



ORIGINALS

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Centralization of the methadone maintenance plan in a hospital pharmacy department in the Community of Madrid

Centralización del plan de mantenimiento con metadona en un servicio de farmacia hospitalaria en la Comunidad de Madrid

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Abstract

In February 2018, Resolution 189/2018 was published in the Autonomous Community of Madrid with the objective of centralizing the procedure for the acquisition, preparation, distribution, and dispensing of methadone to Centres for the Comprehensive Care of Drug Addiction Patients within the Madrid Health Service under the responsibility of a Hospital Pharmacy Service.

The Hospital Pharmacy Service began this activity in March 2018. This is the first time that the comprehensive management of a methadone maintenance plan has been centralized in an Hospital Pharmacy Service for the care of drug-dependent patients in the Autonomous Community of Madrid.

At the beginning of the Project, the previous workflow was analysed, the pharmaceutical laboratory was adapted, and the methadone acquisition procedure was designed. A communication channel with the Centres for the Comprehensive Care of Drug Addiction Patients was implemented and application forms were designed. Corresponding control procedures were established given that the medication under consideration was a narcotic.

Standard procedures for the acquisition of methadone, of containers for personalized dosing in Centres for the Comprehensive Care of Drug

Resumen

En febrero de 2018 se publicó en la Comunidad de Madrid la Resolución 189/2018 con el objetivo de centralizar el procedimiento de adquisición, elaboración, distribución y dispensación de metadona a los Centros de Atención Integral a Drogodependientes del Servicio Madrileño de Salud bajo la responsabilidad de un servicio de farmacia hospitalaria.

El servicio de farmacia hospitalaria inició esta actividad en marzo de 2018, siendo la primera vez que se centraliza en un servicio de farmacia hospitalaria la gestión integral del plan de mantenimiento con metadona para la atención de pacientes drogodependientes en la Comunidad de Madrid.

Al inicio del proyecto se analizó el circuito anterior, se adaptó el laboratorio de farmacotecnia y se diseñó el procedimiento de adquisición de metadona. Se implementó una vía de comunicación con los Centros de Atención Integral a Drogodependientes, diseñándose formularios de solicitud y se establecieron los correspondientes procedimientos de control derivados de su naturaleza estupefaciente.

Se han diseñado y adjudicado, cumpliendo la Ley de Contratos de la Administración Pública, procedimientos normalizados para la adquisición

KEYWORDS

Methadone; Opiate substitution treatment; Opiate alkaloids; Heroin dependence; Pharmaceutical preparations; Pharmacy service hospital; Patient safety.

PALABRAS CLAVE

Metadona; Tratamiento de sustitución de opiáceos; Alcaloides opiáceos; Dependencia de heroína; Preparaciones farmacéuticas; Servicio de farmacia en hospital; Seguridad del paciente.



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Addiction Patients, and transport routes were designed and contracted out through public tender in compliance with the Public Administration Contract Law. A tender has also been awarded for the implementation of a computerized management system and automated dispensing systems, which are currently undergoing installation.

The pharmacotherapeutic protocol of the Methadone Maintenance Plan of the Autonomous Community of Madrid is also being updated.

Over 18 months, 5,300 L of methadone solution have been prepared and 2,844 individual prescriptions have been dispensed.

High levels of perceived satisfaction were reported via a questionnaire administered to the Centre for the Comprehensive Care of Drug Addiction Patients staff. The response rate was 92%. Overall satisfaction was very satisfied/quite satisfied (91%) and satisfied (9%). These results highlight the high level of satisfaction (quite satisfied or very satisfied: 81.8%) with the effectiveness and speed of resolution of incidents by the Hospital Pharmacy Service staff.

This process incorporates the knowledge and experience of hospital pharmacists into this healthcare field, as well as taking advantage of existing resources, facilities, and procedures. All these aspects lead to an efficient, effective, and safe approach to this clinical-care activity and enable a change in the pharmacotherapeutic health care model for opioid-dependent patients.

