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RESEARCH ARTICLE

RETROSPECTIVE EVALUATION ON PATIENT SCREENING AND COUNSELING SERVICE ON DIRECT-ACTING ANTIVIRALS AGAINST HEPATITIS C

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ABSTRACT

OBJECTIVE

Drug-drug interactions and risk of hepatitis B reactivation potentially affect treatment outcomes of direct-acting antivirals (DAA) against hepatitis C. A comprehensive pharmacist screening and counseling service was implemented in a Hong Kong hospital, which aims to optimize the efficacy and safety of DAA therapy while minimizing the risk of drug wastage. The objective of the service review is to explore potential roles of pharmacist in hepatitis C management.

DESIGN

We retrospectively evaluate all cases under service from June 2017 to September 2018.

MAIN OUTCOME MEASURES

Outcomes measured include drug-related problems (DRP) identified, treatment discontinuation and failure rates.

RESULTS

There were 44 cases under provision of service, all completed therapy except 1 died from underlying disease. 25 DRPs, predominantly categorized as drug-drug interactions, were documented. The interactions commonly involved acid-lowering agents. 1 case was noted with inadvertently lengthening of treatment duration. No cases of treatment failure or hepatitis B reactivation were reported.

CONCLUSION

The safety concerns and high cost of DAA have created a new challenge to healthcare providers. Comprehensive screening and counseling by pharmacists are valuable to ensure safe and effective use of DAA, hence reducing unnecessary drug wastage.

KEYWORDS

direct-acting antivirals, hepatitis C, pharmacist, medication review, drug wastage

INTRODUCTION

Hepatitis C is a contagious liver disease caused by hepatitis C virus (HCV). Around 75-85% of patients infected by HCV become chronically infected. In Hong Kong, infection rate has been estimated to be less than 0.5% for the general population. [1] If left untreated, 15–30% of chronic cases would develop cirrhosis within 20 years, causing substantial mortality from liver failure and hepatocellular carcinoma (HCC). [2]

The major aim of anti-HCV treatment is to eradicate HCV, which has been shown to prevent liver-related complications including HCC and need for liver transplantation. [3] Conventional interferon-based regimen

leads to sustained virologic response (SVR) in only 40-65% of cases. [4] The unfavorable adverse event profile further compromises treatment outcomes due to early discontinuation of treatment. Since 2011, the ongoing development of direct-acting antivirals (DAA) has achieved >90% SVR with improved tolerability. [5] Nonetheless, the high cost of DAA therapy has limited the access to new treatment worldwide. [6, 7] Concerns for drug-drug interaction and risk of hepatitis B virus (HBV) reactivation may also affect treatment efficacy and safety.

In view of the potential risk and huge cost of DAA therapy, a comprehensive pharmacist screening and counseling service has been implemented in a Hong Kong public hospital since 2017. The service aims to maximize the clinical benefits while minimizing the risk of treatment failure and subsequent drug wastage. The purpose of this study was to explore the potential role of pharmacist in hepatitis C management under the service model.

METHODS

The study retrospectively reviewed all cases under the pharmacy screening and counseling service since June 2017 to September 2018 for evaluation. All patients were included if any of the following DAA was prescribed: sofosbuvir/ledipasvir,ombitasvir/paritaprevir/ritonavir/dasa-buvir, sofosbuvir/velpatasvir, asunaprevir/daclatasvir or sofosbuvir, with or without ribavirin. Patients were excluded if the DAA therapy was started outside the hospital.

SERVICE SETTING

The service for clinical screening and counseling for hepatitis C patients on DAA therapy was established under the collaboration of gastrointestinal specialists and pharmacists in United Christian Hospital, a public hospital under Hong Kong Hospital Authority. Within the service framework, all patients first prescribed with DAA were referred to clinical pharmacist for medication review. For each case, clinical pharmacist reviewed the appropriateness of the DAA regimen based on the HCV genotype, prior treatment history, baseline liver and renal function. Particular focus was made on patient's medical history and medication profile to check for potential drug-drug interaction and other disease precautions, for instance, risk of HBV reactivation. After the regimen verification, clinical pharmacist provided patient counseling on the administration schedule of DAA, possible adverse drug reactions including preventive and self-management measures, as well as the importance of medication adherence. While DAA therapy typically ranges from 8 to 24 weeks, pharmacist dispensed the medications as short refills every 4 to 6 weeks. If any drug-related problems were identified during initial review or subsequent refills, appropriate advice was provided for issues manageable at pharmacy level. Otherwise, the case was referred back to specialist clinic for further work-up by physicians. Throughout the service, the procurement team was informed of each individual's regimen schedule to ensure a subsequent supply of the medication.

DATA COLLECTION

Patient demographics and relevant clinical data, including medical history, medication profile, HCV genotype, HBV serology, SVR at 12 weeks (SVR 12), renal and liver function, were collected from the electronic medical record. Documented drug-related problems (DRPs) and pharmacist intervention were retrieved from pharmacist notes of the service.

OUTCOMES

Primary outcome was the number and type of drug-related problems identified under the service. Secondary outcomes include treatment discontinuation and failure rates.

