Nigerian Veterinary Journal
Vol 34 (4) 870-876
REVIEW

Clinical Biochemistry as a Prognostic Tool in The Management of the Critically-ill Patient

AKINRINMADE, J.F.[1] and AKINRINDE, A.S.[2]

[1]Department of Veterinary Surgery and Reproduction, Faculty of Veterinary Medicine, University of Ibadan, Nigeria; [2]Department of Veterinary Physiology, Biochemistry and Pharmacology, Faculty of Veterinary Medicine, University of Ibadan, Nigeria. Corresponding author: E- mail address: leyesteve2000@yahoo.com, Telephone: +23407064368126

INTRODUCTION

The veterinarian's primary role involves the use of scientific knowledge and skills for the protection of animal health and the relief of animal suffering. Scientific knowledge in this sense would include the range of approaches from mere observation of signs to the use of sophisticated methods available for the management and treatment of animal ailments. The information gained from serum biochemistry, for example, would substantiate physical examination coupled with medical history to provide excellent basis for judgment with respect to the nature of the disease, the extent of tissue and organ damage and selection of appropriate treatment (Schalm et al., 1975). The Critically-ill patient describes those with diseases that are life-threatening such that they need constant monitoring and usually have secondary involvement of a number of organ systems, regardless of the primary organ dysfunction, and therefore require total body care (Burrows, 1981).

The average Nigerian veterinarian has long relied largely on mere observation of signs and physical examination of patients in coming up with a diagnosis of disease or the prediction of the chances of survival of his patients and the formulation of appropriate therapeutic strategies. The result is that many patients are lost to practice that is merely based on what can be physically seen, while less attention is paid to determining the underlying aetiology. Also lost is the professional and moral dignity of the veterinarian as clients would tend to question the clinical competence of the doctor. While economic considerations hinder, to a large extent, the application of standard laboratory evidence to veterinary practice in Nigeria, it is important to understand that best practices need to be embraced in order to bring the Nigerian veterinary practice in consonance with what obtains in the rest of the world.

This paper attempts to evaluate the current contribution of biochemical markers in the management of veterinary patients, and especially the critically-ill patient. Most, if not all, diseases are manifestations of abnormalities of molecules, chemical reactions or biochemical processes. Biochemical tests are performed for four main reasons: diagnosis, monitoring, prognosis and screening. When used appropriately, biochemical tests can contribute substantially to the overall care of the patient. The critically-ill patient is especially implicated for the use of clinical

biochemistry tools as valuable information can be obtained from measured parameters that can offer advantage in prediction of the outcome of diseases. Despite the observed importance of clinical chemistry and laboratory medicine in clinical medicine, the attitude of Nigerian veterinarians in practice towards the use of laboratory tests appear to be very minimal, or even non-existent in some cases. In keeping with contemporary global best practices, practicing veterinarians in Nigeria must seek to employ this invaluable tool. It is hoped that this paper will create the needed awareness among Nigerian veterinarians in employing clinical biochemistry in the management of patients, towards improving veterinary practice in the country. Keywords: Clinical biochemistry, Nigeria, Veterinarian, critically-ill patient

What is Clinical Biochemistry?

Clinical Biochemistry refers to that branch of laboratory medicine in which chemical and biochemical methods are applied to the study of disease (Gaw et al, 1999). In theory, this embraces all non-morphological studies, but in practice, it is usually, though not exclusively, confined to studies on blood and urine, although analyses are made on other body fluids (Gaw, et al, 1999). Clinical biochemistry can be a useful aid to the veterinary practitioner for the diagnosis of disease, and is one of a number of laboratory investigations which are employed (Douglass and Eckersall, 1985).

Biochemical investigations are involved, to varying degrees, in every branch of clinical medicine. The results of biochemical tests may be of use in diagnosis and in monitoring of treatment. Biochemical tests may also be of value in screening for disease or in assessing the prognosis, once a diagnosis has been made. The biochemistry laboratory is often involved in research into the biochemical basis of disease and in clinical trials of new drugs. Clinical biochemistry provides a variety of non-invasive tools that can be used as prognostic markers for the management of animal patients. The repertoire of common tests carried out in the clinical biochemistry laboratory is presented in Table I.