Introduction

Methadone was synthesized in the 1940s. It is a pure synthetic opioid agonist with strong affinity for and activity at the μ -opioid receptors. It is marginally more potent than morphine and has a longer duration of action, but has a lower euphoric effect¹. Thus, methadone is an alternative to morphine in that it has the same analgesic properties but has milder adverse effects².

In 1964, it was first used in clinical rehabilitation programs for opiate addictions such as those associated with heroin. These programs were developed by a research team at the Rockefeller University of New York³ and are known as methadone maintenance programs (MMPs). They were developed after World War II to treat heroin addictions in response to the sharp increase in consumption and deaths related to this substance in the late 1950s and early 1960s in New York City^{4,5}.

Methadone was the first opioid substitute employed in the United States, Australia, and Europe and continues to be the most widely used today. Its use has been clearly shown to reduce illicit heroin use, drug overdose deaths, frequency of injection, and HIV transmission⁶. It also improves the patients' quality of life, including positive changes in health and in social and physical functioning^{7,8}. It has been shown that oral methadone maintenance treatments are effective for individual patients, improve public health, and are cost-effective^{9,10}.

In Spain, heroin use peaked in the 1980s¹¹. The first Spanish regulations on the prescription and dispensing of methadone for the treatment of opiate dependence appeared in 1983. However, it was not until 1990 that the prescription criteria were standardised and methadone treatment became widespread. Since then, a series of laws on the regulation and implementation of MMPs have been passed¹²⁻¹⁶ and continue to be developed¹⁷.

In the CAM, the General Sub-Directorate for Addiction Health Care (SGAA) was incorporated into the General Directorate for the Coordination of Health Care by Decree 125/2017 of October 17 of the Governing Council, which establishes the organisational structure of the Madrid Health Service. The General Directorate assumed powers over "the planning and coordination of resources for treatment, rehabilitation, and reintegration available to the Public Administrations in the matter of drug dependence, as well as resources belonging to privately owned institutions that receive public funds within the Community for addiction health care tasks".

The SGAA coordinates a network of centres and services in the CAM that provide health care to patients with drug use and dependence problems. They help around 22,000 people each year. Approximately 16%

sición de metadona, envases para la dosificación personalizada en los Centros de Atención Integral a Drogodependientes y rutas de transporte. Asimismo, se ha adjudicado un concurso para la implementación de un sistema informático de gestión y sistemas automatizados de dispensación, actualmente en vías de instalación.

También se está actualizando el protocolo farmacoterapéutico del Plan de mantenimiento con metadona de la Comunidad de Madrid.

En año y medio se han elaborado 5.300 litros de metadona solución y se han dispensado 2.844 prescripciones individualizadas.

Disponemos de resultados de calidad percibida por los profesionales de los Centros de Atención Integral a Drogodependientes mediante una encuesta de satisfacción. La tasa de respuesta fue del 92%. El grado de satisfacción global fue: 91% muy satisfecho/bastante satisfecho y 9% satisfecho. Destaca el alto grado de satisfacción (bastante o muy satisfecho) del 81,8% con la eficacia y rapidez de la resolución de incidencias por parte de los profesionales del servicio de farmacia.

Este proceso permite incorporar el conocimiento y experiencia de los farmacéuticos especialistas a este ámbito asistencial, así como aprovechar recursos, instalaciones y procedimientos ya existentes. Todo ello redundará en un abordaje eficiente, eficaz y seguro de esta actividad clínico-asistencial y posibilitará un cambio de modelo de asistencia farmacoterapéutica de los pacientes dependientes de opiáceos.

of these patients are prescribed methadone as an opiate substitute for the treatment of heroin-related addiction disorders.

As a result of the aforementioned organisational change, Resolution 189/2018¹⁸ was implemented, which tasked a Hospital Pharmacy Service (HPS) with supplying methadone to the Centres for the Comprehensive Care of Drug Addiction Patients (CAIDs) of the Madrid Health Care Service SGAA. The aim of this Resolution was to centralize the acquisition, preparation, distribution, and dispensing of methadone by the HPS. This initiative represented a first step in changing the pharmacotherapeutic health care model for the treatment of the patients in the program. To date, between 3,000 and 5,000 patients are receiving methadone in the 27 CAIDs across the CAM.