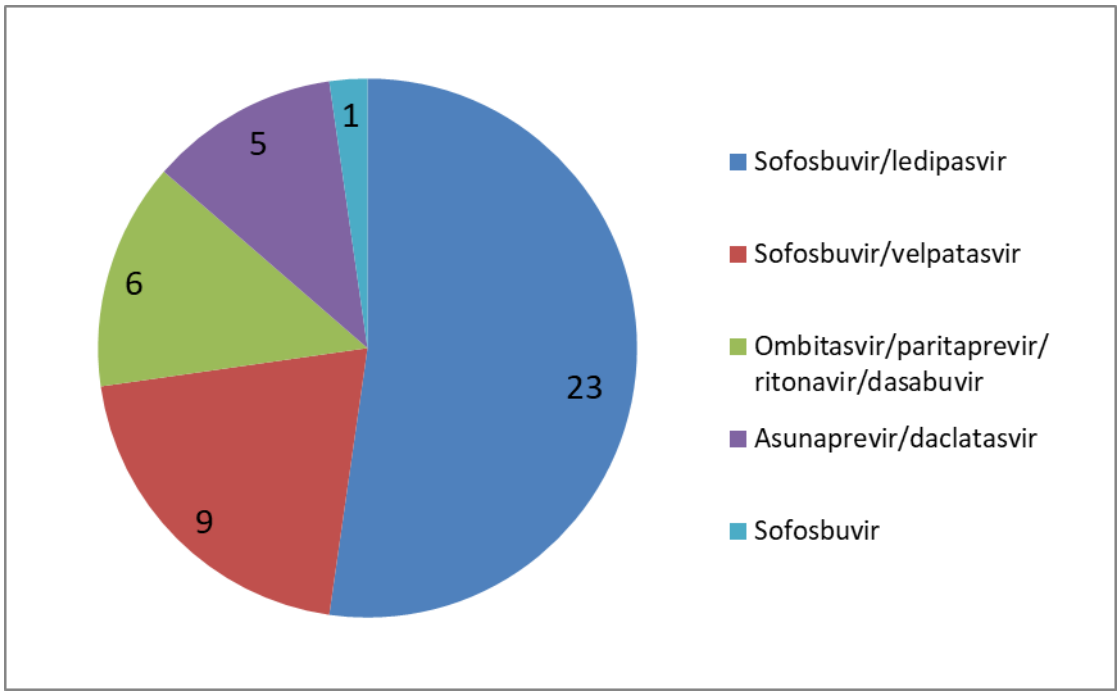
FINDINGS

Within the captioned period, a total of 44 cases were referred to the service. Table 1 illustrated the baseline demographics of the cases. 42 cases completed the DAA therapy uneventfully, and 1 case required regimen modification due to ribavirin intolerance. 1 case deceased from underlying advanced cirrhosis during the DAA therapy

TABLE 1. PATIENT DEMOGRAPHICS (N=44)

CHARACTERISTIC		NUMBER (%)
MEAN AGE (± SD)		61.5 ± 9.2
SEX – MALE		28 (63.6)
CIRRHOSIS	Child Pugh class A	28 (63.6)
	Child Pugh class B	1 (2.3)
	Child Pugh class C	2 (4.5)
PRESENCE OF HBSAG		3 (6.8)
TREATMENT EXPERIENCED		19 (43.2)
CO-MORBIDITY	Hypertension	22 (50)
	Diabetes Mellitus	11 (25)
	Gastrointestinal disorders	10 (22.7)
	Hepatocellular carcinoma	7 (15.9)
MEAN NUMBER OF MEDICATIONS (± SD)		4.3 ± 2.7

