Effect of a Cooperation Strategy between Primary Care Physicians and Hospital Liver Units on HBV Care in Campania, Italy

Rosa Zampino,1,2 Nicolina Capoluongo,3 Adriana Boemio,1 Margherita Macera,3 Martina Vitrone,1 Luigi Elio Adinolfi,1 Pietro Filippini,3 Evangelista Sagnelli,3 Caterina Sagnelli,4 Emanuele Durante-Mangoni,2,4 and Nicola Coppola3

1Department of Medical, Surgical, Neurological, Metabolic and Geriatric Sciences, University of Campania "L. Vanvitelli", Italy
2Unit of Infectious & Transplant Medicine, "V. Monaldi" Hospital, AORN dei Colli, Naples, Italy
3Infectious Diseases Unit, Department of Mental and Physical Health and Preventive Medicine, University of Campania "L. Vanvitelli", Italy
4Department of Precision Medicine, University of Campania "L. Vanvitelli", Italy

Correspondence should be addressed to Rosa Zampino; rosa.zampino@unicampania.it

Received 1 April 2018; Revised 30 June 2018; Accepted 8 July 2018; Published 26 July 2018

Aims. This study is aimed at assessing the efficacy of an active search and treat strategy for HBV-infected subjects in an endemic area (Campania, Italy). To do this, we created a cooperation bundle between 24 General Practitioners (GPs) and 3 Hospital Liver Units (HLU). We assessed whether this strategy improved the detection of HBV infection in patients at risk and the overall quality of care, with the aim of reducing liver disease progression.

Methods. We estimated that, among about 20,000 patients cared for by the 24 GPs, approximately 280 patients unaware of or underestimating HBV infection would be found. Identified patients were to be referred to the HLU for clinical evaluation and treatment from February 2016 for 12 months.

Results. Unexpectedly, screening and enrolment were poor (48 patients only). GP workloads, patient financial difficulties, and patients’ refusal were the major causes of enrolment failure according to GPs. All patients referred to HLU completed the program; most of them were HBV inactive carriers.

Conclusions. This program failed to scavenge chronic HBV-infected patients in an endemic area and establish a successful clinical collaboration between GPs and HLU. Underlying reasons are diverse and call for new strategies to implement cooperation between primary care providers and hospital specialists.

1. Introduction

In recent decades, a progressive reduction in the incidence of acute hepatitis B (AHB) and the prevalence of HBV-related chronic hepatitis has been observed in endemic areas, such as the Campania region of Italy, as a result of improved socioeconomic conditions and universal vaccination [1–3]. The current incidence of AHB is about 1/100,000 inhabitants per year, 15% of cases involving the immigrant population [4], and the prevalence of HBsAg carriers is estimated at nearly 1% in the native population and 3-10% in documented immigrants (regular immigrants who arrived in Italy for economic reasons and have now stable work and residency). It is estimated that 600,000 Italians and nearly 250,000 immigrants are chronic carriers of HBV infection, of whom 50% and 70%, respectively, are unaware of their virological condition [4]. These subjects may transmit HBV infection and remain untreated, even when treatment is warranted [4].

Italian General Practitioners (GPs) are the physicians providing primary care and are usually overwhelmed by a considerable number of patients with symptomatic diseases, leaving them little time for asymptomatic patients, such as
most HBsAg-positive patients. Consequently, most of them are not referred to a hepatologist for screening, follow-up, treatment (when necessary), and the implementation of preventive measures [5, 6]. Previous experience showed the benefit of GP involvement in screening strategies to reduce the number of undiagnosed hepatic infections and clarify the prevalence and correlates of the different risk factors [7, 8]. This cooperation could improve the quality of care and the cost-benefit ratio.

We applied a clinical bundle to first actively screen, identify, and treat HBV infection in subjects unaware of their virological condition in Campania, Italy, and refer them to a Hospital Liver Unit (HLU) for clinical evaluation and antiviral treatment, when indicated. A second aim was to create a network between GPs and hepatology specialists to improve the quality of care (diagnosis, clinical evaluation, follow-up, and treatment). The ultimate aim was to reduce the progression of liver disease to cirrhosis, the development of hepatocellular carcinoma (HCC), the risk of in-house and sexual transmission of HBV infection, and the cost of management.

