Clinical pharmacology profile of care in Hepatology clinic

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Summary

Since 2010, the Clinical Gastroenterology and Hepatology Division of the Central Institute of Hospital das Clínicas of the University of São Paulo Medical School (HC-FMUSP, in the Portuguese acronym) has been developing specialized electives assistance activities in the Outpatient Specialty Clinic, Secondary Level, in São Paulo NGA-63 Várzea do Carmo. The objective of this study was to analyze the pharmacotherapeutic profile of patients. This is a cross-sectional and retrospective study in which patients were seen at the Hepatology sector and the results were submitted to descriptive statistics. During the study period, 492 patients were treated at the clinic, with a mean age of 58.9 years and frequency of 61.2% female and 74.8% living in São Paulo. This population was served by various other medical specialties (cardiology and endocrine among others) and the major liver diagnoses were: chronic hepatitis B and C and fatty liver. Comorbidities were also identified, such as diabetes, hypertension and dyslipidemia. Most patients took their medication in the Basic Health Units. We found that 30% of patients use of more than five medications and the most prescribed were omeprazole 208 (42.3%), metformin 132 (26.8%) and losartan 80 (16.3%). Because it is an adult/elderly population, with several comorbidities and polymedication, it is important to be aware of the rational use of medication. The multidisciplinary team is important in applying correct conducts for the safe use of medicines, to reduce the burden on health spending and improving the quality of life of patients.

Keywords: hepatitis, drug, polypharmacy, ambulatory care, hematology, omeprazole.

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Introduction

The system of referral and counter-referral of the Unified Health System (SUS, in the Portuguese acronym) is the two-way referral of patients between the different levels of complexity of the services. The first means the referral of patients from a service of lower complexity to a service of greater complexity, assisting the patient and scheduling their procedure. Counter-referral, in turn, is when the patient can be sent back to their service of origin for treatment maintenance and follow-up.[1]

The referral and counter-referral network is developed on the basis of four components that function in an integrated manner. Primary Health Care (PHC) services are the patient's place of entry for the entire network; secondary care is made up of specialized outpatient clinics and hospitals of medium complexity; the tertiary network aggregates high-complexity hospitals. All are supported by logistics systems, regulation, health transport and electronic health records, as well as support systems, pharmaceutical assistance, diagnostic and therapeutic support.[2]

The Hospital das Clínicas of the University of São Paulo Medical School (HC-FMUSP, in the Portuguese acronym) has a Liver Care project that functions in line with the SUS referral and counter-referral system, in the NGA-63 Várzea do Carmo Outpatient Specialty Clinic, Health Assistance Management Center, in São Paulo.

This service unit has three pharmacies: one outpatient, one for specialized components and one for oncologic medication focused on the care of patients being treated for breast and prostate cancer.

The Hepatology sector in Várzea do Carmo has a database created from a questionnaire that records the drugs used by patients and the place where they collect their prescriptions. In this database, in addition to patient demographics, there is also information about diagnosis, medical specialties, use of medicines, facilities dispensing these patients' prescriptions, the possibility of acquiring them in the event they are not available for free, and data revealing their knowledge about the drugs they use.

The main services performed at Várzea do Carmo Medical Hepatology Outpatient Clinic are for viral hepatitis and hepatic steatosis. Therefore, it is important, in order to guarantee adequate assistance to the patient, to understand their profile in light of the concepts of polypharmacy. Polymedication, according to Bjerrum et al., is also known as minor polymedication, when the patient uses two to four drugs, and major polymedication, which is when there are five or more drugs of daily and continuous use.[3]

Our study, based on the database mentioned above, uses this concept to address the profile of patients seen at the Várzea do Carmo Hepatology Outpatient Clinic.

Objective

To analyze the pharmacotherapeutic profile of patients attended by the Clinical Hepatology sector in the Outpatient Specialty Clinic, Secondary Level, Várzea do Carmo, according to the definition of polypharmacy.

