Evaluation of HBV-DNA Monitoring after Completion of Chemotherapy using a PDCA Cycle following Introduction of a Support System Provided by a Multidisciplinary Team of Quality Management in Cancer Medicine

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Abstract: *Background:* Reactivation of the hepatitis B virus (HBV) during or after chemotherapy remains a notable clinical concern, particularly among patients with previous exposure to HBV. However, in clinical practice, adherence to HBV-DNA monitoring after completing chemotherapy is often sub-optimal.

Methods: We developed and implemented a support system based on the plan–do–check–act (PDCA) cycle to ensure 12-month HBV-DNA monitoring after the completion of chemotherapy. This system was designed to enable continuous follow-up after a cessation of chemotherapy, and a multidisciplinary team of quality management in cancer medicine established a feedback system to provide timely information for physicians. Adherence to HBV-DNA monitoring before and after introduction of the system was compared, and the reasons for discontinuation were investigated.

Results: Compared with the pre-intervention group, there was a significant improvement in the rate of HBV-DNA monitoring in the post-intervention group ($p < 0.01$). In this group, 16 patients (33.3%) were lost to follow-up after chemotherapy due to death or transition to hospice or home-based care.

Conclusions: The support system provided by a multidisciplinary team of quality management in cancer medicine effectively improved adherence to HBV-DNA monitoring after the completion of chemotherapy. However, it also revealed that some patients could not be followed up immediately after the completion of treatment given their deteriorating general condition.

Keywords: PDCA cycle, HBV reactivation, chemotherapy, multidisciplinary team of quality management in cancer medicine, HBV-DNA monitoring.

INTRODUCTION

The reactivation of the hepatitis B virus (HBV) that can occur during and after chemotherapy is a clinically relevant issue, particularly in patients with a history of HBV infection [1-3]. Japanese guidelines recommend regular monitoring of HBV-DNA during and after chemotherapy in patients with past HBV infections [4]. However, adherence to post-treatment HBV-DNA monitoring is often inadequate in clinical settings [5,6]. With a view toward improving adherence to HBV-DNA monitoring after the completion of chemotherapy, we developed a follow-up system utilizing the plan-do-check-act (PDCA) cycle [7]. Using this PDCA methodology, a multidisciplinary team of quality management in cancer medicine, comprising physicians, pharmacists, nurses, and other healthcare professionals, worked collaboratively to achieve continuous HBV-DNA monitoring for 12 months after the completion of chemotherapy in patients with previous HBV infection. Our aim in this study was to evaluate whether this team-based PDCA approach could improve the rate of HBV-DNA monitoring among patients after the cessation of chemotherapy compared with the period prior to intervention.

METHODS

We established a follow-up system conducted based on the PDCA cycle to enhance adherence to

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HBV-DNA monitoring after the completion of chemotherapy. The procedure adopted is as follows.

Plan: A standardized monitoring schedule was designed based on monthly HBV-DNA testing for hematological malignancies and at 3-months intervals for solid tumors, and was maintained for up to 12 months following a cessation of chemotherapy. Taking into consideration the outpatient visit intervals, a delay of up to 1 month was permitted. A tracking system was developed to support this process.

Do: This system was applied in the case of patients who received chemotherapy between January 2023 and August 2024. Patients who completed chemotherapy in August 2021 were followed up until August 2022, which corresponds to the follow-up period in 12 months. The interval from September to December 2022 was considered as a preparation period.

Check: Adherence to monitoring was evaluated based on review of medical records and laboratory data, and feedback was provided to the attending physicians. We also examined the causes of loss to follow-up according to defined criteria.

Act: On the basis of the findings, strategies for further improvement were considered among the members of the team of quality management in cancer medicine.

The study was conducted at the Nagoya Memorial Hospital and included patients who had received any form of systemic chemotherapy for hematological or solid malignancies and subsequently completed their treatment during the study period. The procedures adopted in the study were initially approved by the Institutional Review Board of the Nagoya Memorial Hospital (approval no. #2013-010).

Patients were divided into the following two groups:

Pre-intervention group: patients who had completed chemotherapy between January 2020 and August 2021 prior to the introduction of new monitoring system.

Post-intervention group: patients who had completed chemotherapy between January 2023 and August 2024 after the initial implementation of the system.

