reviewing and interpreting information for their clinical colleagues who were under considerable pressure dealing with increased patient volumes and with limited time to read and evaluate new data as they were published. While enthusiasm for any drug that could aid in this disease was understandably high, it was important to take an appropriately critical approach in evaluating the risk/benefit ratios, particularly given that there were no randomized controlled trials demonstrating the efficacy of any agent for the treatment of COVID-19.

Critical care pharmacist and clinical trials

Although all ongoing clinical trials were suspended during the crisis, the COPIL integrated the ICU into seven clinical trials. As a member of the clinical research team, the CCP contacted clinical trial promotion teams and took part in feasibility studies. He helped to determine patient eligibility, to assure protocol follow-up and patient safety establishing computerized protocols including drugs and biological examinations. With the haemobiologist, he developed one clinical trial using thrombin generation assay and another focusing on antiplatelets to treat critically ill COVID-19 patients (high platelet activity in the SARS-CoV2 inducing coagulopathy). Other projects are in process. However, some of these projects may be compromised with the pandemic evolution.

Discussion—Conclusion

The role of the CCP has evolved during the COVID-19 pandemic with new institutional responsibilities, ICU and pharmacy coordination, implementation of actions to secure practices, training of new professionals called in reinforcement, monitoring literature and clinical research initiatives and finally devising new therapeutic strategies (sedation or neuromuscular blocking strategies). Some strategies can be reactivated if necessary (double concentration mixture sufentanil/midazolam or pre-prepared syringes of cisatracurium besilate). Others are now routine practice such as the Anaconda® inhaled sedation strategy. In addition to health product availability, another challenge was to mobilize as many relevant healthcare professionals as possible, including the CCP, to support the critical care practitioners in managing their severe COVID-19 patients [23]. Although the CCP is accustomed to the rhythm of working in an ICU, the extra workload during the pandemic to ensure optimal patient care along with the twice daily COPIL meetings, was untenable in the long term. It was clear that we were understaffed in our hospital as a team: the two CCPs were unable to attend the daily medical visits and only intervened for medication management on request of the clinical staff. Unfortunately, we lacked the resources to reinforce our team with back-up from other pharmacists [24]. Nevertheless, the CCP was proud to have been a key actor, at both an ICU department and institutional level, and to have served our ICU patients as efficiently as possible during the pandemic. Overall, and especially during this unprecedented public health crisis, the CCP is placing itself as an expert in health products whose missions are only made possible by flawless coordination between the ICU and the pharmacy. This tight network is the vector for optimal management of health products which was a major challenge during this period.

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Disclosure of interest

The authors declare that they have no competing interest.

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