Table I: The Clinical Biochemistry repertoire

Core biochemical tests	Specialized tests	Other tests
Electrolytes (Na, K, Cl, HCO_3	Hormones	Blood gases (PCO_2, PO_2)
Urea and creatinine	Trace elements	pH
Total protein and albumin	Vitamins	Lactate
Aminotransferases (ALT and AST)	DNA analyses	
Alkaline phosphatase (ALP)	Lipids and lipoproteins (serum triglycerides)	
Glucose	Serum cholesterol	
Gamma-glutamyl transferase		
Bilirubin		

Source: Gaw et al. (1999) Clinical Biochemistry: An illustrated color text. 2nd edition

Information from clinical test results will be of value only if it is accurate and relevant, and if its significance is appreciated by the clinician so that it can be used appropriately to guide clinical decision-making. The success of biochemical tests depends on appropriate sample collection and analysis and the monitoring of factors that can influence biochemical variables. Such factors include age, sex, stress, nutritional status, drugs etc. (Brommer et al, 2001) Errors that affect the results of biochemical tests may be pre-analytical (e.g. patient/sample misidentification; inappropriate test

request; errors in sample collection; inappropriate container, handling, storage and transportation), analytical (e.g. equipment malfunction, sample mix-ups, undetected failure in quality control) or post-analytical (e.g. improper data entry, erroneous validation of analytical data). Errors, can however, be minimized by scrupulous adherence to robust, agreed protocols at every stage of the testing process: this means a lot more than ensuring that the analysis is performed correctly.

Reference ranges in Clinical Biochemistry

Biochemical test results are usually compared to a reference range considered to represent the normal healthy state. Most reference ranges are usually chosen to include 95% of the values found in healthy volunteers, and hence, by definition, 5% of the population will have a result out of the reference range (Bangert et al, 2008; Malati, 2009). In practice there are no rigid limits demarcating the diseased population from the healthy; however, the further a result is from the limits of the range, the more likely it is to represent pathology. In some situations it is useful to define 'action limits', where appropriate intervention should be made in response to a biochemical result. It is important to note, however, that a test result within the reference range does not necessarily imply that there is no disease and a test result outside the reference range does not indicate disease. Also, the ranges found in healthy individuals from different breeds vary for some analytes. Since, biochemical variables can be influenced by intrinsic factors such as the breed of the animal, it is important that reference ranges be defined for specific localities (Brommer et al, 2001). International guidelines (e.g. by International Federation of Clinical Chemistry (IFCC) and International Council for Standardization in Hematology (ICSH), the Clinical Laboratory Standard Institute (CLSI) formerly known as National Committee for Clinical Laboratory Standards (NCCLS) recommend that every country must establish reference intervals for healthy individuals belonging to a group of homogeneous population. It is disheartening to note that as at today, none of the veterinary teaching hospitals in all the veterinary schools in Nigeria has laboratory reference values as obtained in other parts of the world. Interpretation of biochemical abnormalities has largely been based on values obtained from different geographic zones.

The Critically-ill patient

The critically-ill patient represents a wide spectrum of disease. They include some trauma patients, animals undergoing cancer chemotherapy, animals with severe respiratory diseases, neurologic disease, pyometra, etc. The underlying feature is that the diseases are life-threatening so that they need constant monitoring and usually have secondary involvement of a number of organ systems, regardless of the primary organ dysfunction, and therefore require total body care (Burrows, 1981).

Critically-ill patients share several common features, particularly the need for diligent monitoring and nursing. Critically-ill patients have fluid, acid-base and electrolyte disturbances, increased caloric requirements and an increased susceptibility to infection (Burrows, 1981).

Certain patients may present with conditions that require predominantly either medical treatments or surgical interventions. However, a surgical condition,

Table II: Physical status classification

Classification	Results of physical examination findings	Examples of physical examination findings	Prognosis for survival
I	Healthy, no underlying disease	No abnormalities	Excellent
II	Geriatric or obese animals. Neonates, local disease with mild systemic disturbance	Controlled diabetes, closed fracture	Excellent
III	Diseases with moderate systemic signs	Anaemia, cachexia. Fever, renal disease, cardiac disease	Good
IV	Disease with severe systemic signs	Shock, uremia, toxaemia, gastric torsion, colic. hemorrahge	Guarded
V	Moribund or comatose	Advanced disease, solitary or multi-systemic organ failure	Poor

for example, may simultaneously be combined with diseases that require a more medical intervention. In both situations, a critical evaluation of necessary laboratory parameters is vital in formulating appropriate intervention (surgical or medical) and in reaching a correct prediction of the outcome of intervention.

