International Journal of Research in Medical Sciences
Juneja A et al. Int J Res Med Sci. 2015 Nov;3(11):3443-3445
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20150919

Technical Note

Understanding statistical concepts in laboratory quality control measures in biomedical research

Atul Juneja[1], Apoorva Anand[2]*

[1]National Institute of Medical Statistics (ICMR), New Delhi, India
[2]National Institute of Biologicals, Noida, U.P., India

Received: 28 September 2015
Accepted: 05 October 2015

***Correspondence:**
Apoorva Anand,
E-mail: apoorvaanand4@gmail.com

ABSTRACT

The purpose of this article is to explore the quality assurance methods in carrying out laboratory investigations on various kits and biological products and analysing the results through statistical approach. This is commonly used in the health care industry where biological investigations have become a very important part. Quality Control/Quality Assurance (QC/QA) refers to the overall management system which includes the organization, planning, data collection, quality control, documentation, evaluation and reporting activities. With the emerging health issues and availability of modern treatment modalities, it is important to provide the patient, clinical diagnosis with the relevant laboratory investigations. It is therefore, important to maintain the quality control of the testing with a standard degree of precision, which in turn is essential for the delivery of the quality patient care. In view of this, statistical approaches that can be adopted to ascertain the quality of the test have been discussed. The communication also discusses components of validity of the biomedical test and its relevance in clinical settings.

Keywords: Quality Control, Normal distribution, Systemic error, Random error, Specificity, Sensitivity

INTRODUCTION

Biological investigations for various health indications have become a very important part of health care system. Quality Control/Quality Assurance (QC/QA) can be defined as the set of planned and systematic activities focused on providing confidence to the quality, the process had undergone. With the emerging health issues and availability of modern treatment modalities, it is important for the clinician to supplement the clinical diagnosis with the laboratory investigations. It is obviously very important to maintain the quality control of the testing procedure, to put it technically with high sensitivity and specificity. It is important to have a quality management system, which monitors the overall process of the entire system, and to ensure with high confidence of being labeled as diseased or non-diseased.[1]

One can well understand the situation of over and under diagnosis considering medical aspects social aspects and also ethical aspects associated with same. Hence it is important to be sure about the investigation results to take an appropriate treatment protocol. It is obvious that one cannot be sure about the outcome with 100 % certainty hence it is desired to ascertain the quality of results with a certain degree of defined precision.[2] Understanding this degree of precision, there is a need to consider statistical aspects with knowledge of background concepts. This communication would address some issues in process of carrying out quality control measure in laboratory investigations on kits and use of statistical theory to check the quality of testing kit in arriving at precise results for the biomedical researchers including clinicians who are directly the users of the these laboratory findings.

Issues in quality control methods

It is important to mention the dimensions, which contribute to the quality control components; these include training of laboratory personnel, conditions in which the specimens are stored, reagents, hardware such as equipment and finally transcription of the results. Above all, reporting of some results require the concept of the clinical condition under consideration and summary statistics attached to it including range of normal values so as to understand the deviation from the normal values and its relevance in disease under consideration. For example minor deviation of blood sugar levels from the normal range may not be a serious issue but deviation in serum creatinine may be a cause of concern and might need further attention by clinician. The lab personnel should be aware of the consequences of over and under reporting. Thus providing the right information with right interpretation to the right place which could be a patient ward or any medical set up through the right quality control measure is the ultimate responsibility of reporting laboratory and its personnel.

Let us try to look at the procedural issues that are ensured to undertake quality control procedures in the lab. There is a need to understand the statistical concepts underlying the process and subsequent guidelines framed for accepting or rejecting the results.[3] In any laboratory to assess the validity of the test standard controls are used which are products like patients sample derived from human serum etc. for which the concentration of the analytes are known. A control could be a normal control where the product contains values in the normal zone and in the abnormal control, the values are derailed. The good laboratory practice requires testing the controls on regular basis. Normally an assay is run for twenty time and data on summary statistics such as mean and standard deviation is generated and plotted with mean±1SD, mean±2SD and mean±3SD which are known as Shewhart control charts. Subsequently Westgard rules are followed to define the specific performance of the test which includes three warning rules and mandatory rules which help us to trigger a caution on the results available from test, the details of which are available in standard text.[1,4] These rules are based on statistical principle which is discussed to its theory and concept in this paper. These rules are based on the subsequent values of the parameter being tested lying within mean±2SD or mean±3SD. This would help us to understand the two types of error which can occur in lab procedures. These are named as systemic or random error. Systemic error as the name indicates is based on some pattern and can be easily corrected by applying a correction factor. It is similar to zero error which we study in physics, where measuring pointer is over or below the zero by some amount which can be added or subtracted depending on the nature of zero error to the value measured by the instrument. In terms of biological assay, the values observed are on one side of the mean and indicate a pattern which could be assessed if the test is conducted in the same conditions and correction factors could be applied. The other error which occurs in the values is the random error. Ideally this is not an error but the natural variation which occurs in the nature. The whole subject of statistics is based on this natural variation. It may be understood that there is true value of the population known as parameter which is estimated through a sample, technically known as statistics. All samples will yield different values of statistics, the variation of which is known as the sampling error. We cannot reach to the population value unless we enumerate the whole population which is near to impossibility.[5] To understand this concept through a biological assay, even if the same sample is tested repeatedly under the same conditions there could be variation in the values because of the variation in the chemical reaction at the molecular level which the human intervention cannot control. These repeated tests may be considered as different samples from the same population and the variations observed among them are nothing but the sampling variation. This variation is known as random error in biological assay. But it is very important to define the magnitude of the range under which the values could be considered as chance variation. It has been defined that the values of the subsequent assays which lie within mean±2SD would be considered as the acceptable range beyond which the quality of testing kit could be questioned. It is based on the property of the normal distribution which states that 95% of the values would lie in mean±2SD and about 97.5% of the values lie within mean±3SD. It may be reminded that there is no value which encompasses 100 % of the values on the distribution as any random value in the distribution has been considered to vary from minus infinity to plus infinity so as to provide a chance to the random variable to take any possible value occurring in nature, i.e. in terms of health, normal person can have abnormal values or diseased can have normal values of biochemical parameter being tested however the probability of such happening would be very less but not zero (as seen through normal distribution). Hence considering mean±2sd would provide a reasonable chance of the value to be part of that distribution beyond which it might be an outlier and would amount to increasing the probability of the value coming from another distribution like normal being labelled as abnormal or vice versa. The principles of observing the quality control laws are based on fundamental principles of statistics.