Method

Cross-sectional study, with retrospective data collection, from March to July 2015, in the Hepatology sector of the Outpatient Specialty Clinic, Secondary Level, São Paulo, State of São Paulo.

The study population included patients who were enrolled in the Hepatology database, aged 18 years or older. Patients whose data were non-existent or incomplete were excluded from the database. The research project was approved by the Research Ethics Committee of HC-FMUSP (CAPPesq) with CAAE: 53491816.1.0000.0068 - Opinion number 1.433.847 on March 2, 2016.

Information on demographics, diagnosis, specialties in which the patient is treated, medications, dosage, information on the patient's knowledge of the use of their medications, the facility dispensing the drugs and the possibility of each patient to acquire the medication in case that particular drug is not available in the network's pharmacies were transported to the REDCAP, a tool for Data Management in Scientific Research. The results were submitted to descriptive statistical analysis and expressed in tables and charts.

Results

Based on the database of the Hepatology and Gastroenterology Department of the Várzea do Carmo Outpatient Specialty Clinic, from March to July 2015, 492 patients were identified after visiting the Hepatology sector, totaling 1,931 consultations in the period. Of the patients treated, 304 (61.79%) were female and 188 (38.21%) were male. The mean age of the general population was 58.87 years, with a standard deviation of ± 13 years. As for place of residence, 368 (74.80%) patients resided in the city of São Paulo, while 124 (25.20%) resided in the greater São Paulo area.

The main liver diagnoses are shown in Table 1.

TABLE 1 The main liver diagnoses in 492 patients investigated.

Main liver diagnosis	Number of patients	Female n (%)	Male n (%)
Hepatitis C	172	89 (51.75%)	83 (48.25%)
Hepatic steatosis	112	77 (68.75%)	35 (31.25%)
Cirrhosis	72	30 (41.67%)	42 (58.33%)
Hepatitis B	35	19 (54.28%)	16 (45.72%)
Under investigation	62	40 (64.51%)	22 (35.49%)
Other diagnoses	78	42 (57.85%)	36 (46.15%)
Total	531*		

*39 patients were diagnosed with more than one condition.

These patients are also assisted by other specialties in the Várzea do Carmo outpatient clinic, at the Clinics Hospital of São Paulo, and in other primary, secondary or tertiary care centers. The most prevalent clinics were those of internal medicine 110 (22.35%), cardiology 98 (19.92%), endocrinology 79 (16.06%), gastroenterology 68 (13.82%), and rheumatology 62 (12.60 %) and ophthalmology 44 (8.94%).

As for the facilities where the patients collected their medications, we noted that: 317 (74.59%) would get them from Primary Health Units (UBS, in the Portuguese acronym), 110 (25.88%) from the Várzea do Carmo Outpatient Specialty Clinic and 36 (8.47%) from HC-FMUSP.

According to the information contained in the database, 373 (87.76%) patients correctly reported the name, quantity and purpose of all medications used daily, while 52 (12.24%) did not know how to give any of the requested information.

Regarding the possibility of acquiring the drug, 258 (60.8%) patients reported having the possibility of buying the medication if the drug was not available for free or when it was a drug that is not listed in the government-funded medication program on a federal, state or municipal level. Another 54 (12.5%) could buy it, depending

on the price of the medication, but 113 (26.7%) reported not being able to purchase the prescribed medication, regardless of the price.

Table 2 demonstrates that omeprazole, metformin, losartan, hydrochlorothiazide, simvastatin and enalapril were the medications most frequently cited by patients in a list of 33 spontaneous citations.

Of the drugs spontaneously reported by patients, treatment for hepatitis B was cited by 12 patients and treatment for hepatitis C by two.

TABLE 2 Distribution of patients according to their medication (n=425).

