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Hospital Pharmacy in the multidisciplinary team of COVID inpatient units

La farmacia hospitalaria en el equipo multidisciplinar de las unidades COVID de hospitalización

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Abstract

Since the implementation of the Antimicrobial Stewardship Programs, hospital pharmacy specialists have collaborated with infectious disease specialists on a regular basis in most hospitals in Spain. Cooperation between these professionals ensures the integrated management of patients with infectious diseases and the appropriate use of antimicrobials in hospitals.

The COVID-19 pandemic forced hospital pharmacists to abruptly suspend all their structured activities and concentrate on the health crisis. Real-time information sharing between different medicine specialties is an effective strategy to generate and maintain treatment protocols adapted to each center, with continuous evidence-based modifications as new publications appear.

Hospital pharmacies had to reorganize their activities to respond to the pandemic. On the one side were patients with COVID-19, and on the other were routine hospital pharmacy tasks, with the added difficulty of adapting to individual protection measures. New communication and collaboration strategies were adopted. Protocols were established for the management of COVID-19 patients, with continuous changes; special medications had to be prepared and distributed; circuits were designed for the home- or institution-based care of patients; internal circuits were created to minimize the movements of hospital staff and professionals caring for COVID-19 patients.

The most effective antiviral drug and anti-inflammatory therapy remains elusive. In this scenario, hospital pharmacists emerge as a key player, as they have a deep understanding of the mechanisms of action of drugs

Resumen

La colaboración entre los especialistas en farmacia hospitalaria y enfermedades infecciosas está implantada en la mayoría de los hospitales españoles desde 2012, a raíz de los Programas de Optimización de Antibióticos. Los objetivos principales de esta colaboración son el abordaje integral de los pacientes con enfermedades infecciosas y el uso adecuado de los antimicrobianos en el hospital.

Las actividades estructuradas y organizadas que los farmacéuticos tenían dentro de los grupos se vieron truncadas por la pandemia por SARS-CoV-2, que requirió una alta dedicación. El intercambio de información en tiempo real entre las especialidades ha sido una vía efectiva para generar y mantener protocolos de tratamiento adaptados a cada centro, con continuas modificaciones basadas en las publicaciones que iban apareciendo.

Los servicios de farmacia se tuvieron que reorganizar para dar respuesta, por un lado, a los pacientes que ingresaban por esta infección, y por otro, para continuar con las actividades anteriores, con las dificultades añadidas que exigían las normativas para la protección del personal sanitario. Hubo que reinventarse para establecer otros sistemas de comunicación y de colaboración, protocolizando el tratamiento farmacológico de estos pacientes, con modificaciones continuas, gestión de medicamentos a través de medicamentos en situaciones especiales, diseño de circuitos para tratar a pacientes en su domicilio y en centros sociosanitarios y modificación de circuitos internos para minimizar los desplazamientos de los profesionales en el hospital, así como del personal que atendía a pacientes con SARS-CoV-2.

KEYWORDS

Hospital Pharmacy Service; COVID-19; Infectious disease; Multidisciplinary team.

PALABRAS CLAVE

Servicio de farmacia hospitalaria; COVID-19; Enfermedades infecciosas; Equipo multidisciplinar.



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and potential interactions. In a setting where experimental drugs preferably tested in clinical trials are being used, the role of hospital pharmacists in interdisciplinary teams has become essential for the optimization of clinical outcomes.

Introduction

The first articles on the relevance of mutual collaboration between hospital pharmacy and infectious disease specialists were published in USA in the 90's¹. In Spain, although there were some significant previous experiences, integration was not massive until 2012, when several scientific societies issued a consensus document on the Antimicrobial Stewardship Programs (ASP), where the role of hospital pharmacists in ASP teams was considered essential². As of today, this program has been implemented in most hospitals of the country.

The objectives of the pharmacists integrated in infectious disease teams include collaborating in the comprehensive approach to patients with infectious diseases, and contributing to the adequate use of antimicrobials in hospitals. To accomplish the first objective, hospital pharmacists take part in decision making on antimicrobial therapies, analyze drug-to-drug interactions, alert on possible allergies, calculate doses based on PK-PD parameters, monitor drug pharmacokinetics, and participate in bedside evaluation of patients. The tasks of hospital pharmacists in relation to the second objective are defined by hospital global strategies and include assessing the quality of antimicrobial use and prescription, taking part in the selection of antimicrobials, and implementing specific strategies to reduce the inadequate use of antimicrobials in different areas of the hospital.

When the SARS-CoV-2 pandemic started to spread beyond Europe, a review was performed of the evidence available on potential antiviral therapies, with few results. We initially retrieved information from previous studies on other types of coronavirus (SARS-CoV-1 and MERS), as they share a similar genetic structure. As a result, some drugs that had never been tested in humans to treat these infections postulated as potential therapeutic candidates. As usual, we investigated the biological mechanisms that would support the efficacy of these therapies³. Remdesivir emerged as the potentially most effective antiviral, although it had only been used for ebola. Arrangements were made for the procurement of this agent, but it was not available and could not be processed as a medication for special situations. Therefore, the only drugs available were lopinavir/r, interferon beta 1b and interferon alfa, although there was no evidence supporting their use in patients with COVID-19 infection⁴.