Table II presents features of physical status classification of veterinary patients (Williams and Owens, 2011). Critically-ill veterinary patients are/include those that are classified as having physical status IV and V, including patients suffering from diseases with severe systemic signs and patients that are moribund or comatose, respectively.

Patients with physical status I – III would generally present fewer complications for management of their conditions. For patients in classes II to V, it is recommended that laboratory tests including total plasma protein levels, urinalysis and a complete chemistry profile be obtained as part of pre-surgical screening to assess the surgical risk. Diseases that involve a major organ system or more than one organ system increase surgical risk. These include patients with major cardiopulmonary abnormalities, renal failure, traumatic bladder rupture urethral obstructions, liver disease, endocrine disorders, diabetes mellitus, etc. The management of patients with physical status IV and V would ideally involve examination of a wide range of biochemical parameters in order to effectively manage their condition. Such patients present as poor surgical risks, and should therefore undergo extensive pre-surgical assessment/screening if they would survive surgery.

Veterinary intensive care may be considered as too expensive for most practitioners, considering the involvement of sophisticated monitoring equipment. Nevertheless, it has developed into the round-the-clock care of the critically-ill patient, with constant monitoring of physical and laboratory parameters, attendance to patient's changing needs and support of physiological and metabolic functions (Burrows, 1981).

Molecular biology tools in clinical biochemistry

Molecular diagnostic tools and detection methods such as nucleic acid amplification are becoming invaluable additions to laboratory testing and clinical evaluation, providing, diagnostic, therapeutic and prognostic information. According to Murray et al (2000), all diseases have genetic bases. Gene identification may provide an indication of the biochemical basis to the disease, thus enabling therapies to be designed (Brown, 1998). During the last few years, a number of genes responsible for inherited diseases have been identified. Once a gene associated with a single gene disorder has been isolated and cloned, it is usually easy to develop a gene-based diagnostic test. This can be used to confirm the diagnosis of an existing condition, as a prognostic indicator that an individual animal will eventually develop a disease, or may be at increased risk of developing disease conditions or to reveal information on a healthy individual animal's carrier status (Soetan and Salako, 2010). Genetics has been used in the diagnosis of mutations in animal diseases including:

1. Cittrullinemia in cattle (Hauge, 1989)
2. Marple syrup urine disease (MSUD) in bovine (Hauge, 1989)
3. Hyperkalemic periodic paralysis (HYPP) in Quarter Horses, a genetic disease observed among quarter horses (Hauge, 1989).
4. Leukocyte adhesion deficiency in Cattle and malignant hyperthermia in pigs.

It is important to note that diagnostic molecular biology is widely used in a number of areas including haematology, immunology and microbiology with possibly the least developed area being clinical biochemistry. However, molecular methods will be increasingly incorporated into all areas of pathology, not to replace current tests but as an aid in evaluating the future risk of disease.

Collection of Baseline data for Biochemical parameters

Reference ranges are sets of values used by a health professional to interpret a set of health professional to interpret a set of medical test results from samples obtained from patients. A reference range is usually defined as the set of values 95 percent of the normal population falls within (that is, 95% prediction interval) (Bangert et al, 2008). It is determined by collecting data from vast numbers of laboratory tests. Factors such as nutrition, age, sex, breed and climate were known to affect biochemical and hematological parameters of clinically healthy dog (Coles, 1986; Awah and Nottidge, 1998). Variations have been observed in these indices between temperate and tropical animals (Awah and Nottidge, 1998). Baseline values established for animal breeds originating from the temperate regions may not be appropriate for use in breeds from the tropical regions. These variations had been thought to be due to the effect of nutrition, climate and sub clinical diseases (Ogunsanmi et al., 1999; Awah and Nottidge, 1998). Although clinical biochemistry is potentially a valuable diagnostic aid in the veterinary care of animals, the interpretation of results in sick animals is often difficult. Any physiologic and pathological changes can be evaluated only if the normal values are available for comparison. Considerable information is available on the normal biochemical test values of domestic animals of exotic breeds kept under different environment and management conditions. It is therefore pertinent that baseline values for animals kept under tropical conditions be sought and established. This is because the use of biochemical values that are derived from exotic breeds for monitoring the health status of indigenous breeds could be misleading.