2. Methods

We contacted two GP associations in Naples and a group of GPs in Caserta to illustrate the program and seek their participation. One of the GP associations did not join the program because of excessive prior workload, while other GPs gave their full availability to participate. In Caserta, of 15 GPs invited, 5 joined the program. GPs use a database for their clinical records, which we thought would be useful tool to screen data and identify patients’ anthropometric measures, clinical history, and current pharmacologic treatment.

Within this network, we tried to apply to a large primary care population methods similar to those successfully used in an ongoing study performed to identify and manage HBV infection in irregular immigrants and refugees [9].

2.1. Study Design. The planned duration of the program was one year. On the basis of chronic HBV infection prevalence in Campania [4] and the number of subjects cared for by the GPs participating in this program, we estimated that in a cohort of about 20,000 subjects (at least 20 GPs randomly involved) approximately 280 citizens with HBV infection would be found. An educational meeting with participating GPs was held to discuss the study protocol and review HBV epidemiology, pathophysiology, and treatment. Posters illustrating the “Scavenge HBV in Campania” program were put up in the GPs’ offices to inform subjects and sensitize them towards HBV infection. The essential role of the GPs in alerting HBV carriers was stressed. A financial support to put up in the GPs’ offices to inform subjects and sensitize them towards HBV infection. The essential role of the GPs in alerting HBV carriers was stressed. A financial support to

The study was conducted in accordance with the rules of the Good Clinical Practice and the protocol and procedures were approved by the Ethics Committee of the University of Campania “L. Vanvitelli”.

3. Results

The program started in February 2016 with the involvement of 25 randomly selected GPs. As only 33 patients from 15 of 25 GP offices were enrolled during the initial 4 months of study, we decided to extend the bundle to all 116 GPs included in the GP association (Figure 2).

3.1. Enrollment. The analysis of the GP databases at the beginning of the study identified 282 known HBsAg-positive patients. However, many of these patients either were not involved by GPs or were misclassified as HBsAg-positive. Moreover, less than 50% of patients who were anticipated to have risk factors for HBV infection and/or elevated ALT were screened. The reasons for such a low enrolment rate
were reported only by a small number of GPs and are summarized in Table 1. GP workloads (many patients with different symptomatic disorders to follow), patients’ financial difficulties, and simple refusal to participate were the most frequently reported. Furthermore, diabetes mellitus and oncohematologic diseases were considered a priority by some GPs compared to possible or asymptomatic liver disease.

Eleven GPs did not refer patients to the specialist liver units stating these were already followed up at other HLU (6 GPs) or due to lack of any HBsAg-positive subject in their patient population (5 GPs) (Figure 2).

An analysis performed by a member of the HLU specialists’ team, who was in direct contact with GPs, revealed common mistakes in the GP databases, with patient misclassification regarding ALT values or HBV status or failure to update past test results. In particular, 30% of patients who were meant to be HBsAg-positive were in fact HBsAg-negative. This likely caused the initial overestimation of the number of patients available for the study.


3.2. Referral to Hospital Liver Units. Although the percentage of HBsAg-positive subjects referred was much lower than expected, among the identified patients, only 4 declined to continue HLU follow-up after screening.

Overall, 44 referred patients as known or presumed HBsAg-positive started screening at the HLU. Of them, 14 (32%) were actually found to be HBsAg-negative when tested at the HLU laboratory and were instead anti-HBs-positive. Thus, 30 HBsAg-positive patients were finally included in the HLU follow-up.

3.3. Specialist Follow-Up. Specialist follow-up was highly successful, as all 30 HBsAg-positive subjects referred concluded the diagnostic, clinical, and therapeutic (where indicated) course. A clinical and laboratory report for the GP was given to each patient at the end of the evaluation and a schedule for the following appointments.