For the patients in both groups, we focused on those who were negative for hepatitis B surface antigen (HBsAg) but positive for either hepatitis B surface antibody (HBsAb) or hepatitis B core antibody (HBcAb), as these patients are considered to be at risk of HBV reactivation. For each group, we assessed the proportion of HBV DNA within 12 months after the completion of chemotherapy, and the efficacy of the multidisciplinary approach was evaluated by comparing the rates of implementation in the pre- and post-intervention groups. The primary outcome of the study was the rate of HBV-DNA monitoring within 12 months after the completion of chemotherapy based on a specific schedule; monthly for hematological and 3-monthly for solid tumors [4,5,8].

Statistical comparisons of the two groups were conducted using Fisher's exact test, at the $p < 0.05$ level of significance. All analyses were performed using EZR software (Saitama Medical Center, Jichi Medical University, Saitama, Japan) [9].

RESULTS

During the pre-intervention period, 259 patients received chemotherapy, among whom, two patients were found to be HBsAg-positive and one patient had been vaccinated prior to treatment. Consequently, 256 patients were eventually deemed eligible for HBV-DNA monitoring. Of these, 56 (21.9%) were HBsAg-negative, although were HBsAb or HBcAb positive and thus required regular HBV-DNA monitoring (Table **1**). During the post-intervention period, 232 patients received chemotherapy. Similarly, two patients were assessed to be HBsAg-positive and four had been vaccinated, resulting in 226 eligible patients. Of these, 48 (21.2%) were HBsAg– / HBsAb or HBcAb positive.

Table **2** shows the cancer types in those patients with an HBsAb- or HBcAb-positive status before and after the introduction of the follow-up system. Hematopoietic malignancies accounted for 23 and 22 cases before and after the intervention, respectively. Among the solid tumors, 33 were identified before and 26 were identified after the intervention. The most common solid cancers were colorectal (9 vs. 8 cases, respectively), followed by lung (4 vs. 6), stomach (4 vs. 2), gynecological (4 vs. 2), and breast (3 vs. 3) cancers. The overall distribution of cancer types during the two periods were found to be similar.

Among the antibody-positive individuals, patients with hematological malignancies and solid tumors, who had become untraceable within 1 and 3 months after the completion of chemotherapy, respectively, were excluded from the present analysis. Consequently, 15 (26.8%) and 16 (33.3%) patients in the pre- and post-

Table 1: Comparison of HBV-DNA Monitoring Before and After the Introduction of Follow- up System

	Pre-intervention (Jan 2020–Aug 2021) n (%)	Post-intervention (Jan 2023–Aug 2024) n (%)
Total patients receiving chemotherapy	259	232
HBsAg+	2	2
Vaccinated	1	4
Eligible patients	256	226
Gender		
Male	136 (53.1)	130 (57.5)
Female	120 (46.9)	96 (42.5)
Age		
Average	70.1	72.1
Median (min-max)	72.5 (5-94)	75 (16-96)
HBsAg testing	256 (100)	226 (100)
HBsAb/HBcAb testing	247 (96.1) / 246（95.7）	217 (96.0) / 215（95.1）
HBsAg– / (HBsAb or HBcAb) +	56 (21.9)	48 (21.2)
Monitored (12-month follow-up)	9 (16.1)	8 (16.7)
Monitored (< 12 month)	14 (25.0)	21 (43.8)
Not monitored	18 (32.1)	3 (6.3)
Excluded (death, hospice, home care, etc.)	15 (26.8)	16 (33.3)
HBV reactivation cases	2 (0.78)	2 (0.88)

Table 2: Cancer Type in Patients with HBsAb or HBcAb-Positive Status Before and After Introduction of the Follow-up System

Diagnosis	Pre-intervention (Jan 2020–Aug 2021) n=56 (%)	Post-intervention (Jan 2023–Aug 2024) n=48 (%)
Hematopoietic	23	22
Solid tumors (total)	33	26
Colorectal	9 (27.3)	8 (30.8)
Stomach	4 (12.1)	2 (7.7)
Pancreatic	1 (3.0)	1 (3.8)
Esophagus	1 (3.0)	1 (3.8)
Biliary	0	3 (11.5)
Breast	3 (33.3)	3 (11.5)
Lung	4 (12.1)	6 (23.1)
Gynecologic	4 (12.1)	2 (7.7)
Urologic	6 (18.2)	0
Sarcomas	1 (3.0)	0

intervention groups, respectively, were excluded from the analyses. Having excluded these individuals, we were able to establish that adherence to HBV-DNA monitoring had undergone a significant improvement from 56.1% (23/41) prior to the intervention to 90.6% (29/32) after the intervention (Figure **1**; Fisher's exact test, $p < 0.01$).