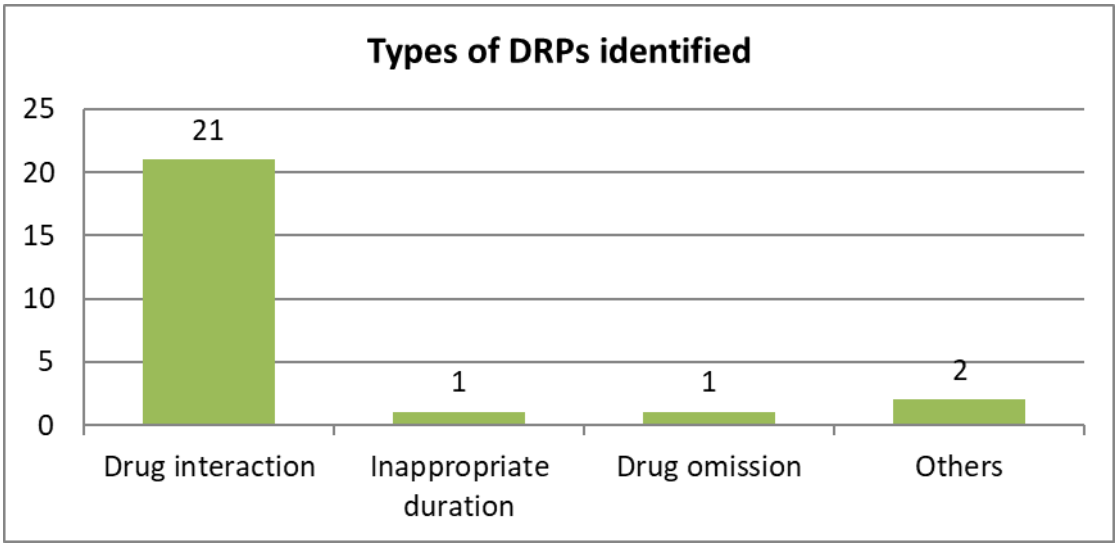
FIGURE 1. DAA PRESCRIPTION PATTERN



For the 43 patients who finished the DAA therapy, no cases of treatment failure were reported in terms of SVR 12 results. Hepatitis B reactivation was not detected in the 3 cases with hepatitis B co-infection. 25 DRPs were identified as illustrated in Figure 2. The most common DRP was drug-drug interaction. Around 62% of the interactions involved acid-lowering agents, while the remaining was attributed to CYP450 inhibitors. Pre-emptive treatment of hepatitis B was omitted in 1 case with hepatitis B co-infection. 1 case was documented with inadvertently prolonged DAA regimen

(24 weeks) beyond standard recommendation (16 weeks). Other DRPs identified involved suboptimal laboratory monitoring. In response to the DRPs, 21 pharmacist interventions were made. 17 cases were provided with pharmacist advice, and 4 required physician referrals.

FIGURE 2. DRPS IDENTIFIED FROM THE SERVICE



DISCUSSION

While various HCV guidelines strongly recommended treatment in nearly all patients with chronic hepatitis C infection, budgeted healthcare providers often prioritized DAA regimen to those with the greatest need due to cost concern. [3, 8, 9] According to the local formulary control, use of DAA was restricted to chronic hepatitis C patients with certain stage of fibrotic changes in liver. Therefore, it was expected to find majority of the patients under service care were suffering from different degree of hepatic impairment. After longstanding history of chronic HCV infection, many patients were approaching elderly ages with co-morbidities including hypertension, diabetes mellitus and gastrointestinal disorders. These co-morbid conditions were managed by physicians from different specialties, so polypharmacy was not uncommon. Even for those non-complicated cases, the choice of DAA alone was already a challenge to healthcare professionals. There were sophisticated pathways in choosing the preferred DAA regimen based on different HCV genotypes and prior treatment history. All these factors put patients at risk for DRPs where pharmacists could contribute.

Despite the limited service scale, it has demonstrated that drug-drug interaction poses a significant obstacle in optimizing DAA therapy. Similar results were reported in other studies evaluating patients on DAA, with or without HIV co-infection. [10, 11] From our results, the interaction was mostly caused by acid-lowering agents. This was likely driven by the prescribing pattern of predominately sofosbuvir/ledipasvir and sofosbuvir/velpatasvir. Acid-lowering agents are extensively used in common gastrointestinal ailments, and furthermore, many of such products are readily available as over-the-counter medicines. Such interaction was easily overlooked as patients might not disclose proactively. Pharmacist input on comprehensive screening and patient counseling could reduce the risk of treatment failure or toxicities due to hidden interaction.

While there is boxed warning by FDA on risk of HBV reactivation for DAA, [12] it is more concerning for Southeast Asia, being one of the endemic regions for HBV infection. [13] As the complication may cause fulminant liver damage, it is the local practice to screen all patients for HBV serology before DAA initiation. Positive cases for hepatitis B surface antigen (HbsAg) were also prescribed with HBV antivirals in addition to DAA, otherwise, intensive monitoring of liver function and HBV DNA were performed. Although only 3 cases were co-infected with HBV in the study cohort, 1 was missed for HBV treatment, suggesting

potential role of pharmacist in HBV screening and monitoring.

As standard of care, medications were dispensed according to the prescription duration, usually until the next medical follow-up. However, in view of the long follow-up interval after first medical follow-up, short medication refills were arranged to facilitate early detection of DRP with prompt intervention by pharmacists. If patients required early treatment interruption, appropriate control in procurement and dispensing could reduce drug wastage. As the local daily DAA treatment cost over US$320–$570, the prevention in drug wastage would translate into huge financial implications for the healthcare system.

As confined by the limited service scale, the study could only discover common risks and challenges in initiating DAA therapy in local population. There was also lack of comparison data on the outcomes of pharmacist intervention. Larger studies covering newer generations of DAA may provide more robust evidence for establishing service models to optimize hepatitis management.

CONCLUSION

The introduction of DAA has created challenge to healthcare providers in hepatitis C management. Patients on DAA commonly encountered DRPs involving drug-drug interactions which may compromise treatment efficacy with huge cost impact. The study provided preliminary evidence on pharmacists' impact on medication management in patients with chronic hepatitis C infection. Through comprehensive medication review and detailed counseling, pharmacists played a role in identifying drug-related problems with prompt intervention to ensure safe and effective use of DAA, thus reducing unnecessary cost wastage.

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