Automation of analytical processes in Immunohematology: Hospital Based-HTA approach

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Abstract— **Problems related to the interpretation of results and clinical consequences of analysis in Immunohematology laboratory are discussed. On the basis of an Hospital-Based HTA (HB-HTA) approach, most common errors of the analytical processes have been highlighted, divided in pre-analytical, analytical and post analytical phase. For each phase, the adoption of automated instruments has enabled a strong reduction of errors, monitored by using indicators related to the analytical phases.**

Keywords— **Hospital-Based HTA, Immunohematology and Transfusion, Automation, Error, telemedicine**

I. Introduction

HTA multidisciplinary approach to the healthcare context is represented by Hospital-Based HTA, supported by the assessments at the hospital level [1]. HB-HTA is founded on four steps, that are: needs assessment; recovery of available technical and economical evidences; selection of purchasing procedures, with the comparison of different technologies; analysis of the impact given by the adopted solution, using adequate indicators. Diagnostic Immunohematology is one of the most critical laboratory activities, which must take into account all the overall cycle of investigations pertaining to transfusion, starting from the appropriateness of the request to the correct use and interpretation of the diagnostic information in the management patient records. Each phase of the immune-hematologic laboratory activities (pre-analytical, analytical and post-analytical phase) can be characterized by errors that may compromise the quality of the examinations, and the resulting therapeutic course of the patient [2]. Adverse reactions due to transfusion errors represented about 70% of all adverse events. Among these, about 20% are transfusion reactions from ABO incompatibility [3].

II. Material and methods

The activity of laboratory in the area of Immunohematology, traditionally divided in pre-analytical, analytical and post-analytical phases, can be affected by mistakes, with negative results on the care of the patients. It's important to investigate every possible lack that it is checked in the analytical process.

Complying with the HB-HTA method, we have decided to create an assessment, to individuate the most relevant problems about laboratory activities, that are the request from the clinicians, the correct evaluation of the exam, and the consequent action on the therapeutic decision.

A. Pre-analytical phase

Literature evidence in the pre-analytical phase shows the great number of: human errors, for incomplete, incorrect or illegible identification of a patient; duplicated or not pertinent requests for laboratory tests; the presence of not acceptable blood samples for the analysis; the execution of incorrect blood taking or wrongly labelled samples; the wrong identification of patients. However, there are some procedures not performed directly in the laboratory, and therefore not subjected to direct control of laboratory personnel, such as requesting the examination, collection and management of the samples, transport of the samples.

B. Analytical phase

In blood assignment phase (analysis of ABO/Rh, irregular antibody screening...), purpose of laboratory clinicians is to use the most suitable test on the appropriate sample, achieving a correct result, aimed at the delivering the right

blood product to the right patient. Errors in the analytical phase may therefore be due to the imprecision of diagnostic tests for low sensitivity and specificity and / or incorrect identification of samples. Particular attention must be given to the correct operation of the instrumentation, to the reagent preparation, to the calibration tasks of analytical systems, and to the activities of Internal Quality Control for all tests.

C. Post-analytical phase

The post-analytical phase encloses the overall quality of all the analytical process. The context of the patient and the donor and the ability of the clinician to use the analysis information properly are very important. Procedures include the transfer of analytical data from the equipment to the information management system, the check of the results and their communication. Therefore a report is created, able to point out possible mistakes, causing alarming results. Similarly to the pre-analytical phase, there are external procedures to the laboratory, that are the post-transfusion follow-up of the patient, the donor look back and the haemovigilance. Due to the inadequate experience about transfusion field, showed by any clinician, errors in the communication and in the interpretation of reports may adversely affect treatment decisions adopted by clinicians.

III. RESULTS

Protocols and strategies can help reduce the number of errors committed during laboratory activities.

In the Department of Immunohematology and Transfusion Medicine in San Matteo Hospital, it was decided to adopt a technological solution, that is an automated analytical system (Fig. 1, IH1000, Bio Rad, Berkeley, California). The analytical process is based on the determination of the antigen/antibody, that is detectable in media called "ID-Cards", consisting of tubes filled with Sephacryl gel. The gel is composed of microspheres with a variable diameter, mixed with antibodies or specific buffers, depending on the reaction that must be observed. For each phase of the analytical process, this system allows to reduce the number of errors, improving safety and outcome of the patient and the donor, and protecting the operator at the same time.