In each of the two treatment groups, there were two cases of HBV reactivation. Of those in the pre-intervention group, one patient had gastric cancer and the other had a hematological malignancy. In the post-intervention group, two patients had hematological malignancies. In total three patients with hematological malignancies (pre-intervention; 1, post-intervention; 2)

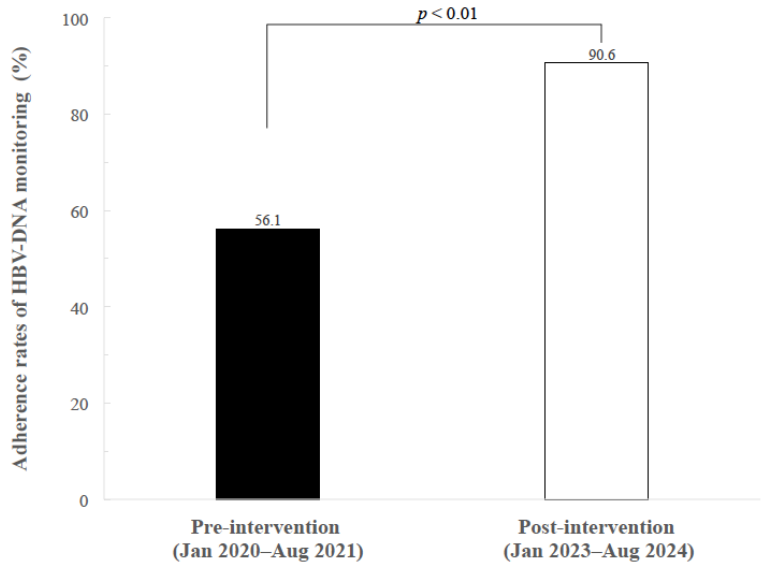

Figure 1: Comparison of adherence rates to HBV-DNA monitoring before and after implementation of the PDCA-based follow-up system.

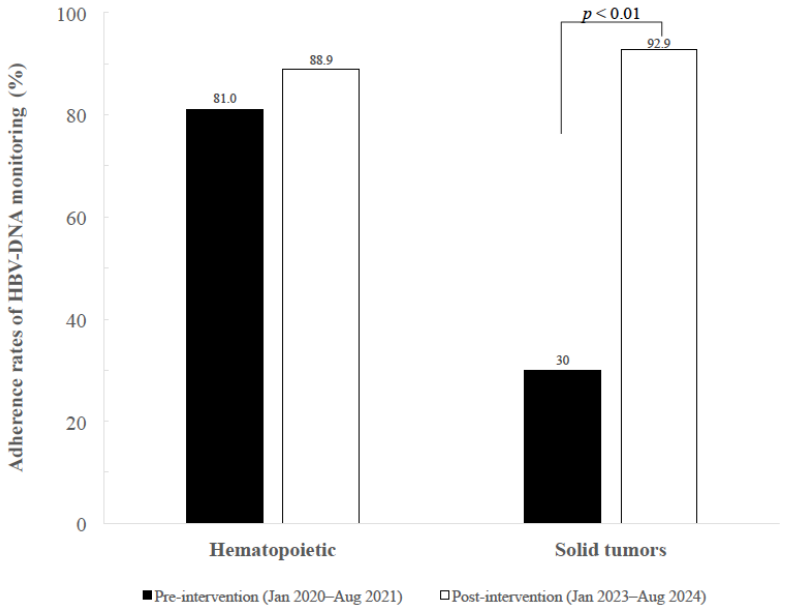

Figure 2: Comparison of adherence rates to HBV-DNA monitoring between hematopoietic malignancies and solid tumors before and after implementation of the PDCA-based follow-up system.

were appropriately monitored for HBV DNA, whereas the patient with gastric cancer was not monitored according to the scheduled intervals. All patients continued to receive chemotherapy whilst also receiving antiviral therapy for HBV infection.