In the first phase, methadone acquisition and production management had to follow the current distribution cycle, dosage, and personalized administration in each CAID.

In the second phase, treatments would be protocolised, standardised, and harmonised through the development of pharmacoclinical prescription and pharmaceutical care protocols. Health care staff and patients at the CAIDs would receive information and training strategies.

Given Resolution 189/2018¹⁸ and the staged approach to the objectives, the HPS assumed its new responsibilities in March 2018. This was the first time that pharmacists specialised in Hospital Pharmacy had conducted this kind of work in the setting of addiction treatment in the Autonomous Community of Madrid. This approach provides a range of opportunities that will facilitate the utilization and optimization of existing resources as well as a change in the pharmacotherapeutic health care model by incorporating the competences, skills, and knowledge of specialist pharmacists in the healthcare process.

This article describes the process of the centralization of the acquisition, preparation, distribution, and dispensing of methadone in the HPS. This process will enable a change in the pharmacotherapeutic health care model for the treatment of MMP patients by incorporating specialist pharmacists into the health care process.

Methods

In the first phase of the project, the workflow followed prior to Resolution 189/2018¹⁸ was analysed to acquire all the resources and materials needed to implement the Centralized Pharmacy Unit in the HPS.

A pharmacotechnical laboratory was set up in the facilities of the HPS and equipped with 500 mL, 1,000 mL, 2,000 mL, and 2,500 mL volumetric flasks, a precision scale, magnetic stirrers, magnets, 800 mL, 2,000 mL, and 3,000 mL beakers, glass rods, a desktop computer, and essential security measures, such as electronic access control and

safe storage, given that the medication under consideration was a narcotic.

Subsequently, procedures for acquiring methadone were established to guarantee supply to the CAIDs. Methadone hydrochloride was acquired through the Spanish Drug Agency and methadone tablets were purchased from the supplying laboratory. Likewise, a new workflow, schedules, route, and security procedures were established to transport the drugs to the CAIDs. At the beginning of the program, methadone was purchased directly from the supplying laboratory. Subsequently, in compliance with the Public Administration Contracts Law, a standard procedure for the acquisition of methadone hydrochloride and methadone tablets was designed and contracted out through public tender.

A communication system was set up between the HPS and the CAIDs and a new email account was created which was exclusive to this program. Two application forms were designed, one for oral methadone solution (Figure 1) and another for methadone tablets (Figure 2). The CAIDs use these forms to send their individualized requests to the HPS.

The HPS Quality Commission drafted and approved six standard operating procedures (SOPs) following the methodology implemented in the HPS in accordance with the ISO 9001:2015 Management System obtained in 2012.

The Pharmacy Service technical staff were trained in the theoretical and practical aspects of the program in order to incorporate them into their daily tasks.

Oral methadone solution

Methadone solution is prepared following the Good Practice Guideline for Drug Preparation in Hospital Pharmacy Services¹⁹ at a concentration of 10 mg/mL according to the National Formulary²⁰. It is made in different volumes depending on the needs of the CAIDs.

Requests vary depending on the number of patients and population served by the CAID or the time of the year. These requests range from 5,000 mg to 200,000 mg of methadone hydrochloride (0.5-20 l). Thus, methadone solution is packaged in 0.5 L batches in order to be able to provide final packaging of 1 L or 2.5 L topaz glass bottles. During preparation, the batches are assigned according to the prescription book, and the corresponding preparation control sheet is completed. The batches dispensed to each CAID are recorded on the sheet, thus guaranteeing the traceability of the product. Once ready, the bottles are labelled, sealed with parafilm, and kept in a refrigerated room at 2 °C to 8 °C under security. The cold room is equipped with a sensor that monitors the temperature and its door remains locked until dispensing.