Validity of test

There are certain situations where one needs to decide on the cut off value, over or below which a person is classified as diseased or non-diseased. This is under the assumption that above quality control measures have been rightly followed and there is no question on the value obtained through the biochemical test. The issue is to decide on cut off value as normal or abnormal. Identifying the right cut off involves exhaustive efforts involving observing large scale clinical data and other biological issues. But it is important to discuss and

understand the consequences of wrongly categorising diseased as non-diseased or otherwise.[6] This concept epidemiologically can be seen through sensitivity- ability to rightly classify diseased as diseased and specificity- ability to classify normal as normal. But it is important for the researcher to understand the concept of picking up right sensitivity or specificity which is analogous to type 1 and type 2 error in statistics, when one is decreased other increases. As the population consists of diseased and non-diseased in mixed form, the test under consideration helps to segregate diseased from non-diseased with some degree of precision which obviously is not perfect. If the disease in consideration is serious and missing the case can amount to serious consequences including mortality, it is important for the test to be more sensitive. But if the test is invasive and expensive and falsely labelling non-diseased as diseased can lead to traumatic situation and over treatment can have serious effects then one needs to concentrate on specificity. Statistical methods such as ROC (Receiver Operator Characteristics Curve) analysis are available to arrive at appropriate cut off point which yields optimum sensitivity and specificity.[7] It may be mentioned that in spite of arriving at best results there is still a margin of miss classification as statistical theory of distribution lends values to random variable from minus infinity to plus infinity as discussed above. In terms of medical decisions the cut off values through ROC analysis optimises sensitivity and specificity which minimises the risk of misclassification. This can be best appreciated by the clinician if he understands the concept of epidemiology through statistical theory.

CONCLUSION

It can be stated said that there will be variations in the values generated under same sample even if the test is conducted in the same environment. The knowledge of statistical concepts can help us to understand the acceptable variation of the results. In clinical terms it can also be stated that diseased and non-diseased are overlapping in nature and we need to minimise this through the discussed concepts of sensitivity, specificity. This article concludes to mention that laboratory issues concerning quality control dimensions but emphasises the need to understand statistical and epidemiological concepts in addition to skills of their specialisation. It is also important for the clinician to have a clear understanding of the magnitude of the probable errors as discussed above so as to appreciate the results available from laboratory to take a decision on treatment protocol.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Cooper G. Basic Lessons in Laboratory Quality Control. Bio-Rad Laboratories, Inc. Quality Systems Division, 2008.
2. Chesher D. Evaluating Assay Precision. The Clinical Biochemist Reviews, 2008. 2015;29(Suppl1):S23. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2556577/.
3. Karkalousos P, Evangelopoulos A. Quality Control in Clinical Laboratories, Athens, Greece, 2011. http://www.intechopen.com/books/applications-and-experiences-of-quality-control/quality-control-in-clinical-laboratories.
4. Manikandan S. Measures of central tendency: Median and mode. J Pharmacol Pharmacother. http://www.jpharmacol.com/text.asp?2011/2/3/214/83300. 2011;2(3):214-5.
5. Swensson B, Wretmann J. Model Assisted Survey Sampling. United States of America: Springer-Verlag, 2003.
6. Coughlin SS, Pickle LW. Sensitivity and specificity-like measures of the validity of a diagnostic test that are corrected for chance agreement. Epidemiology. 1992;3(2):178-81.
7. Fawcett T. An introduction to ROC analysis [Internet]. 1st ed. Pattern Recognition Letter; 2005. https://ccrma.stanford.edu/workshops/mir2009/references/ROCintro.pdf.

Cite this article as: Juneja A, Anand A. Understanding statistical concepts in laboratory quality control measures in biomedical research. Int J Res Med Sci 2015;3:3443-5.