Medications	Total	Percentage (%)
Omeprazole	208	42.28
Metformin	132	26.83
Losartan	80	16.26
Hydrochlorothiazide	77	15.65
Simvastatin	67	13.62
Enalapril	62	12.60
Propranolol	60	12.20
Levothyroxine	53	10.77
Amlodipine	50	10.16
Atenolol	50	10.16
Acetylsalicylic acid	40	8.13
Insulin	35	7.11
Spironolactone	32	6.50
Captopril	26	5.28
Furosemide	25	5.08
Dipyrone	24	4.88
Glicazide	24	4.88
Calcium	23	4.67
Vitamin D3	23	4.67
Alendronate	18	3.66
Paracetamol	17	3.46
Glibenclamide	14	2.85
Domperidone	13	2.64
Pantoprazole	11	2.24
Prednisone	11	2.24
Bromopride	10	2.03
Fluoxetine	9	1.83
Lactulose	9	1.83
Tenofovir	7	1.42
Entecavir	4	0.81
Interferon	2	0.41
Ribavirin	2	0.41
Adefovir	1	0.20
Other	219	44.51

As for use of medication, we found that 425 (86.38%) patients used some medication, while only 67 (13.62%) did not use any. Therefore, 425 patients will be investigated for polypharmacy. Table 3 and Chart 1 show the patient's classification according to Bjerrum et al.[3]

TABLE 3 The pharmacotherapeutic profile according to the classification by Bjerrum et al. with the five drugs most often prescribed to patients on minor polymedication and the ten most often prescribed to patients on major polymedication.

Drug	Minor polymedication n=425	Major polymedication n=425
Omeprazole	154 (36.23%)	86 (20.23%)
Metformin	72 (16.94%)	62 (14.58%)
Losartan	43 (10.11%)	44 (10.35%)
Hydrochlorothiazide	43 (10.11%)	34 (8.00%)
Enalapril	38 (8.94%)	34 (8.00%)
Amlodipine	–	33 (7.76%)
Simvastatin	–	33 (7.76%)
Acetylsalicylic acid	–	32 (7.52%)
Propranolol	–	25 (5.88%)
Levothyroxine	–	24 (5.64%)

Discussion

The sex and age distribution found in our study is in line with what we expected. Likewise, the distribution of diagnoses among the population served is in accordance with the distribution of these conditions in the general population.

The study demonstrates that a patient can be treated simultaneously at the primary, secondary and even tertiary level of care. The factor keeping a particular patient in tertiary care is the medicines he or she uses, that is, if they are not available in primary or secondary care.

Within this scope, where it is observed that these patients will continue to require specialized or ultra-specialized services, i.e. tertiary care, we are able to say that the concern for rational use of medicines is of note.[2]

Our patients collect their medication from different facilities such as Primary Care Units, the Várzea do Carmo Outpatient Specialty Clinic and the FMUSP Hospital das Clínicas. For the same reasons cited above, dispensing centers are also classified according to complexity and not all medicines are available from the same location.

From a viewpoint of the safe and rational use of medication, there is control over the use of medical prescriptions, because each dispensing facility indicates in