Laboratory activity was analyzed in a period between April and December 2012. In the first 4 months, laboratory operators learned the utilization of IH-1000, maintaining the old laboratory equipment. From August to December 2012, the activity passed completely to IH-1000 equipment, showing a strong growth in the number of tests on donors and patients. In Table 1 the results of analysis are shown.

Fig. 1 Automation equipment IH1000, Bio Rad

Table. 1 Comparison between two periods of utilization of IH-1000

Quantity (#)	Old equipment (from April to July 2012)	IH-1000 equipment (from August to December 2012)
# patients tested	3000	7500
# donors tested	500	600
# AB0 tests on patients	500	2500
# AB0 tests on donors	500	4000
# AB0 tests on indirect reverse group	3500	8000
# Type and Screen tests	500	6000
# Trio Coombs tests	200	500
# Crossmatch C tests	1000	3500
# Crossmatch BR tests	200	3000

A. Automation in pre-analytical phase

The automated equipment identifies the resources required to start the analytical process, by setting a reading of bar codes of the items inside the instrument, and comparing them with the resources needed to run the selected test. The unambiguous identification of the input sample is given by the link with the information management system of the Department and of the Hospital, that collects all the requests. The equipment also controls the lot number and the expiration date of the used devices (reagents, ID-Cards, thinners), the level of liquid reagents and solutions, and the presence of clots in the hydraulic circuit during the process of dispensing. Problems related to the use of expired products and the failures of the instrument caused by the obstructions (clots, fibrin) are therefore solved.

The instrument has an optical sensor for the identification of test tubes accidentally loaded with the stopper, and acceptance options of test tubes of different sizes can be configured, such as pediatric samples.

Logs of events and display areas for loading samples and reagents are available for the operator, ensuring a view of the current status of each loaded rack. The warehouse of ID-Cards is displayed on the monitor, with information on the amount, location and type, ensuring the operator to have the possibility to know the availability of ID-Cards for tests. By software management IH-Com, the operator can combine several different types of tests, creating customized job profiles. The software module contains the Reflex Test, that ensures the possibility to perform more tests on the basis of previous results or requests defined by the user, with reference to patient parameters such as age and sex.

B. Automation in analytical phase

The analytical cycle (dispensation of ID-Cards, incubation, centrifugation, reading and interpretation) is completely inside the instrument, protected by a front panel whose opening is detected by the instrumental control software. In this way, no external element can affect the process, and there are not risks of contamination to the outside. The analytical phase begins with the identification, by the carrier arm, of the ID-Card type loaded on each support, while samples and reagents are identified during the loading rack. More precisely, the uploading of the rack of samples and reagents takes place frontally and in dedicated positions, to minimize possible errors of insertion and optimize the activity and the continuity of the work. Tubes are equipped with a bar code, for the recognition of the positive samples, avoiding errors due to incorrect matching between sample and patient, and between patient and donor. Expired reagents and solvents are identified and discarded by the system, by reading the bar code on the package.

The logic random access allows the operator to process the samples in the order of insertion, ensuring optimal management of urgency. In fact, it is possible to automatically load some rack, equipped with specific barcode, which allow to discriminate samples priority, enabling the instrument to handle them immediately. Priorities are performed automatically by optimizing the cycles of centrifugation and incubation that could be in progress. The instrument is equipped with automated accessories (3 centrifuges, 2 arm / needle dispensers, double wash equipment of tanks and exhaust) that allow the optimization of the working flow, with the ability to load a large number of samples, and the continuity of the work even in the presence of an hardware failure (auto-backup).

The reading of the ID-cards is via color camera high definition, and it is based on the detection of antigen-antibody complexes. The camera provides a picture of the reaction and evaluates the results for the corresponding ID-Card. The result of the reaction for each microtube can be positive for 4 degrees (+ + + +, + + +, + +, +), negative (-), undefined (?), or with double erythrocyte population (Dp) (Fig. 2).

