Indigenous IRMA Kit for Routine Estimation of Serum Thyroglobulin in Thyroid Cancer Patients

Radiation Medicine Centre, BARC
Completing a Decade of Accomplishment

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Introduction

Radiation Medicine Centre (RMC) is one of the largest referral bases in India for the management of patients with various thyroid disorders including differentiated thyroid cancer (DTC) [1]. Constant efforts are being put in both *in-vivo* and *in-vitro* diagnostics for better care and management of the patients. RMC is a pioneer in Nuclear Medicine and due to its established infrastructure, various radioisotopic assays for thyroid analytes [Total T4, Free T4, anti-thyroid peroxidase autoantibody (TPOAb), serum thyroglobulin (Tg) and anti-Tg autoantibody (TgAb)] have been developed and validated here and some of them also found its applications for routine *in-vitro* patient services. Serum Tg is one of these in-house developed assays which was first developed in RMC and is still being used as a 'tumor marker' in the monitoring of thyroid cancer patients for almost 40 years. Thyroid cancer is the most common type of endocrine malignancy. About 90% of thyroid neoplasms are differentiated thyroid cancers with low malignant potential and a very good prognosis [2]. Serum Tg measurement is clinically useful for the postoperative monitoring of patients diagnosed with DTC with detectable and/or increasing Tg concentration indicating possible recurrent or persisting disease.

Evolution of Tg Assays at RMC: From where we Begin! A Look Back at the Past

At our Centre, in the early 80s, patient's sera were initially quantitated for serum Tg by an in-house developed radioimmunoassay (RIA) procedure [3]. The assay involved a primary incubation of radiolabelled Tg (^{125}I-Tg) and rabbit anti-Tg for 72 h and an additional 18 h incubation for precipitation of antigen-antibody (Ag-Ab) complex with goat anti-rabbit serum (GARS) in combination with S. aureus. Thus, in all, it took 90 h to report on a test sample. Therefore, there was a need to significantly reduce the overall total reporting time. Towards this, the initial approach had been to modify the second incubation step by using goat anti-rabbit antibody coated-magnetic particle (GAR-Ig-MP) as a mobile solid-phase in the separation system of the assay instead of GARS and S. aureus. With this method, the second incubation period was significantly reduced from 18 h to 2 h and facilitated an easy centrifugation-free separation system to separate the bound fraction from the free [4]. During this period, the sample load had started increasing gradually. Due to the long turnaround time (TAT) required by Tg RIA, the assay was performed once a week. RIA for Tg suffers from practical disadvantages [5] and due to these shortcomings, commercial assays favor the immunometric assay (IMA) format which comparatively offers higher sensitivity and precision with shorter TAT enabling quick reporting. Thus, this was the period when we decided to switch over from RIA to immunoradiometric assay (IRMA). Hence, to cater to the increasing patient load we switched over to imported commercial IRMA kits (a window period). The commercial kits being highly expensive prompted us to standardize a two-step solid-phase IRMA using antibodies coupled to Magnetic particles (MP) and polystyrene-coated tubes (CT) as different solid-phases. Among the two developed IRMA formats, the CT-IRMA had better possibilities to be implemented for routine use in terms of sensitivity, precision and automation with a significant reduction in the TAT (14 h) thereby making the reporting time rapid. Figs.1-6 depicts the various steps involved in the manual immobilization of antibodies (one of the laborious steps in the production of in-house Tg IRMA kits).

Thus, the CT-IRMA came into routine practice for monitoring thyroid cancer patients from Nov 2013 onwards which is still being used satisfactorily in RMC. So far, we have produced approximately 2000 Tg IRMA kits and have analyzed more than 40,000 serum samples for Tg estimation in the follow-up cases of thyroid cancer patients. The cost of a commercial (Izotop) Tg IRMA kit is approximately Rs. 17,500/kit (100 Determinations) whereas an RMC-Tg IRMA kit costs approximately Rs. 2500/kit (100 Determinations). Hence, the overall cost of 2000 commercial kits would be approximately Rs. 35 million whereas for in-house kits it is Rs. 5 million. Hence RMC, BARC has saved the expenditure of Rs. 30 million and in addition, has generated a revenue of approximately Rs. 4 million from 40,000 samples in the last decade.

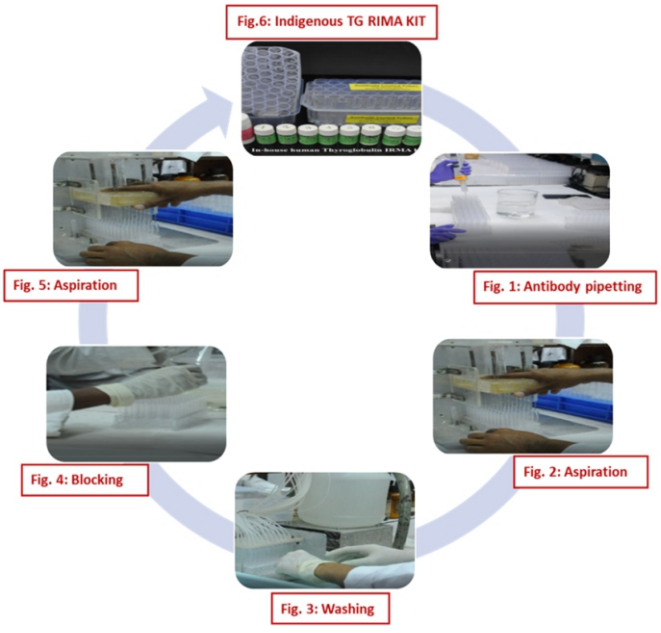

Fig.1-6: Various steps involved in the manual immobilization of antibodies at RMC for in-house TG IRMA kit production.

Conclusion

This report concludes that RMC, BARC have completed a decade of accomplishment by taking a step forward towards self-reliance (Atmanirbhar Bharat) in securing the stock of entirely indigenously produced and highly economical Tg IRMA kits for routine thyroid cancer patient use. Thus, RMC has continued to deliver on its mandate the application of radiation technology solutions to address societal issues in the areas of healthcare and medicine.

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