Subgroup analysis revealed that the improvement in adherence among patients with solid tumors was statistically significant (Fisher's exact test, $p < 0.01$). In contrast, patients with hematological malignancies originally had relatively high rates of adherence, which further increased subsequent to intervention (Figure **2**).

DISCUSSION

According to Japanese guidelines, HBV-DNA is scheduled to be monitored monthly for hematological malignancies and at 3-month intervals for solid tumors [4]. Prior to the introduction of the support system provided by the multidisciplinary team of quality management in cancer medicine, HBV DNA testing was completely physician-dependent. At present, our system enables the attending physicians to receive feedback from a quality management team through medical record tool at first and then direct

communication as a second step when HBV DNA testing is not performed.

Our findings in this study revealed that baseline HBV serological testing was performed for a majority of the assessed patients, with a higher rate of testing compared with those previously reported in Japan [10]. On the basis of the findings of continuous observations using a follow-up system, we were able to establish that adherence to HBV-DNA monitoring declined over time subsequent to the completion of chemotherapy.

The degree of improvement was particularly evident among patients with solid tumors. That the rate of adherence was higher in the case of patients with hematological malignancies than in those with solid tumors can be ascribed to the fact that the risk of HBV reactivation when using regimens such as rituximab-based chemotherapy, is generally perceived by physicians to be higher in the former patients [11,12]. These findings are consistent with those previously reported indicating that physicians are more vigilant when assessing patients with hematological malignancies [8,13].

During the post-intervention period, 33.3% of the assessed patients (n = 16) became untraceable owing to their deteriorating general conditions and were accordingly excluded from the analysis. The primary contributary factors in this regard were disease progression leading to death (n = 9), transfer to hospice care (n = 3), transition to home-based care (n = 3) or emergency transfer with subsequent death at another hospital (n = 1). These events reflect a limitation of hospital-based monitoring, as patients may no longer be followed-up within the same institution following disease progression. Therefore, it remains debatable as to whether continuous HBV-DNA monitoring is meaningful in the context of patients with a very limited life expectancy, ranging from only a few weeks to a few months. In this regard, there are currently no clear clinical indicators or guidelines as to when monitoring can be reasonably discontinued. Nevertheless, our team continues to assess the current barriers to continuous HBV-DNA monitoring and consider strategies for the management of HBV reactivation during or after chemotherapy using the PDCA cycle.

CONCLUSIONS

The implementation of our support system provided by a multidisciplinary team of quality management in cancer medicine was assessed to contribute to a significant improvement in a 12-month adherence to HBV-DNA monitoring following the discontinuation of chemotherapy, with particular impressive gains seen among patients with solid tumors. Notably, this improvement was observed among patients who continued follow-up at our institution. In addition, our analysis highlight the clinical reality that many patients become untraceable owing to deteriorating general conditions after the completion of chemotherapy.

LIST OF ABBREVIATIONS

PDCA = plan-do-check-act

HBV = hepatitis B virus

HBsAg = hepatitis B surface antigen

HBsAb = hepatitis B surface antibody

HBcAb = hepatitis B core antibody

HBV-DNA = hepatitis B virus deoxyribonucleic acid

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was approved by the Ethical Review Board of the Nagoya Memorial Hospital (approval number: #2013-010) and was conducted in compliance with the “Ethical Guidelines for Medical and Health Research Involving Human Subjects”. Information regarding the study inclusion was posted on the hospital’s homepage, and consent was obtained via the opt-out method.

CONFLICTS OF INTERESTS

The authors declare that they have no potential conflicts of interest regarding the research, authorship, or publication of this article.

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Not applicable.

AUTHORS’ CONTRIBUTIONS

SH, KN, and SK contributed to the study design and conceptualization. SH, YS, TK, and YK were involved in the PDCA-based activity of Quality Management team in cancer medicine. SH and KI drafted and revised the manuscript. SH reviewed the medical records. SH and SY performed the statistical analysis. All authors reviewed and approved the final version of the manuscript.

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