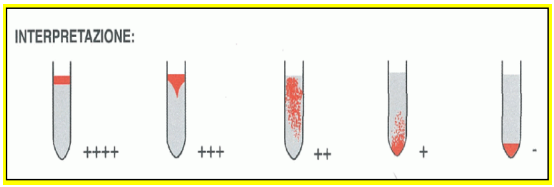

Fig. 2 Kinds of possible reactions

The sequence of steps followed by a test (dispensation, incubation, centrifugation, reading) is represented by a screen, that shows the status and timing of the test. The screen showing relevant maintenance gives to the operator the options for the weekly maintenance and system initialization. Some of the maintenance activities have a daily periodicity (the check of the outer surface of the tool and of work plan), others a weekly one (washing water circuit with dedicated solution and cleaning device for removing the ID-cards). The initialization and the control of the modules and of the work plan are performed, during the start and the stop of the equipment.

The system is equipped with a quality control module that allows the verification of the used reagents. The strategy for the controls can be set by the operator, and controls validity time is monitored by the system. Then the instrument can detect the presence of clots in the needle: the user is guided by instrument itself in the cleaning procedure of the needle, while the second needle ends the dispensation in progress, ensuring work continuity.

C. Automation in post-analytical phase

The system allows the processing of reports as shown in the current guidelines, considering all the necessary information for the correct interpretation of the results:

- The name of Department which writes the report;
- The patient/donor identification;
- The date of the sample and of the report;
- The indication about the exam done;
- The results of the exam;
- The reporting of any discrepancies
- The information about significant events that may interact with the results;
- Any notes
- The pictures of the wells with their score of reaction

Through the management software of the system, users can validate results. The results that contain inconsistencies (discrepant results, doubts) or that need deepening tests are shown (antibody screening tests or cross-posi-tive, sub-

groups, RhD weak). It's 'also possible to set a double validation.

The system proposes an elaboration and a clear display of the results, allowing the operators to enlarge the selected wells, to modify and then confirm the results interpreted by the analyzer.

The system is composed of basic elements (a module of reading images of ID-Cards, a module for user authentication, an user interface module, a module for the supervision, a module for automatic interpretation) that communicate as HTTP traffic. Clinical physicians may at any time remotely connect to server computers in the blood transfusion service, for viewing and validating the results. In addition to an increased safety, the use of telemedicine ensures a better organization in the blood assignment, with consequent optimization and reduction of costs for the hospital.

IV. Discussions

Transfusion Medicine regards collection, processing and distribution of blood components and blood products. Problems shall be continuously identified, corrected and monitored, implementing any interventions in an attempt to improve the performance and the patient and donor health [4].

As defined in the last crucial step of Hospital-Based HTA, any appropriate performance indicators must be used for monitoring automation.

Monitoring indicators, grouped in relation to the phases of laboratory work, are adopted in order to check the main error situations that could happen.

The indicators are shown below:

1. Pre-analytical phase: appropriateness in the application of examinations; patient and donor satisfaction; indicators on the transport of specimens; percentage of misidentification; optimization of the technician time for the management of the specimens;

2. Analytical phase: validity of the tests; use of human and material resources; organizational changes; treatment times of the samples;

3. Post-analytical phase: time required for the availability of results; accuracy of laboratory reports; clinicians satisfaction for the service offered by laboratory work; appropriateness of the request for further analytical tests.

V. Conclusions

Health Technology Assessment is a useful tool to provide as objective as possible criteria, in order to decide on future investments of resources in the healthcare sector. In this context it was decided to evaluate the immunodiagnostics field, especially critical sector of transfusion medicine, according to a perspective of Hospital-Based HTA.

The major problems that may arise during the phases of acquisition requests, execution of tests, interpretation, reporting, counseling and eventual assignment of the blood were identified, on the basis of available information sources.

The help of automation ensures high activity through continuous loading, work autonomy (walk away), a chance for uninterrupted monitoring of the state of the instrument, a guaranteed traceability for all requests, a safe management and interpretation of the results.

Last but not least, the telemedicine module assures user-friendly work processes, with increases in the efficiency and effectiveness of validation tests, and rationalization of available resources.

The introduction of automation equipment must still be followed by a monitoring of its performance and of the organizational changes, through the identification and the analysis of previously evaluated and defined indicators.

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