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Advances in Biochemistry & Applications in Medicine

Chapter 1

Quality Control in a Clinical Laboratory

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Abstract

Quality Control (QC) is carried out in the laboratory to find out and reduce the errors in the analytical phase of the testing system prior to the release of reports of the patients. High quality laboratory results involve commitment to all phases of testing system including pre-analytical, analytical and post-analytical phases. Pre-analytical phase includes those factors which affect the laboratory results prior to the handling of the sample in the clinical laboratory. Post-analytical factors are those which affect the results after the analytical phase is complete. Quality control involves implementation of both Internal Quality Control (IQC) and External Quality Control (EQC) which is known as Proficiency Testing (PT). Internal quality control is performed daily in the laboratory using controls whose values are known, where as external quality control includes the participation of the laboratory in an external quality assessment scheme which is used as a test of competency.

The interpretation of quality control data is done with the help of both graphical and statistical tools. Quality control data is most commonly visualized with the help of Quality Control (QC) charts which include Levey-Jennings (LJ) Charts and Westgard Rules. Both are useful in detecting trends or shifts observed from the average target value. Corrective and Preventive Action (CAPA) is an important path towards improvement and effectiveness of quality management system in a laboratory. The root cause analysis of any problem or deviation can be easily done by implementing CAPA in the

laboratory.

In this chapter, quality control in a clinical laboratory has been discussed with respect to potential errors in the laboratory, statistical quality control (SQC) tools, the procedures used to maintain quality in laboratory, corrective and preventive action (CAPA) and clinical audit of the laboratory.

Key Words: Quality control (QC); Corrective and preventive action (CAPA); Proficiency testing (PT); Internal quality control (IQC) and External quality control (EQC)

1. Introduction

Quality control (QC) in a clinical laboratory plays an important role in detecting deficiencies and reducing errors in laboratory's analytical process prior to the release of patient's results. The purpose of quality control in the clinical laboratory is to ensure that the results being reported are accurate and precise. There have been many developments in the laboratory testing system. These are pre-analytic (sample processing), analytic (chemical analysis of analyte) and post-analytic (data management) after the introduction of total laboratory automation (TLA). New management techniques have been developed to control the quality and appropriateness of results. The use of internal quality control (IQC) and external quality control (EQC) have helped the laboratories to continually improve the quality control of laboratory. In order to achieve the precision, accuracy and reliability of laboratory test results, accreditation and external quality assessment (EQA) are very important procedures [1].

2. Sources of Laboratory Errors

There are a number of potential errors which can affect the quality of the clinical laboratory results.These errors can occur in pre-analytical, analytical and post-analytical phases. All the three phases can be targeted individually for improving quality, although it is well published that most errors occur in the pre- and post-analytical phases [2,3,4].

2.1. Pre-analytical Phase

These are the errors which occur in the pre-analytical phase and create an impact on the patient's sample before it is analysed in the laboratory. There are a number of things which can go wrong from the time when the sample is collected from the patient till it is transported to the laboratory for analysis. These errors are as follows:

- **Wrong patient information:** The particulars such as name, gender, age, ward, patient's posture, effects of exercise, dietary effects, medical history, pregnancy, effects of drugs and alcohol etc. can affect the values of analytes.

- **Improper collection of the blood sample:** The results will be affected if the sample is collected in a vacutainer other than the one which is recommended for analysis of a particular

analyte for e.g. vacutainer containing sodium citrate is used in place of sodium fluoride for analysis of plasma glucose.

- **Inadequate quantity of the sample:** An insufficient quantity of sample cannot be processed for all the analytes which have been requested by the clinician.

- **Improper handling of the sample:** Improper handling of the sample can lead to haemolysis of the sample before it reaches the laboratory for analysis. Grossly haemolysed sample should always be rejected as lysis of blood cells leads to release of certain intracellular chemicals and enzymes which will lead to increase in levels of potassium, phosphates and transaminases.

