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CHRONIC VIRAL HEPATITIS C MICRO-ELIMINATION PROGRAM USING TELEMEDICINE.

THE MEXICAN EXPERIENCE

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ABSTRACT

Background
Infection with hepatitis C virus (HCV) is a global health problem; chronic infection induces the development of fibrosis and cirrhosis together with all their related complications. The use of direct-acting antiviral (DAA) drugs has proven highly effective. Telemedicine is a present-day resource that brings treatment closer to distant areas and may result in savings.

Objective
To implement a microelimination program for HCV using DAAs with support from a telemedicine program to minimize expenses.
Patients and methods
The program was developed at the Medical Services department of Petróleos Mexicanos (SMPM) with national coverage; patients diagnosed with chronic hepatitis C were included. These were classified into locals and outsiders. Treatment for foreign patients was indicated, monitored, and completed through telemedicine, thus avoiding their transport to the country’s capital city, in order to save up on transportation costs and travel allowances.

Results
A total of 136 patients, 74 locals and 62 outsiders participated. Transfer was avoided for 62 patients (45.5%), which meant that telemedicine resulted in USD 3,176.20 savings per patient, with overall savings of USD 196,924.40 from cost minimization. A total of 30 patients remained untreated for lack of medication, hence coverage amounted to 86%. Sustained virological response (SVR) was achieved in 99% of cases. Only 2 patients had treatment failure. Adverse events included headache and fatigue in 5% of the sample.

Conclusions: With the aid of a telemedicine approach significant savings were achieved by minimizing costs, since nearly half of patients were outsiders. Coverage reached 86%. Treatment with DAAs was successful for 99% of our cases.

Keywords
Hepatitis C, telemedicine, sustained viral response, direct-acting antiviral, liver cirrhosis, liver fibrosis.

INTRODUCTION
Infection with hepatitis C virus (HCV) is a global health issue. According to recent estimations by the World Health Organization (WHO), it affects around 71 million people worldwide [1]. In Mexico seroprevalence was reported to be 0.16% for individuals between 15 and 49 years of age, and 0.18% for those older than 50. Mexico has the second highest chronic hepatitis C rate in Latin America, considering that only 30% of
cases are diagnosed and, sadly, only 0.6 % receive treatment [2]. At diagnosis, almost 30 % already exhibit advanced fibrosis or cirrhosis [3]. Before 2011, standard treatment for active infection with HCV was a combination of pegylated interferon alpha plus ribavirin (peg-IFNα/RBV), with effectiveness ranging from 30 % to 50 % [4]. Since 2011 direct-acting antivirals (DAAs) have become available, with an effectiveness greater than 90 % and fewer side effects [5]. This higher therapeutic effectiveness has been associated with a significant reduction in death risk from cirrhosis and liver cancer [6]. The micro-elimination strategy involves treating specific population segments to ensure non-transmission of the virus, thus limiting infection cycles. Such strategies have been implemented in multiple countries and populations, including intravenous drug users in Spain [8] and Great Britain [9], patients with thalassemia in Italy [10], and the Netherlands population [11]. Furthermore, telemedicine is known to have been particularly useful in cities with scattered populations or large territories. The WHO defines telemedicine as “the provision of health services when distance is a critical factor by using novel communication technologies for valid information sharing regarding the diagnosis, treatment, and prevention of disease” [7]. Since 2000, the Servicio Médico de Petróleos Mexicanos (SMPM) has available a fiber-optic network that connects all hospitals and clinics in the Mexican Republic. We report herein the results of a nation-wide SMPM program for the micro-elimination of infection with HCV using telemedicine for resource savings within a cost minimization concept.

PATIENTS AND METHODS

Patients
Patients diagnosed with HCV were included and categorized as either locals or outsiders. They all underwent the following tests: viral load, genotype, subtype, grade of fibrosis (using Fibrotest® or transient elastography), liver ultrasound, and alpha-fetoprotein. When grade of fibrosis was F4 (cirrhosis) the Child-Pugh score was calculated. Patients were excluded who had any malignancy with estimated survival lower than 1 year, whether hepatic or not, and who withheld their informed consent to sharing data. The
informed consent form was approved by the local Ethics Committee (*Comité de Ética en Investigación, CONBIOETICA-09-CEI-007-20180529*).

**Methods**

Local patients were treated in a tertiary hospital in the country’s capital city, and patients residing outside Mexico City (outsiders) never traveled to the capital—all their visits were performed by non-specialist physicians in their area, with advice and guidance from an hepatologist through telemedicine. Cost estimations per outsider entitled to SMPM care every time he/she attends a medical appointment in the capital city includes a round-trip air ticket plus travel allowances and lodging for 3 days; in addition, these costs are also paid for an accompanying family member, which renders the expense twice as big. Without the telemedicine program every outsider patient previously required visiting the tertiary center in the capital on 6 occasions—the first one to open a case record and order initial testing; the second visit to review initial testing results and decide an antiviral therapy; the third and fourth visits during treatment for patient monitoring and follow-up; the fifth one at treatment completion for patient assessment and viral load testing; the sixth, final visit to assess sustained viral response (SVR) and discharge the patient to his/her regional site when appropriate. Costs attributed to cirrhosis complications were not included in this protocol (endoscopy, ligation, diuretics, etc.).

