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Development and Evaluation of a Laboratory Information System-Based Auto-Dilution and Manual Dilution Algorithm for Alpha-Fetoprotein Assay

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Korea is known as a hepatitis B virus-endemic area with a high incidence of hepatocellular carcinoma (HCC) [1]. Alpha-fetoprotein (AFP) is the most widely used tumor marker for monitoring HCC in clinical practices. The serum AFP level is <10 ng/mL in healthy adults, but patients with HCC show a very wide distribution of AFP levels. AFP level is known to increase in 60-70% of patients with HCC [2]. In addition, 8.2-30.1% of these patients have high levels of AFP (e.g., levels of >400 ng/mL) [3, 4]. Tyson et al. [5] reported that 29% of patients with hepatitis C-related HCC had elevated AFP levels of >1,000 ng/mL.

AFP levels are currently determined by immunoassay in most clinical laboratories. As the analytical measurement range (AMR) of AFP assay reagents cannot cover all the clinically important range of AFP levels, it is necessary to dilute and retest the specimens with high AFP levels.

At our institution, we measure AFP levels by using the chemiluminescent microparticle immunoassay (ARCHITECH i2000SR system; Abbott Laboratories, Abbott Park, IL, USA) with the ARCHITECT AFP Reagent kit (Abbott Laboratories). The AMR of the assay reagent is 0.4-350 ng/mL. However, the manufacturer has made the following recommendation: if the AFP level of the original samples is >200 ng/mL, the original samples are automatically retested by the instrument with a fixed-dilution ratio of 1:16.7 to rule out "hook effect." In addition, if the AFP levels of auto-diluted samples are >5,845 ng/mL (350×16.7), the original samples are manually diluted. These dilution processes not only waste assay reagents but increase turnaround time (TAT) as well. Therefore, we developed an auto-dilution and manual dilution algorithm by using the laboratory information system (LIS) to minimize the number of AFP dilution analyses and reduce TAT.

We developed an auto-dilution and manual dilution algorithm, taking into consideration both the measurement range of the AFP reagent and the fixed-dilution rate of the instrument (Fig. 1). When previous AFP results were not available or the previous AFP results were <200 ng/mL, samples were, then, briefly tested without diluting them. Previous AFP results were defined as results that were obtained within 8 weeks prior to the current AFP assay. The instrument automatically diluted the original samples if the previous AFP results were within the 200-5,000 ng/mL range. In addition, if the previous AFP results were >5,000 ng/mL, corresponding sample racks were immediately ejected from the instrument with a particular flag sign, and the tests were subsequently performed following the manual dilution procedure conducted by laboratory personnel.

In total, 11,297 samples were ordered for AFP assay from June to September 2012. Among them, the developed algorithm