Methadone tablets

Methadone tablets are also dispensed to CAIDs according to individualized prescriptions made by the medical staff in each CAID. Each dose is packaged individually per patient and an information leaflet is

Figure 1. Application form for 1% methadone solution.

Hospital Universitario Infanta Leonor <small>Hospital Virgen de la Luz</small>	
HOJA DE SOLICITUD DE METADONA AL 1% AL SERVICIO DE FARMACIA	
FECHA DE SOLICITUD:	_____
FECHA DE ENTREGA:	_____
DESTINATARIO:	SERVICIO DE FARMACIA HOSPITAL UNIVERSITARIO INFANTA LEONOR
A LA ATENCIÓN DE:	SERVICIO DE FARMACIA HOSPITAL UNIVERSITARIO INFANTA LEONOR
REMITE:	
NOMBRE DEL CENTRO:	
ASUNTO: SUMINISTRO DE SOLUCIÓN DE CLORHIDRATO DE METADONA	
Se solicita la cantidad de _____ mg de SOLUCIÓN DE CLORHIDRATO DE METADONA 1% necesarios para este Centro desde el día _____ hasta el día _____.	
Fdo. (Nombre y apellido) (Responsable asistencial del CAID/Unidad o persona en la que delegue)	
REMITIR POR CORREO ELECTRONICO farmetadona.hvl@salud.madrid.org	

Figure 2. Application form for methadone tablets.

Hospital Universitario Infanta Leonor <small>Hospital Virgen de la Luz</small>	
HOJA DE SOLICITUD DE METADONA COMPRIMIDOS (METASEDIN®) AL SERVICIO DE FARMACIA	
Datos del médico responsable de la prescripción:	
FECHA:	_____
MÉDICO:	_____
Nº DE COLEGIADO:	_____
CENTRO PRESCRIPTOR:	_____
TELÉFONO:	_____
FECHA TOPE DE RECEPCIÓN: (hacer coincidir con rúbrica manijero)	_____
FIRMA Y SELLO:	_____
Fdo.:	(Nombre y apellidos)
Datos del paciente:	
NOMBRE:	_____
PRESCRIPCIÓN METASEDIN®:	_____
DOSIS DIARIA:	_____
NÚMERO DE DÍAS:	(máx 35)
Nº comprimidos totales METASEDIN® 5 mg:	_____
Nº comprimidos totales METASEDIN® 30 mg:	_____
Nº comprimidos totales METASEDIN® 40 mg:	_____
Solicitud de metadona comprimidos (METASEDIN®) para reposición de stock:	
Nº comp. METASEDIN® 5 mg:	_____
Nº comp. METASEDIN® 30 mg:	_____
Nº comp. METASEDIN® 40 mg:	_____
Fdo.:	(Nombre y apellidos)
(Responsable asistencial del CAID/Unidad o persona en la que delegue)	
REMITIR POR CORREO ELECTRONICO farmetadona.hvl@salud.madrid.org	

included with each dose according to the pharmaceutical form of methadone.

Finally, a weekly work schedule was established in which four days were allotted for the preparation of methadone solution and one day for the preparation of individualized prescriptions for methadone tablets.

Transport and distribution

A standard procedure was designed for the transportation and distribution of methadone hydrochloride and methadone tablets. This procedure was contracted out through public tender in accordance with Public Administration Contracts Law.

Firstly, the transport route was created by assigning one day of the week to each CAID. Safety and security conditions were established. The containers are transported in flexible cooler bags with padded separators between the bottles to prevent impacts and breakage during transport. As a control and safety mechanism, a daily transport, delivery, and return control form was established between the HPS and the transport company workers. This form includes the number and volume of the methadone solution containers, total milligrams requested by each CAID, and whether or not individualized treatments with methadone tablets have been requested. The form also contains a final section in which the CAID stamps and confirms that the delivery has been completed correctly.

The HPS is also responsible for reviewing the accounts of each CAID through the daily dispensing records and accounting balance sheets, which are sent via e-mail, thus guaranteeing the correct use and control of the medication.