3.4. Data of HBsAg Patients Enrolled. Table 2 summarizes clinical, biochemical, and virological data of the 30 patients enrolled. Twenty-seven patients were Italian and 3 were immigrants (2 from Benin and 1 from Brasil). They had a median age of 59.5 years and a median BMI of 27 and were mostly free of significant comorbidities. Among them, a high prevalence of HBV inactive carriers was observed, defined as presence of serum antibodies to HBeAg (anti-HBe), undetectable or low (< 2,000 IU/ml) HBV DNA levels, and normal ALT [11]. HBV DNA was undetectable in 8 patients. No patient showed HCV or HDV coinfection. Liver disease was generally mild, with liver function tests within normal values and no signs of liver disease progression and/or HCC. Liver fibrosis assessment was performed by transient elastography in 15 patients (median 5.4 kPa, range 4.0 - 12). This test was not performed in patients with undetectable HBV DNA or in those who refused. However, all patients started a standard clinical follow-up. Ultrasound evaluation was performed in all patients: a bright liver echo-pattern was observed in 6 patients, a coarse pattern was observed in 2 patients, and signs of portal hypertension (increased portal vein and/or spleen diameter) were present in 3 patients. No other clear alteration in the liver echo-pattern was described in the remaining patients.

Household spread of the virus or surgery and dental procedures were the most common risk factors for HBV infection. More than 30% of the analysed patients consumed alcohol daily. Only 2 patients needed antiviral treatment and were started on entecavir and tenofovir, respectively.

4. Discussion

This study shows that, despite our structured attempt to establish a cooperation between GPs and HLU specialists, we failed to effectively identify all HBsAg-positive cared subjects and significantly reduce the number of those not receiving specialist care. In fact, our results highlight the obstacles to an effective primary care detection of hepatitis B infection in an endemic area, the Campania region of Italy.

The major drawback of our bundle was the poor effectiveness of HBV screening. GPs reported that enrolment failure was related to their “excessive workload”, consisting in too many patients to care for with different and complex diseases, coupled with difficulties in practical organization and simultaneous engagement with other ongoing projects in unrelated fields of medicine. After early detecting these difficulties, we extended the number of GPs involved in the program, in the hope that additional GPs would be more successful in their screening efforts. As a matter of fact, only
Overall and only 30 were finally assessed. 48 of the 282 anticipated HBV-positive patients were referred for evaluation. In the “scavenged” HBV patients, the most frequent risk factors were related to iatrogenic transmission; this is in agreement with the senior age of most patients and an infection acquired many years before.

Cooperation with GPs is necessary to “scavenge” asymptomatic diseases in the general population. Studies in other settings reported variable results in the screening and evaluation of liver diseases of different etiologies. Some studies identified problems in screening or basic knowledge [7, 8, 14–18], and others obtained very good results [19, 20].

Although our experience was not entirely satisfactory, we are firmly convinced that the involvement of primary care providers in the management of HBV infection is pivotal. Starting from the results of this study, we hypothesize some approaches to implement the outcome of such studies.

(i) Organizing periodic (i.e., every 2-3 months) educational meetings to raise GPs awareness on specific epidemiologic and clinical problems.

(ii) Organizing periodic hospital meetings between GPs and specialists to discuss the results obtained and critically assess the ongoing programs.

(iii) Alerting the population through media information campaigns, so that they, themselves, ask their GPs for screening and subsequent clinical investigation.

(iv) Offering GPs public financial incentives proportional to their enrolment commitment.

(v) Offering free screening tests for indigent subjects.

(vi) Strengthening the idea of patient well-being and scientific and/or social gratification to stimulate study participation.

Data Availability

This manuscript is the description of a cooperative approach between primary care physicians and liver units and offers suggestions to improve this kind of cooperation. Numerical data concern only 30 patients involved in the study and are clearly shown in the manuscript and table.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Acknowledgments

This work has been supported by an unrestricted grant from Gilead Science Ltd., goShape Program 2015 (Grant no. 000/IHQ/15-09//1686).

References