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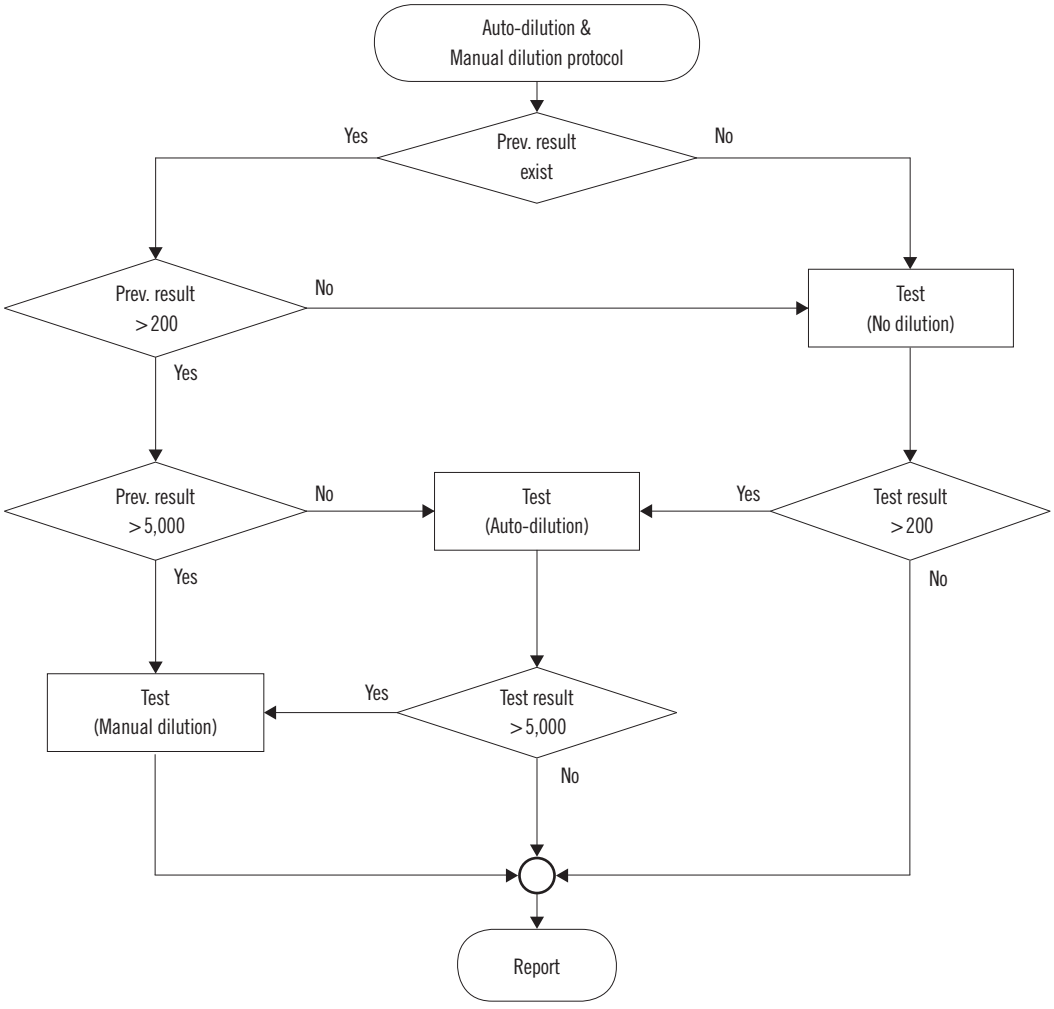

Fig. 1. Flow chart of the auto-dilution and manual dilution algorithm for the alpha-fetoprotein (AFP) assay. The upper linearity limit of AFP assay without dilution is 200 ng/mL for the ARCHITECT AFP reagent kit. The 5,000 ng/mL is an arbitrary value that is approximately 85% of the upper detection limit of the ARCHITECH i2000SR system for AFP assay.

was evaluated using 10,947 samples, excluding 350 samples for prenatal screening. Previous AFP assay results were available for 8,745 of the total 10,947 samples (79.9%). Of these 8,745 samples, 479 (479/8,745; 5.5%), and 169 (169/8,745; 1.9%) had previous AFP assay results that were 200-5,000 ng/mL and >5,000 ng/mL, respectively.

By applying the developed auto-dilution algorithm, one assay step could be omitted by automatically diluting the original samples with previous AFP results of 200-5,000 ng/mL (i.e., 479 samples). Starting from the time of aspiration of the sample in the instrument, it takes approximately 29 min to obtain the result of an AFP assay. As the original samples were not analyzed, the TAT could be shortened by more than 29 min in these samples. In no cases were the AFP values obtained by dilution analysis lower than the lowest limit of detection. Similarly, 2 assay steps, including the measurement of the original sample and the auto-dilution assay, could be omitted by manual dilution in samples with previous AFP results of >5,000 ng/mL (i.e., 169 samples). The TAT was shortened by more than 58 min in these cases. Consequently, 8.4% of the reagents could be conserved, and the TAT was shortened by 29 to 58 min by applying the auto-dilution algorithm in patients with previous AFP results.

In conclusion, the LIS-based auto-dilution and manual dilution algorithm for the AFP assay shortened the TAT and conserved reagents. Application of this auto-dilution and manual dilution algorithm based on the patient's previous results to the automated immunoassay system could allow for more cost-effective laboratory practices in clinical laboratories.

Authors' Disclosures of Potential Conflicts of Interest

No potential conflicts of interest relevant to this article were reported.

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