Daily workflow

Each CAID sends the request forms for methadone solution and methadone tablet prescriptions via email one week in advance. The data are anonymised by sending encrypted files with a separate key provided by the CAIDs. HPS administrative staff receive, record, and file requests. The pharmacist reviews and validates the requests and then organizes the weekly schedule. Methadone solution and individualized methadone tablet treatments are prepared according to the schedule. After the pharmaceutical validation of the compounding process, the route forms are filled in and two copies are made. Each day, the carrier collects the methadone according to the route sheet and weekly schedule. The carrier signs one of the copies, which is given to the administrative staff for its subsequent filing. The second copy is given to the carrier and the delivery cycle begins. Upon delivery, each CAID verifies that the methadone delivered corresponds to what has been requested. If everything is correct, the CAID stamps the delivery in the corresponding section of the form. This procedure is repeated at each CAID on the scheduled transport route, such that by the end of the day the form contains every CAID's stamp. The carrier returns this form to the HPS and it is archived as proof that the

methadone was correctly shipped and dispensed that day. In case of discrepancy, the CAID communicates with the HPS so that the issue can be resolved.

A questionnaire on perceived quality was designed to determine each CAID's level of satisfaction with the centralization program. The questionnaire comprised a seven-item Likert-type scale (Table 1) with five possible replies: not satisfied, little satisfied, satisfied, quite satisfied, and very satisfied. It was sent to 24 CAIDs via email through the Google® Forms platform.

Results

Over the first year, standard procedures were designed for the acquisition of methadone, of containers for personalized dosing in the CAIDs, and for the transportation of methadone from the Hospital to the CAIDs. These procedures were contracted out through public tender in compliance with the Public Administration Contracts Law. The HPS pharmacist staff established all the technical specifications, needs, and assessment criteria.

The HPS serves a network of 27 CAIDs with between 3,000 and 5,000 patients in the MMP.

A total of 5,293.5 L of methadone solution has been produced since the beginning of the project between April 2018 and September 2019. Specifically, the HPS produced 76 1 L batches of methadone 10 mg/mL and 2,087 2.5 L batches of methadone 10 mg/mL (total, 5,217.5 L). Thus, approximately 53 kg (52,935 g) of methadone hydrochloride were consumed. Of the total produced, 5,242.75 L were dispensed.

A total of 2,844 individualized requests were dispensed comprising 151,579 methadone tablets in the form of 32,857 5 mg tablets, 62,164 30 mg tablets, and 56,558 40 mg tablets. Tablets were dispensed for the following reasons: the development of intolerance to methadone in solution, travelling for holidays or personal or work reasons, or showing good control and adherence.

There was a monthly average of 138.7 dispensed requests, although this value increased 3-fold in the summer months. This was because many patients changed from methadone solution to tablets to make travel easier or for holiday reasons.

The total purchasing cost was € 63,100.9 (methadone hydrochloride: € 43,993.8; methadone tablets: € 19,117.1).

In line with the legal requirements on the control of narcotic drugs (Royal Decree 1675/2012 of December 14), over the last 18 months 7,934 files containing the daily dispensing records and accounting balance sheets of all the CAIDs have been reviewed. This decree regulates official prescriptions and special requirements for the prescription and dispensing of narcotic drugs for human and veterinary use²¹.

In the second phase, a public tender was launched to acquire a software management system and automated methadone dispensing systems. It was awarded in March 2019 and is currently being implemented in the CAIDs. The pharmacotherapeutic protocol of the MMP of the CAM is being updated in collaboration with a multidisciplinary team made up of health

Table 1. Satisfaction questionnaire

Question
1. What is your level of satisfaction with the degree to which the Hospital Pharmacy Service has adapted to the centralization process?
2. What is your general level of satisfaction with the information that the Hospital Pharmacy Service provided at the start of the process and over the first year?
3. What is your level of satisfaction with the ease by which you can contact the Hospital Pharmacy Service staff?
4. What is your level of satisfaction with the speed and efficiency of Hospital Pharmacy Service staff in resolving incidents?
5. What is your general level of satisfaction with your interactions with the Hospital Pharmacy Service staff?
6. What is your general level of satisfaction with service quality provided by the Hospital Pharmacy Service?
7. What is your general level of satisfaction with the Hospital Pharmacy Service?

care staff from the CAIDs, the HPS, the Subdirectorate of Pharmacy and medical products, and the Subdirectorate of Addictions.

