Clinical Pharmacists Intervention to Optimize the Management of a Patient with Chronic Hepatitis B: A Case Report

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Abstract
Hepatitis B infection is caused by the hepatitis B virus which infects the liver leading to hepatocellular inflammation and necrosis. Infected persons can either present with acute or chronic disease. Persons may also present with asymptomatic infection, mild disease, severe or rarely fulminant hepatitis. Acute hepatitis B is often associated with acute inflammation and hepatocellular necrosis, usually self-limiting. Chronic hepatitis B infection is however defined as persistent hepatitis B virus infection, which is the presence of detectable hepatitis B surface antigen in the blood or serum for more than six months, with or without active viral replication and evidence of hepatocellular injury and inflammation. We present a case of a young African adult male with chronic hepatitis B infection who reported to the community pharmacy to purchase a medication. Upon further questioning, pharmaceutical care issues identified by the clinical pharmacist included the need for initial patient assessment, clinical evaluation and laboratory investigations at a hospital before recommendation of medication therapy, invalid prescription, wrong choice of pharmacological agent as first-line antiviral therapy, and the need for patient counselling. Interventions by the clinical pharmacist resulted in patient being seen at the hepatobiliary clinic of a tertiary teaching hospital. This led to optimized patient management, positive patient outcomes and improved quality of life.

Keywords: Clinical pharmacist, Intervention, Chronic hepatitis B, Community pharmacy

Case Presentation

A 30-year-old African male reported to a community pharmacy with an invalid prescription for "tablet lamivudine 300mg daily". The clinical pharmacist at post realized that vital information such as name and address of the prescriber, date of the prescription, name and address of the patient, duration of therapy and prescriber's signature had not been indicated on the prescription. Upon further questioning by the pharmacist, the patient explained that he attended a routine health screening in his community and was informed of a positive hepatitis B test. He was therefore advised by a member of the screening team to do a complete hepatitis profile test at a laboratory which confirmed that he had hepatitis B, after which a person prescribed for him tablet lamivudine 300mg daily.

The clinical pharmacist declined to supply the medication since the prescription was not valid, and the medication had been prescribed outside a hospital setting without the authorization of a prescriber. Furthermore, the pharmacist observed that initial patient assessment, clinical evaluation and other essential laboratory investigations had not been conducted before the medication was prescribed. It was also noticed that tablet lamivudine is not the recommended first-line antiviral medication for management of chronic hepatitis B (CHB) infection, and the medication had been prescribed without thorough patient counselling on the indications for treatment, including likely benefits and side-effects.

The pharmacist therefore counselled the patient extensively on CHB, its course of disease, mode of transmission and the cofactors likely to accelerate disease progression. The patient was then advised to visit a nearby hospital, from where he was referred to the hepatobiliary clinic of a tertiary teaching hospital for thorough assessment and investigations. The clinical Pharmacist followed up on the patient and ensured that he visited the hepatobiliary clinic. The pharmacist further

communicated with, and liaised with the medical team during patient's review and assessment at the hospital.

At the hepatobiliary clinic, the patient explained to the doctors that he had no complaints. He added that a pharmacist advised him to seek for medical attention when he attempted to buy a medication recommended for him after a positive hepatitis B profile test. Patient's social history revealed that he was not married and had no child. He had a girlfriend who resided in a different house in his community. He was sexually active and admitted to engaging in unprotected sexual intercourse with his girlfriend. Patient added that he lived alone in a rented apartment close to his family house where his mother and sisters resided, and that he often visited his family house to see his mother and sisters. The patient was a pupil teacher who did not take alcohol or smoke and had no history of recreational drug use. His past medical history revealed a previous *Salmonella typhi* infection 8 years ago, apart from which he could be described as being in a good state of health. He had no history of surgery or blood transfusion. Patient also had no known family history of hepatitis B infection, CHB infection, cirrhosis and hepatocellular carcinoma (HCC). He added that his father died three years ago with cause of death unknown to him.