Separate admittance flowcharts were established for COVID-19 patients and isolation measures and possible treatments were adopted. However, health professionals in Western countries could not understand how an unknown virus that had caused the outbreak of a respiratory disease in a distant city of Asia could have jeopardized our modern, advanced and technological society and placed the humanity in a critical situation as the plague or the 1918 Spanish flu did. The high infectivity and rapid spread of SARS-CoV-2 caused such an avalanche of patients that health services collapsed across the country. We were not prepared to face this change, which caused chaos and forced us to improvise.

Real-time information sharing has been an effective way to contain panic and guide clinicians and epidemiologists in planning the management of the pandemic. The most prestigious journals started to publish the experiences of professionals with the disease. The lack of information and urgent need for evidence that supported therapeutic strategies led editors of high-impact journals to adopt less strict criteria for publication. As a result, numerous suboptimal-quality articles that showed inconsistent results were published, with a high impact on the treatment of SARS-CoV-2. Local treatment protocols were continuously modified based on the publications released, incorporating combinations of antivirals and antimicrobials, which were demonstrated later to be ineffective: what was good yesterday has become useless today⁵. The need to treat patients

A día de hoy, se desconoce el mejor fármaco antiviral y el mejor tratamiento antiinflamatorio, pero la colaboración del farmacéutico hospitalario es fundamental, pues dispone del conocimiento de los mecanismos de acción de fármacos tan diferentes y de las interacciones que pueden ocasionar. La urgente necesidad de utilizar fármacos experimentales, preferiblemente dentro de ensayos clínicos, coloca al farmacéutico en un papel clave dentro del equipo interdisciplinario imprescindible para conseguir los mejores resultados.

whose state worsened rapidly driving them to the Unit of Critical Care and death hindered the development of well-designed clinical trials that could have helped find the best treatment for SARS-CoV-2. Consequently, 16,507 publications have been indexed in PubMed since January 2020 versus only 11 clinical trials.

Strategies adopted

The well-structured, organized activity of pharmacists and ASP in infectious disease teams were disrupted by the pandemic. Hospital pharmacies had to reorganize to respond to the pandemic. On the one side were patients with COVID-19, and on the other were routine hospital pharmacy tasks, with the added difficulty of adapting to individual protection measures. New communication and collaboration systems were implemented to face the situation.

At the beginning of the pandemic, the first step was to establish a standard protocol for the pharmacologic management of patients. This protocol was initially based on the protocol published by the Ministry of Health, which indicated the patients who needed treatment, the treatments to be used, the way they were administered, their associated contraindications and main adverse reactions, and drug-to-drug interactions. As these protocols were constantly modified, updates were incorporated to the electronic prescription system. The medications included in these protocols (lopinavir/r, hydroxychloroquine, azithromycin) were associated with a high rate of drug-to-drug interactions, which were encoded in the electronic prescription system. This way, when a treatment with a moderate-severe interaction was prescribed, an alert popped up. To reduce movement of professionals within the hospital, all medications were available in automatic drug dispensers and stocks were increased to prevent that pharmacy staff had to go to SARS-CoV-2 wards.

This way, access to intensive care boxes was minimized. To such purpose, posology was adapted for medications to be administered once or twice daily, and antimicrobials were administered by continuous infusion wherever possible (beta-lactams and vancomycin).

Other problems we faced but never imagined was that there was a shortage of the drugs which were progressively incorporated to treatment protocols. Procurement was performed individually, which required an intensive use of human and technical resources for many weeks. For this reason, we set up a central registry of individualized orders for a more effective supervision.

As the pandemic continued to evolve and more information was published on this infection, an outpatient regimen for the early treatment of patients with mild COVID-19 infection was established. Treatment kits were delivered to asymptomatic relatives in the ER to avoid the visits of the patients to the hospital. A medication delivery system was created to send drugs to nursing homes, which were fitted with medical equipment.

We have learned that the course of this disease is divided into two clearly differentiated stages⁶: the first stage starts with the rapid replication of the virus in the respiratory tract. At this stage, antivirals will probably play a crucial role; in the second stage, host immunologic response to the pulmonary disease caused by the virus ("cytokine storm") stimulates disease progression. At this stage, medications to control hyperinflammatory response are the cornerstone of treatment. Recent studies demonstrate the impact of thrombotic and ischemic events on the prognosis of COVID-19 infection and highlight the importance of an adequate anticoagulation therapy⁷. Ventilatory support and the treatment of nosocomial infections in intensive care units have been crucial to the improvement of patients with severe COVID-19 infection.

Lessons learned. Future applicability in pharmacy services

The most effective antiviral and anti-inflammatory therapies still remain elusive, as does the way these therapies must be combined at each stage of the disease.

Nevertheless, it is reasonable to think that outcomes will improve if the viral load in the airways is reduced before a hyperinflammatory response occurs. The role of hospital pharmacists is essential, as they have a deep understanding of the mechanisms of action and interactions of medications. The urgent need to use experimental drugs preferably being tested in ongoing clinical trials gives the hospital pharmacist a

key role in interdisciplinary teams, which is essential to the optimization of outcomes⁸.

As long as an effective treatment is not available, prevention emerges as the cornerstone for the control of the disease. Lockdown, social distancing, hand washing, and the use of masks have been effective in containing the pandemic until a vaccine is discovered. However, SARS-CoV-2 differentiates from other types of coronavirus by its ability to replicate in the airways of asymptomatic individuals or in the preclinical stage of the disease, which facilitates asymptomatic transmission⁹. This is the true "Achilles heel" that hinders the control of the pandemic. New strategies will be necessary for the identification and isolation of new cases and the minimization of nosocomial infection.

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