- **Incorrect sample storage:** If a sample has not been properly stored or a blood sample has been left overnight before being sent to the laboratory, it will become haemolysed in 24 hours especially at a warm temperature.

- **Other factors:** Heat and exposure to light can change the actual value of many analytes in routine clinical chemistry such as photo-degradation of bilirubin by light exposure.

2.2. Analytical Phase

The analytical phase begins from the time when the patient's specimen is prepared for analysis to the time when the test result becomes available. Potential analytical errors which may affect the quality of the results obtained include sample measurement, sample pre-treatment, reagent volume measurement, sample and reagent mixing, incubation, reaction timing, and calculations. These errors may arise in conjunction with the supplementary use of analytical equipment such as glassware, pipettes etc., which may not have been properly washed and calibrated. The quality of the reagents and the deionized water used for reconstitution of calibrators and controls will also have a critical influence on the values generated. It is very important that the reagents should be prepared according to the instructions given by the manufacturer and also the reagents should be properly stored when not in use.

During the analytical phase, the quality of the laboratory can be maintained by running internal quality control (IQC) daily and participating in external quality assessment (EQA). In addition, specific rules need to be followed for accepting and rejecting the analytical run. The use of analytical methods with a high degree of accuracy and precision as well as the proper maintenance of the equipment also help in reducing analytical errors. Commonly, the analytical errors are seen after the use of deionized water with high conductivity, expired reagents and controls and calibrators, blockade in aspiration system of reagents and samples [1]. The responsibility of the laboratory professional lies in appropriately analysing EQA/PT samples and reports, detecting trends or bias in reports that may not be apparent in a single result, in-

vestigate root causes producing unacceptable performances, apply and monitor appropriate action for removing the underlying causes, verify the effectiveness and above all determine whether the problem affected clinical decision making [5].

2.3. Post-Analytical Phase

Post-analytical phase mainly deals with the reporting of results after the completion of analytical phase in a timely manner and in an accepted format that can be understood and correctly interpreted by health care professionals. The most common post-analytical errors include the reports being not legible and also delay in delivering the reports to the clinician or the patients [1,6].

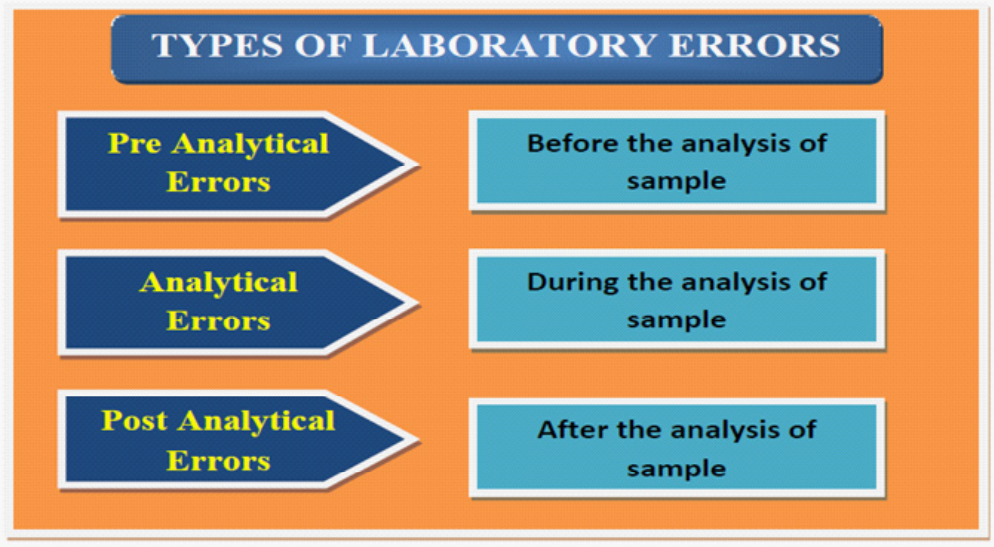

Figure 1: Types of errors in a clinical laboratory

3. Terms and definitions used in clinical laboratory

Analytical errors influence the accuracy, precision, sensitivity, specificity and reproducibility and repeatability of the analytical methods [1].