In total, 22 CAIDs completed the questionnaire (response rate, 92%). Regarding the overall level of satisfaction, 50% were very satisfied, 41% were quite satisfied, and 9% were satisfied. The results are shown in figure 3.

Discussion

In Spain, MMPs have been analysed in different healthcare settings, such as outpatient centres, drug addict care centres, and community pharmacies. Publications related to these MMPs vary by the care modality in each Autonomous Community. In general, they present the results from different perspectives (e.g. by analysing effectiveness, economic aspects, or perceived quality through patient satisfaction questionnaires^{8,11,17,22,32}). However, these results are related to objectives that differ from those of this article in that they address MMPs. In contrast, we describe the centralization of acquisition, preparation, distribution, and dispensing of methadone to the CAIDs in the CAM and the role of the pharmacist in this process. Thus, the results of this article cannot be compared with previously published results, given the degree of implementation up to this point in time.

In the CAM, methadone can be dispensed from the CAIDs or from community pharmacies that are within the Madrid Pharmacy Offices MMP. This MMP was created in 1997 in collaboration by the Ministry of Health and Social Affairs (Anti-Drug Agency) and the Official College of Pharmacists of Madrid³³.

However, the procedure for acquiring, preparing, distributing, and dispensing methadone to CAIDs had never been centralized in the CAM. In this Community, this pioneering experience has been conducted under the direction and responsibility of an HPS. This is the first time that specialist pharmacists have performed health care tasks in the setting of addictions. This has led to a number of benefits.

Firstly, the health resources of the Madrid Health Service have been optimized, due, on the one hand, to using the resources of the HPS with minimal adaptation, and on the other hand, to designing standard procedures for the acquisition of methadone, of containers for personalized dosing in the CAIDs, and for the transportation of methadone. These procedures were contracted out through public tender in compliance with the Public Administration Contracts Law. These initiatives have increased efficiency in the process, thus contributing to the sustainability of the health care system.

Secondly, the reduction of inter-centre variability through the creation of standardized work procedures has facilitated the unification and homogenization of the processes.

The quality of the medicine has also been improved by centralizing the preparation of methadone solution in a single HPS. In addition to having better facilities, the HPS prepares master formulas following the Good Practice Guideline for Drug Preparation in Hospital Pharmacy Services¹⁹ and has a traceability system that covers the entire the manufacturing process. These actions have increased patient safety.

However, these processes must be planned in advance such that the HPS can guarantee supplies to all the CAIDs given the high number of patients included in the MMP and the large amount of methadone solution needed for preparation.

The results of the questionnaire on perceived quality show a high level of satisfaction in the CAIDs. It should be noted that no score less than satisfied has been recorded and the lowest response was "satisfied" and that the predominant response was "very satisfied". Other outstanding results were the high level of satisfaction with the efficiency and speed of the resolution of incidents by the HPS staff (81.8% "very satisfied" or "quite satisfied") and with the attention and treatment received from the HPS staff (95.4% "very satisfied" or "quite satisfied").