Relevant signs identified and documented after thorough patient evaluation included no history of jaundice, abdominal pain, pruritus, pale stool, darkened skin, nausea or anorexia. Patient was anicteric, afebrile, and not pale. His chest was clear, and his abdomen was soft and non-tender. The patient also added that he had no history of easy fatigability and mid-upper quadrant pain or discomfort. Patient's risk factors included his African race, male sex, low socioeconomic status, no previous hepatitis B test or vaccination and engaging in unprotected sex. The patient had not taken any prescription medications within the past six months prior to being seen at the hospital and had no known allergies. He admitted that he had no routine exercise schedule, and that according to his mother, he did not receive any childhood vaccination during infancy. He was observed to be very cooperative and attentive, both at the community pharmacy and the hospital, and had no suspected medication adherence concerns.

Laboratory investigations conducted at the hospital revealed that the patient's liver function test and full blood count results were within normal limits. His haemoglobin count was 14.8g/dL (normal 11.0-18.0g/dL), platelet count was 268 $x10^{12}$/L (normal 150-450 $x10^{12}$/L), and white blood cell count was 7.49 $x10^{9}$/L (normal 2.5-8.5 $x10^{9}$ /L). Patient's level of aspartate aminotransferase (AST) was 28 U/L (normal 15-46U/L), alanine aminotransferase (ALT) was 29U/L (normal 13-69U/L) and alkaline phosphatase (ALP) was 40U/L (normal 38-126U/L). Patient's albumin level was 45g/L (normal 35.0-50.0g/L). He tested negative for hepatitis C virus. His hepatitis B profile test revealed that he was hepatitis B surface antigen (HBsAg) reactive, hepatitis B surface antibody (Anti-HBs) non-reactive, hepatitis B e-antigen (HBeAg) non-reactive, hepatitis B e-antibody (HBeAb) reactive and hepatitis B core antibody (HBcAb) reactive. Comments from the hepatitis B profile test confirmed that he had CHB infection with non-replicating virus. His hepatitis B viral deoxyribonucleic acid (DNA) load was 321 IU/mL, alpha-fetoprotein (AFP) was 7.37 IU/mL (normal<10 IU/mL) and he had an aspartate aminotransferase to platelet ratio index (APRI) Score of 0.261. The patient's abdomino-pelvic ultrasound scan was normal, indicating that his liver was of average size measuring 142.8mm midclavicular line (MCL) with homogeneous echo pattern. No focal mass or diffuse lesions were identified, and no intra or extra hepatic bile duct dilation was observed. Based on the patient assessment, clinical evaluation and laboratory investigations, the patient's medical problem was confirmed by the doctors at the hospital as CHB infection with non-replicating virus. Patient could therefore be described as being in the immune inactive phase. With an ALT level of 29U/L, HBV DNA load of 321 IU/mL, an APRI Score of 0.261, the medical team decided that patient did not require pharmacological therapy, and as such he was not given any antiviral medication. He was however referred to the gastrointestinal clinic, where he was asked to report in six months for further monitoring for disease progression.

Discussion

This report highlights the important role of a clinical pharmacist's interventions in the management of patients with chronic diseases such as CHB infection at community pharmacies. Pharmaceutical care issues identified by the pharmacist included the need for initial patient assessment, clinical evaluation and laboratory investigations at a hospital before recommendation of medication therapy, inappropriate pharmacotherapy outside the hospital setting, inappropriate choice of medication as first-line antiviral therapy, presentation of an invalid prescription and the need for patient counselling on his medical condition.