3.1. Accuracy

Accuracy refers to the degree of agreement between a measured value and its 'true' value. It is generally measured by direct comparison to a reference value or more commonly by using quality control serum, with an accurate value assigned to it by the manufacturer.

3.2. Precision

Precision refers to the reproducibility or the agreement between replicate measurements. Precision is quantitatively expressed as Standard Deviation (SD) or more precisely as Coefficient of Variation (CV) of the results in a set of replicate measurements. Hence good precision means least CV. Ideally a laboratory should be striving for both good accuracy and precision.

3.3. Specificity

Specificity describes to the ability of a method to measure solely the component of interest. A lack of specificity could lead to a falsely elevated result where the test is measuring components other than the analyte of interest.

3.4. Sensitivity

Sensitivity is the ability to detect small quantities of a measured component. It will subsequently affect both precision and accuracy, when attempting to measure levels at the bottom end of the clinical range.

3.5. Repeatability

It is the degree of agreement between successive measurements which have been done on the same sample under similar conditions (e.g. same analyzer, same user, same laboratory, same methods, and same reagent lot) within in a very short time.

4. Statistical Tools Used in Laboratory for Quality Control

It is a well-known fact that treatment of patients depends to a great extent on the reports generated by the clinical laboratory. So, the results generated by the laboratory should be accurate. The laboratory data which is generated need to be summarized in order to monitor test performance known as quality control. This is known as descriptive statistics. It can be described by their center, spread and shape.

4.1. Normal Distribution

Normal or Gaussian distribution (N) is the basis of statistical quality control theory. This distribution chart is a biaxial bell shaped diagram (X/Y) in which X-axis shows the values of a variable's observation and Y-axis shows the frequency of each value. The distribution curve or Gaussian curve indicate that about 68% of all values would fall within 1SD from the mean or average value, 95% would be expected to fall within 2SD and 99.7% would be expected to fall within 3SD value. If the value falls between 1SD range, it indicates a good control [1].

A. Measures of Center

(i) Mean

It is the most commonly used term. Mean ($\bar{x}$) is defined as the arithmetic average of a group of values and is determined by summing the values and dividing by the number of values.

$$\bar{x} = (\Sigma xi) / n$$

Where; $\bar{x}$ = mean, Σ = add up, x_i = all of the values, n = number

(ii) Median Value

Median value (M) is the value which divides the variable observations into two equal parts and represents the center of the distribution. It is often used with skewed data.

(iii) Mode Value

Mode value (Mo) is the value with the highest frequency and is used to describe the data with two centers (bimodal).

B. Measure of Spread of the Data around the Mean

(i). Standard Deviation

Standard deviation (SD or s) is the measure of dispersion of a group of values around the mean. It is derived from the curve of normal distribution and is used to assess precision.

$$s = \sqrt{\frac{1}{N-1}\sum_{i=1}^{N}\left(x_i - \bar{x}\right)^2}$$

Where; s = standard deviation, $\bar{x}$ = mean, Σ = add up, x_i = all of the values, n = number

(ii). Coefficient of Variation

The coefficient of variation (CV) is defined as the ratio of standard deviation to the mean and is expressed as percentage. It is another measure of percentage of imprecision.

CV = (S/ $\overline{x}$) X 100

Where; CV = coefficient of variation, s = standard deviation, $\bar{x}$ = mean

(Iii). Standard Deviation Index

It is the difference between indiviual value subtracted from the group mean divided by the SD of the group also known as Z- statistic. It is used for peer-group comparison.

5. Quality Control in Laboratory

Quality control is an aspect of quality assessment that is used to maintain the quality in laboratory. This can be done with the help of internal quality control and external quality control [1].

5.1. Internal Quality Control

Internal quality control (IQC) is performed daily in the laboratory and involves the use of calibrated glassware, reagents and equipment. The laboratory staff should be qualified professionals. There is a recommendation to use atleast two control levels for each analyte. The samples are internally evaluated in the laboratory. The main purpose of IQC is the precision (repeatability or reproducibility) of the method.