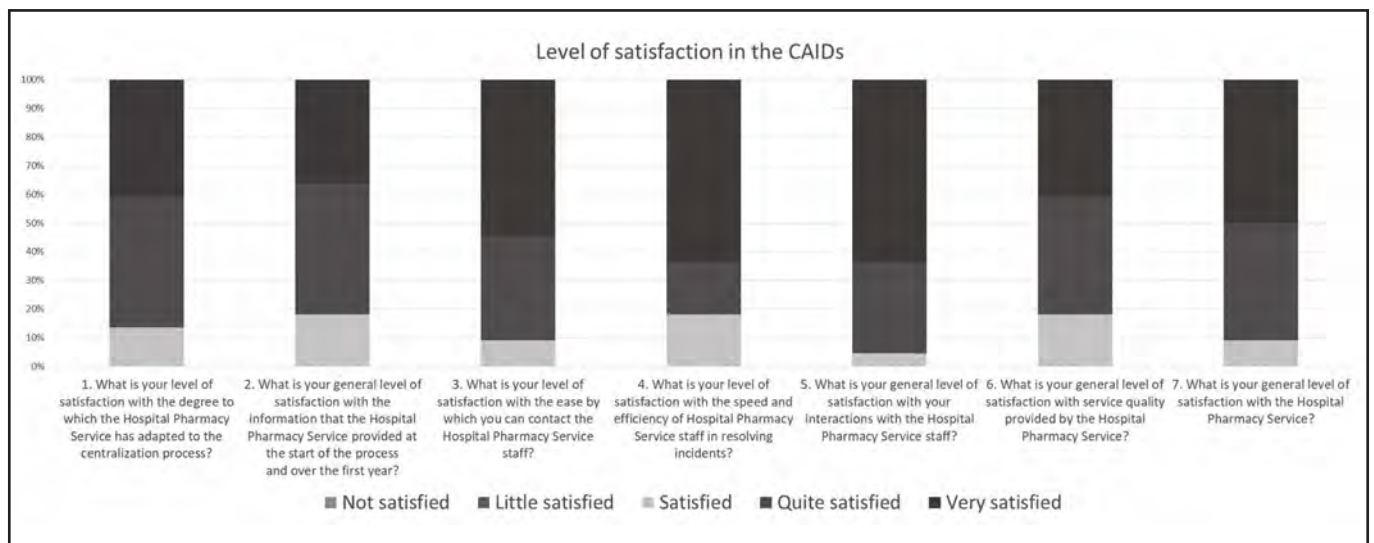
The lack of a computerized system for prescribing, dispensing, and administration of methadone stands out as a limitation to the centralization of the MMP. Among other benefits, such a system would enable prescribing doctors, specialist pharmacists, and other staff in the CAID to completely trace prescriptions and provide them with an electronic medical record containing the clinical aspects and pharmacotherapeutic history of the patient. They would then have complete information on the effectiveness, safety, and efficacy of methadone treatment as well as adherence to treatment.

From this limitation arise our next challenges and improvements that we want to contribute, such as the implementation of a software that integrates all the processes related to the use of methadone. In addition, a process is already underway to further integrate specialist pharmacists in the multidisciplinary clinical teams caring for drug addiction patients, thus providing added value and improving health outcomes³². Specialist pharmacists and other Madrid Health Service staff are updating the pharmacotherapeutic protocol of the MMP of the CAM.

In addition, possible improvements to the formulation of methadone solution are currently being studied due its short period of stability²⁰. One possibility is the addition of preservatives. The physicochemical and microbiological stability of the formula are also being studied in order to increase its "beyond use date". These improvements will improve organizational aspects of the workflow and increase adaptability to the individual dispensing needs of patients.

In conclusion, we highlight that the entire first phase of the project has been consolidated, the initial objectives of Resolution 189/2018¹⁸ have

Figure 3. Level of satisfaction in the CAIDs.



been fulfilled, and that this workflow can serve as a model for other autonomous communities. The centralization of the MMP in the HPS facilitates changes to the pharmacotherapeutic health care model by incorporating the competencies, skills, and knowledge of hospital pharmacists into the health care process of opiate-dependent patients. To the greatest extent possible, it also makes available the experience and resources needed to address this health care challenge, thus benefitting patients and other staff and contributing to the sustainability of the health care system.

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Conflict of interests

No conflict of interests.

Presentation at Congresses

This work has been presented at the 64th Congress of the Sociedad Española de Farmacia Hospitalaria held in Seville from 17 to 19 October 2019.

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