Inappropriate pharmacotherapy outside the hospital seEng

The goal of antiviral therapy for CHB is to reduce or prevent adverse outcomes such as necroinflammatory change and hepatic fibrosis leading to progressive liver disease, cirrhosis, decompensated cirrhosis and liver failure, HCC and death (Lampertico *et al*., 2017; Terrault *et al*., 2018). Initiating antiviral therapy is usually based on a combined assessment of the stage of liver disease from clinical features, and increasingly on blood or ultrasound-based non-invasive techniques, together with levels of serum ALT and HBV DNA (World Health Organization, 2015; Lampertico *et al*., 2017; Terrault *et al*., 2018; Kim, 2019). The decision to treat is usually clear in persons who present with life-threatening or advanced liver disease, such as acute liver failure, and compensated or decompensated cirrhosis and acute-on-chronic liver failure. In persons who have not yet progressed to cirrhosis, treatment plans are also based on ALT and HBV DNA levels (World Health Organization, 2015). It is important that antiviral therapy is targeted to the active phases of CHB when the risks of disease progression are greatest and, conversely, when persons with minimal fibrosis and low risk of CHB progression are identified, as they do not require antiviral therapy(World Health Organization, 2015; Terrault *et al*., 2018). Several guidelines recommend that as a priority, antiviral therapy is not recommended and can be deferred in persons without clinical evidence of cirrhosis or based on APRI score ≤2

in adults, who have persistently normal ALT levels and low levels of HBV replication (HBV DNA <2000 IU/mL) regardless of HBeAg status or age (World Health Organization, 2015; Lampertico *et al*., 2017; Terrault *et al*., 2018; Kim, 2019). Therefore, prescription of tablet lamivudine 300mg daily outside a hospital setting after the patient repeatedly tested positive to the hepatitis B profile test was not in conformity with recommendations by the guidelines and findings from several studies (World Health Organization, 2015; Lampertico *et al*., 2017; Terrault *et al*., 2018; Kim, 2019).

Inappropriate choice of medication as first-line antiviral therapy

Antiviral medications approved for the management of CHB include lamivudine, adefovir, entecavir, telbivudine, tenofovir, emtricitabine, standard and pegylated interferon (PEG-IFN) (World Health Organization, 2015; Sarin *et al*., 2016; Tang *et al*., 2018). In all adults, adolescents and children aged 12 years or older, in whom antiviral therapy is indicated, the Nucleot(s)ide Analogs (NAs) which possess a high barrier to drug resistance such as tenofovir or entecavir are recommended ''(World Health Organization, 2015; Lampertico *et al*., 2017; Terrault *et al*., 2018; Kim, 2019). Some studies have also revealed that NAs with a low barrier to resistance such as lamivudine, adefovir and telbivudine can lead to drug resistance and are not recommended as the first-line antiviral therapy for the management of CHB (Hanlon, Lindblad and Gray, 2004; Bishop *et al*., 2019; Hamada *et al*., 2019). Therefore, choice of tablet lamivudine for the patient was inappropriate. Furthermore, some studies have shown renal functional decline that is frequently observed during the pharmacological treatment of CHB can exert adverse effects on overall patient prognosis (Shin *et al*., 2016; Kayaaslan and Guner, 2017). As a result, it is recommended that the measurement of baseline renal function and assessment of baseline risk for renal dysfunction are considered in all persons prior to the initiation of antiviral therapy (World Health Organization, 2015; Shin *et al*., 2016; Kayaaslan and Guner, 2017). This was not done before recommendation of tablet lamivudine for the patient, inconsistent with recommendations from guidelines and studies. Through the encouragement of the pharmacist, the patient was seen at the hepatobiliary clinic of a tertiary teaching hospital for further evaluation and management. This helped to identify the stage of patient's CHB and influenced the decision of the multidisciplinary team not to offer pharmacological management based on findings after thorough patient assessment (World Health Organization, 2015; Lampertico *et al*., 2017; Terrault *et al*., 2018; Kim, 2019).