5.2. External Quality Control

External quality control (EQC) or proficiency testing (PT) is performed as a test of competency. It includes the participation of the laboratory in an external quality assessment scheme which provides samples for analysis every month. They have to be analyzed by the laboratory professionals using the same procedures as used for testing of quality control samples and patient samples. The results obtained from analysis of EQC samples are reported to the outside agency running external quality assessment scheme (EQAS). They then provide a report for the participating laboratory based on mean, coefficient of variation and standard deviation index of the all the participating laboratories.

5.3. Quality Control Charts (QC Charts)

Quality control charts (QC charts) have historically been used to examine prior QC results within a particular range diagrammatically. QC charts are used to represent the values of control material within the defined upper and lower limit.

The Levey Jennings (L-J) Chart

The use of Levey Jennings chart (L-J chart) is one of the most commonly used charts to monitor quality control results. It is a graphical method for displaying the values of controls. The control values are plotted versus the days of the month which is indicated on the x-axis and value of controls as mean±1SD, mean±2SD and mean±3SD are indicated on the y-axis. The deviation of the results from the mean especially, when the results are greater mean±2SD from the mean, indicate the rejection of run.

5.4. Westgard Rules

It involves the use of multiple control rules which help in improving the performance of quality control. It also helps in deciding whether the analytical run is in control or out of control. These are defined as follows:

- **Westgard 2_{2S} rule:** It is violated when 2 consecutive control values for the same level fall or both controls in the same run outside the mean±2SD. This run has to be rejected.

• **Westgard 4_{1S} rule:** It is violated if four consecutive control values exceed the same limit (mean ± 1SD) and this may indicate the need to perform instrument maintenance or reagent calibration.

• **Westgard 1_{3S} rule:** It is violated when either of the two control values fall outside mean ±3SD. The assay run is rejected when a single control value exceeds the mean plus 3SD or mean minus 3SD.

• **Westgard 4_{S} rule:** It is violated when one control value exceeds the mean by +2SD and the other control value exceeds the mean by -2SD. The range between the two results will therefore exceed 4SD hence the run is rejected.

• **Westgard 10_{x} rule:** This rule is violated when the last 10 consecutive control values are on the same side of the mean or target value. So the run has to be rejected.

6. Corrective Action and Preventive Action (CAPA)

Corrective action is that action which should be used to stop the occurrence of non-conformities. Preventive action is that which should give the opportunity to prevent potential non-conformities. Corrective action has to be taken when there is a problem. If a problem does not exist, preventive action has to be taken. Once the run is rejected on the basis of quality control results, the problem is to be solved by taking corrective action, so that results become accurate. Corrective action starts with the root cause analysis which forms the most important part of corrective action. The root cause analysis should be done by the laboratory staff familiar with the problem. The results of the corrective action taken need to be recorded and monitoring should be done to verify the completion of actions taken and also to see its effectiveness. The corrective and preventive action process includes following steps [7]:

a. Reviewing and defining the problem or non-conformity.

b. Finding the cause of problem.

c. Develop an action plan to correct the problem and prevent the recurrence.

d. Implementing the plan.

e. Evaluating the effectiveness of the correction in preventing the problem.

7. Clinical Audit of the Laboratory

In addition to participating in external quality assessment schemes, laboratories are also subject to clinical audit. This is a systemic and critical assessment of the general performance of the laboratory against its own declared standards and procedures and against nationally

agreed standards. In the context of analytical procedures, the audit evaluates the laboratory performance in terms of the appropriateness of the use of the tests offered by the laboratory, the clinical interpretations of the results and the procedures that operate for the receipt, analysis and reporting of the test samples. The objective of the audit is to ensure that the patient receives the best possible care and support in a cost-effective way. The audit is normally undertaken by junior doctors, laboratory staff, and assessors from the agencies. Clinical audit is carried out primarily for the local benefit of the laboratory and its staff and ultimately for the patient [8].

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