**Telemedicine project**

The project started out in January 2017 to facilitate that patients with chronic infection with HCV could be assessed at their local Health Unit by their primary care practitioners in a fast, timely manner to receive their treatment without having to travel to Mexico City. Primary care physicians were at all times advised on decision making by a hepatologist by means of virtual conferencing through telemedicine. The aim was to receive at the tertiary level only those patients who required it because of severe side effects of treatment or disease decompensation. Therapy regimens were prescribed according to patient characteristics, and included the following: a) sofosbuvir/ledipasvir; b)
sorosbuvir/velpatasvir; c) elbasvir/grazoprevir; and d) the combination of ombitasvir/paritaprevir/ritonavir plus dasabuvir. Every treatment to be prescribed for HCV was reviewed, as were likely interactions with other drugs, which were acknowledged for each case by consulting the website https://www.hep-druginteractions.org/, sponsored by the University of Liverpool.

**Cost analysis**

The cost analysis was performed as a cost minimization analysis, and we considered travel costs from the regional units to the tertiary site. For calculations we considered that a patient’s and companion’s transfer represented on average a total of 529.40 dollars, hence six round trips represented a mean of 3176.2 ± 1246.25 dollars. The total cost for medication, imaging, and lab tests was estimated at 9,314.54 dollars on average, for a mean of 9,314.6 ± 210.8 dollars per patient.

**Statistical analysis**

Intervention results were deemed equivalent for both groups. Cost minimization estimates were based on the savings resulting from six visits per patient for the total number of patients. Percentages and frequencies were used for the analysis of patient characteristics. Means and standard deviations were used for costs. Comparisons between groups were performed using median tests for independent groups with a significance (alpha) level lower than 0.05. The statistical software SPSS version 23.0 (Chicago, Illinois, USA) was used.

**RESULTS**

A total of 156 patients were diagnosed with HCV; of these, 136, 74 locals and 62 outsiders, were included. Their main characteristics are listed in table 1. SVR was achieved in 99 % of subjects; only 2 patients failed to respond to treatment. Reported adverse events included headache and fatigue in 5 % of case; no serious side effects were reported.
The total treatment budget for all patients was estimated at USD 1,463,710.00; of this amount, USD 689,280.40 was for locals and USD 774,429.60 was for outsiders. Traveling was avoided for 62 patients (45.5%), which represented savings of USD 3,176.20 per patient for an overall cost minimization of USD 196,924,40 (Fig. 1), and a final spent budget of 1,266,785.60 dollars. Differences were found in median values between locals and outsiders—USD 9,355.5 vs 12,996.7, respectively; p < 0.001. Thirty patients remained to be treated because of unavailable medication, and coverage amounted to 86% of patients diagnosed with HCV.

DISCUSSION
At the Medical Department, Petróleos Mexicanos a strategy was designed for the micro-elimination of infection with HCV using DAAs and telemedicine. We have shown that it is possible to integrate actions for the primary and secondary levels of health care using current electronic tools, and that this also represents savings for the health system. We obtained SVR in a high percentage of patients on DAAs, with benefits including the prevention of progression to liver cirrhosis and, in those already with cirrhosis, avoiding decompensation, with a better prognosis for the mid-long term and a positive impact on quality of life [25-26]. DAA selection must be made by experts in this disease, which in countries such as ours, with a highly scattered population and few specialists, all of them working at tertiary institutions, represents a significant limitation. Outsiders represented a high percentage (45%), hence the impact on savings (cost minimization) was significant. While estimates only dealt with transportation costs and travel allowances, the program also had an impact on sick leave days and the risks run by patients and their partners during their journey, most particularly now during the COVID-19 pandemic, this being the reason why we believe telemedicine will have a still more important role. The SMPM will possibly reach the goal set by the WHO regarding the elimination of HCV infection by 2030 using DAAs with proven efficacy and safety, and the aid of telemedicine.
REFERENCES


Table 1. Characteristics of patients (n = 136)

<table>
<thead>
<tr>
<th>Location</th>
<th>Locals / Outsiders</th>
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<tbody>
<tr>
<td></td>
<td>74 (54.4%) / 62 (45.5 %)</td>
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<table>
<thead>
<tr>
<th>Gender</th>
<th>Male / Female</th>
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<tr>
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<td>95 (70 %) / 41 (30 %)</td>
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<table>
<thead>
<tr>
<th>Age:</th>
<th>61.3 ± 11.4 years</th>
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<table>
<thead>
<tr>
<th>Genotype</th>
<th>1 = 92 (67.6 %)</th>
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<tbody>
<tr>
<td></td>
<td>2 = 42 (30.9 %)</td>
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<tr>
<td></td>
<td>3 = 2 (1.5 %)</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Grade of fibrosis</th>
<th>Not significant or minor / Advanced or cirrhosis</th>
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<tr>
<td></td>
<td>64 (47 %) / 72 (53 %)</td>
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<thead>
<tr>
<th>Child-Pugh classification (n = 72)</th>
<th>A = 62 (86.1 %)</th>
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<tbody>
<tr>
<td></td>
<td>B = 9 (12.5 %)</td>
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<tr>
<td></td>
<td>C = 1 (1.3 %)</td>
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<th>Treatment</th>
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<tr>
<td>Sofosbuvir / Velpatasvir = 78 (57.3 %)</td>
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<tr>
<td>Sofosbuvir / Ledipasvir = 47 (34.5 %)</td>
</tr>
<tr>
<td>Elbasvir / Grazoprevir = 5 (3.6 %)</td>
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<tr>
<td>Ombitasvir / Paritaprevir / Ritonavir plus dasabuvir = 6 (4.4 %)</td>
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</tbody>
</table>
Figure 1. Cumulative costs for locals and foreigners (travel allowances + transfers), total costs (foreigners + locals) and savings (difference between foreigners and locals), and actual expense for foreigners (telemedicine cost – transfers avoided to a tertiary site).

* p < 0.001, median test.