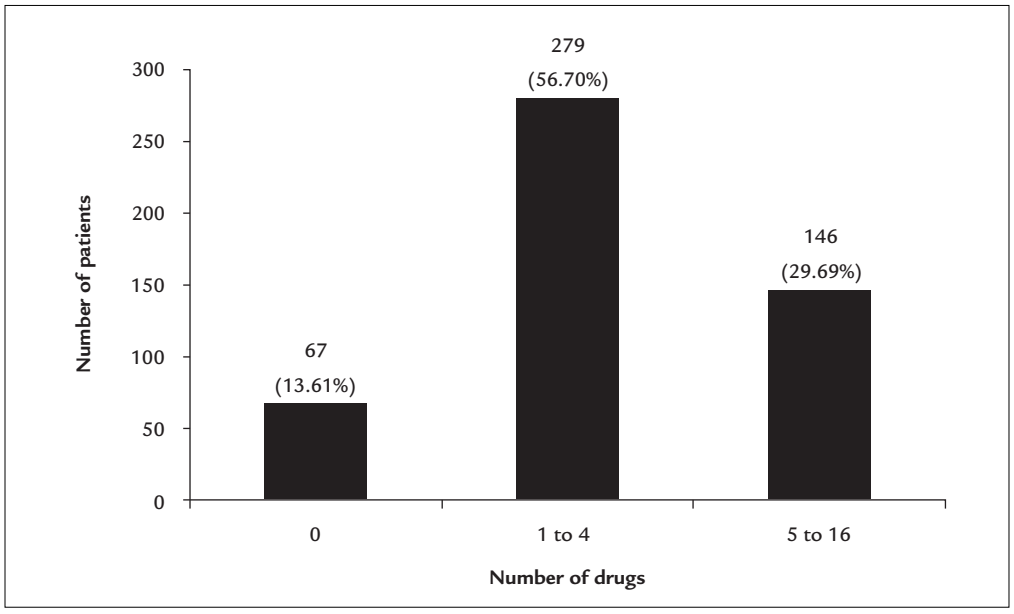

CHART 1 Number of patients vs. number of drugs (n=492).

the prescription that the drug was delivered. However, a patient who consults with more than one prescribing physician can have the same prescription repeated and, with different prescriptions, receive more medication than needed.

Comparing the above data with the information obtained in the database about the patients' lack of knowledge about their medications, misuse is a possibility. In addition, too much medication in a patient's possession can lead to self-medication, either through overuse or sharing.

Considering also that some patients mentioned the impossibility of acquiring prescription items if these drugs were not available for free, care about rational use is even more justified as a measure to avoid shortage and waste that can burden the public service.

Omeprazole is one of the drugs most frequently mentioned by patients, which, outside the scope of gastroenterology, raises the question of whether the drug is being used rationally. Omeprazole may alter the metabolism of other drugs by enhancing or reducing their effects, exposing patients to unnecessary side effects and drug interactions without proper monitoring.[4-6]

Regarding the findings of medication use, the 67 patients who do not use any medication are those that are still under investigation, through laboratory tests. There were still no medical prescriptions for these patients at the time of the study and therefore they were excluded from the analysis.

Comparing the drugs most often mentioned with the diseases for which they are indicated, we found:

- Type 2 diabetes mellitus: biguanine (metformin).
- High blood pressure: diuretics (hydrochlorothiazide), angiotensin converting enzyme inhibitor (enalapril), angiotensin receptor antagonists (losartan).
- Dyslipidemia: hydroxymethylglutaryl-coenzyme A (HMG-CoA) reductase inhibitor (simvastatin).

Diabetes is growing worldwide; it is estimated that 382 million people have the disease and that it should reach 471 million people by 2035.[4] Systemic hypertension showed prevalence > 30% in Brazilian cities in recent years, which means blood pressure (BP) levels ≥ 140/90 mmHg.[7]

Dyslipidemia, a growing disease in Brazil and the world, is one of the risk factors for overweight, along with diabetes. Without medical follow-up, dyslipidemia and obesity may directly affect hepatic steatosis, the second most frequently cited diagnosis. Steatosis can progress to hepatitis and cirrhosis.[8-17]

Comparing the mean age of patients (58 years) and their comorbidities (compatible with the age of these patients and the need for chronic medication use), we found justification for the observation of polypharmacy in all patients.

Based on the classification by Bjerrum et al., we were able to correlate medications and diagnoses. Among the cases of minor polymedication, we found diabetes mellitus and systemic hypertension, while major polymedication was also found in cases of diabetes mellitus and hypertension but with additional drug treatment, which indicates

worsening of the disease.[3] In some cases, there is also the possibility of complications caused by liver disease, such as portal hypertension with the use of propranolol and problems related to hepatitis C and its treatment, including hypothyroidism, which requires levothyroxine.[18]

The observation that only 12 of the 35 patients with hepatitis B virus cite medications for the treatment of this disease is suggestive that inactive diseases may be present in the remaining patients.