CONCLUSION

Clinical biochemistry is a potentially valuable aid in the management of the veterinary patient. Its use in veterinary care will, to a large extent, improve the capability of veterinarians to protect animal health and relieve suffering, especially in the critically-ill patient. When combined with physical examination and medical history, it can provide an excellent basis for decision-making in the care of patients. It therefore becomes highly imperative for veterinarians in the 21st century to seek to employ this invaluable tool in the management of patients. Correct interpretation of biochemical test results, however, relies on the availability of reference ranges that are specific for breeds and climatic regions. In this respect, it would be highly beneficial for Veterinary teaching hospitals in the country to vigorously pursue the establishment of reference ranges for predominant breeds of domesticated animals domiciled in their respective catchment regions.

REFERENCES

AWAH and NOTTIDGE, H.O. (1998): Serum biochemical Parameters in Clinically Healthy Dogs in Ibadan. Trop. Vet. 16: 123-129.

BANGERT, S.K., MARSHALL, W.J. and LEONARD, W. (2008). Clinical biochemistry: metabolic and clinical aspects. Philadelphia: Churchill Livingstone/Elsevier. p. 19.

BROMMER, H., SLOET van OLDRUISTENBORGH - OSTERBAAN, M.M. and KESSELS, B. (2001) Hematological and Biochemical characteristics of Dutch warm blood foals managed under three different rearing conditions from birth to 5 months of age Vet Q. 23 (2): 92-95

BROWN, T.A. (1998): Gene Cloning. An Introduction, 3rd Edition. Stanley Thornes Publishers Ltd., U.K.

BURROWS, C.F. (1981): Veterinary Intensive care. J. Small Anim. Pract. 22: 231-252

CLSI (2008) How to define and determine Reference Intervals in the Clinical Laboratory; Approved Guidelines. 2nd ed. Clinical and Laboratory Standards Institute (CLSI Document no. C28- A2 20 (13) pp. 1-38.

COLES, E.H. (1986): Veterinary Clinical Pathology 4th Edition. W.B. Saunders Co. Philadelphia.

DOUGLASS, T.A. and ECKERSALL, P.D. (1985) Clinical Biochemistry in Veterinary Practice: Results of a survey by questionnaire J. Small Anim. Pract. 26:363-367.

GAW, A., COWAN, R.A., O'REILLY, D.J., STEWART, M.J. and SHEPHERD, J. (1999) Clinical Biochemistry: An Illustrated color text. Churchill Livingstone. Second Edition pp 2-7.

HAUGE, J.G. (1989): DNA Technology in Diagnosis, Breeding and Therapy, In: Clinical Biochemistry of Domestic Animals Ed. Kaneko JJ (1989). 3rd Ed. Academic Press. Inc., New York. pp. 21-44.

MALATI, T. (2009): Whether Western normative laboratory values used for clinical diagnosis are applicable to Indian population? An overview on Reference interval. Indian Journal of Clinical Biochemistry 24(2): 111-122.

MURRAY R. K., GRANNER D. K., MAYER P. A., RODWELL V. W. (2000): Harper's Biochemistry, 25th Edition, McGraw-Hill. Health Profession Division, USA.

OGUNSANMI, A.O., AKPAVIE, S.O. and ANOSA, V.O. (1990) Serum Biochemistry Changes in West African Dward Sheep. Experimentally Infected With Trypanosomia brucei. Rev Elev. Med. Vet. Pay Trop. 47(2): 195-200.

SCHALM, O.W., JAIN, N.C., and CARROLL, E.J. (1975): Veterinary haematology. 3rd edition Lea and

Febiger Philadelphia,U.S.A. pp. 13, 123, 136.

SOETAN, K..O. and SALAKO, A.E. (2010) The importance of genetics in the diagnosis of animal diseases- a review. African Journal of Biotechnology Vol. 9(4), pp. 402-408.

SOLBERG, H.E. (1993) A guide to IFCC recommendations on reference value. J Int Fed Clin Chem 5: 160-4.

WILLIAM, D. and OWENS, M.D. (2011): American society of anaesthesiologists Physical status classification system is not a risk classification system. Anesthesiology 94(2): 378.