The need for patient counselling on CHB

Cofactors that are likely to accelerate disease progression, the risk and modes of onward disease transmission and the need for long-term follow up should be explained to patients with CHB. Individuals who are HBsAg positive should, in addition, be counselled to adopt correct and consistent condom use during sexual intercourse if their partners are neither HBV immune nor have been vaccinated. Furthermore, patients should be advised not to share razors, toothbrushes or other personal care items with their partners or other persons in their household. Patients should be advised not to donate blood, organs or sperm and follow standard universal precautions with open cuts or bleeding. Household members and sexual partners of persons with CHB are at increased risk of HBV infection and should be vaccinated if they test negative for hepatitis B virus serological markers(World Health Organization, 2015; Terrault *et al*., 2018). CHB patients must be counselled on healthy eating habits since the optimization of body weight and treatment of metabolic complications such as diabetes and dyslipidaemia, are recommended to prevent concurrent development of metabolic syndrome and fatty liver(Hepler and Strand, 1990; Al-Quteimat and Amer, 2016; Soumya *et al*., 2016; Alves da Costa, van Mil and Alvarez-Risco, 2019). As such, thorough counselling offered to the patient by the clinical pharmacist helped to enlighten patient about his medical condition and empowered him to honour scheduled hospital visits and make healthy decisions (Wong *et al*., 2014; Chan *et al*., 2017; Yip *et al*., 2018; Merli *et al*., 2019).

Monitoring of persons who do not yet meet the criteria for antiviral therapy is recommended to ensure swift identification of a change in patient clinical status. The change in patient clinical status could manifest as the development of clinical features of cirrhosis or an APRI score >2 in adults, development of HCC or a rise in ALT or HBV DNA levels. These changes may be indicators of progression to active disease requiring treatment. It is recommended that parameters such as the ALT levels, AST, HBsAg, HBeAg, and HBV DNA levels are monitored together with non-invasive tests such as APRI score, at least, annually (Seto *et al*., 2014; Lampertico et al., 2017; Terrault et al., 2018). Therefore involvement of the clinical pharmacist in ensuring that the patient keeps to his follow up schedules by reporting to the gastrointestinal clinic every 6 months for monitoring of his parameters helped to optimize patient's care (Seto *et al*., 2014; Lampertico *et al*., 2017; Terrault *et al*., 2018).

Presentation of an invalid prescription

A study conducted on the quality of written prescriptions of general practitioners in Pakistan revealed that the use of structured prescriptions improve the quality of written prescription in terms of completeness and legibility (Raza *et al*., 2016). According to the WHO, information such as name and address of the prescriber, date of the prescription, name of the medication prescribed with strength and dosage form, the total amount of medication to be dispensed or duration of therapy, directions for use, name and address of the patient and prescriber's signature are important features that are looked out for on prescriptions by pharmacists (De Vries *et al*. 2014, Smith, 2019). One of the crucial roles played by clinical pharmacists is to ensure that all prescriptions are legally complete and clinically appropriate for patients. Thus, pharmacists are required to ascertain that all information that are essential for selection and dispensing of the appropriate medication are available on the prescription. Pharmacists are also expected to take the necessary actions to ensure that any information that is missing or ambiguous is verified on the prescription before the prescribed medication is dispensed. Such action may include

returning the prescription to the prescriber for missing information to be added and inaccurate information corrected (Smith, 2019). Action taken by the clinical pharmacist not to dispense the medication due to invalidity of prescription was therefore consistent with recommendations from a cross-sectional study conducted by Soumaya R *et al*. on drug dispensing practices of pharmacists(Soumya *et al*., 2016).

Conclusion

Clinical pharmacists' interventions in community pharmacies can lead to optimized patient management.

Consent

Informed consent was obtained from the patient in the publication of this case report.

Conflicts of Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

Funding Statement

This research did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sectors.

Acknowledgment

The authors would like to thank Dr. Asare Offei, consultant hepatobiliary surgeon, Department of Surgery, Korle Bu Teaching Hospital for his assistance in management of the patient.

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