A patient with an inactive disease requires specific tests such as normal alanine aminotransferase (ALT) and serum HBV DNA levels below 2,000 IU/mL. The serological profile observed is HBeAg-negative in patients with chronic inactive hepatitis. To confirm the diagnosis of inactive disease over time, it is necessary to perform periodic examinations such as ALT, on a quarterly basis, and measurements of HBV DNA and serum HBsAg levels every 12 months to confirm viral elimination. Given these criteria, pharmacological treatment is not recommended, but medical follow-up of these patients is of paramount importance,[19,20] maintaining them in the secondary care system.

Only two patients out of 172 cited pharmacological treatment for hepatitis C, which may be due to the risk-benefit assessment of drugs available at the time, given their adverse reactions, such as anemia, thrombocytopenia, rash, neutropenia and more. The therapeutic arsenal for the treatment of chronic hepatitis C (ICD-10: 18.2) in the study period was: alpha-interferon 2b, alpha-2 interferon 2a and 2b, ribavirin, epoetin alpha, filgrastim, telaprevir and boceprevir, according to the Clinical Protocol and Therapeutic Guidelines for Chronic Viral Hepatitis C and Coinfections, published in 2013.[21]

With the proposed inclusion of new drugs (sofosbuvir, daclatasvir and semiprevir), which have proven efficacy and minimal adverse reactions, we chose in most cases to await the release of the new drugs. These drugs are currently part of the Clinical Protocol and Therapeutic Guidelines for Chronic Viral Hepatitis C and Coinfections published in 2015, and patients who meet the criteria of this protocol may already benefit from treatment.[22,23]

Conclusion

The results demonstrated that the study population is adult or elderly, with several comorbidities and, therefore, users of polymedication. The fact that patients in general have access to several prescribing physicians and thus the possibility of duplicity of prescriptions is important to ensure rational use of the drug in a multiprofessional team.

The patients treated have diagnoses that are consistent with the Hepatology sector, demonstrating that the referral and counter-referral system can remove this patient from the tertiary health system, but this does not make his or her care less complex, since the patient remains allocated in the three levels of attention.

Resumo

Perfil clínico farmacológico dos atendimentos no ambulatório de Hepatologia

Desde 2010, a Divisão de Gastroenterologia e Hepatologia Clínica do Instituto Central do HC-FMUSP tem desenvolvido atividades assistenciais eletivas especializadas em Hepatologia no Ambulatório de Especialidades Nível Secundário de São Paulo no Estado de São Paulo NGA-63 Várzea do Carmo. O objetivo do estudo é analisar o perfil farmacoterapêutico dos pacientes. Trata-se de um estudo transversal e retrospectivo, no qual pacientes foram atendidos pelo setor de Hepatologia e os dados encontrados foram submetidos à estatística descritiva. Os resultados demonstraram que 492 pacientes foram atendidos nesse ambulatório durante o período do estudo com a média de idade de 58,9 anos, frequência de 61,2% do sexo feminino e 74,8% residindo na capital paulista. Essa população foi atendida por outras diferentes especialidades médicas (cardiologia e endócrino, entre outras), e os principais diagnósticos hepáticos foram hepatite crônica B e C e esteatose hepática. Também foram identificadas comorbidades como diabetes, hipertensão arterial e dislipidemia. Boa parte da população tende a retirar a sua medicação nas Unidades Básicas de Saúde. Foi verificado que 30% dos pacientes fazem uso de mais de cinco medicamentos, sendo os mais prescritos o omeprazol (208; 42,3%), metformina (132; 26,8%) e losartana (80; 16,3%). Por se tratar de uma população adulta/idosa, com diversas comorbidades e com polimedicação, é importante estar atento ao uso racional do medicamento. O atendimento da equipe multiprofissional é importante para aplicar tomadas de condutas corretas para a segurança no uso de medicamentos e diminuir a oneração em gastos em saúde, melhorando a qualidade de vida do paciente.

Palavras-chave: hepatites, medicamento, polifarmácia, assistência ambulatorial, hepatologia, omeprazol.

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