DOI: 10.7860/JCDR/2016/22338.8738

Case Report

Biochemistry Section

Is dilution important: Factitious Total Creatine Kinase in case of Rhabdomyolysis?

SUNIL KUMAR NANDA[1], ASHA DINAKARAN[2], LOPAMUDRA RAY[3]

ABSTRACT

Factitious test reports may result in incorrect diagnosis and incorrect management. Such incorrect diagnosis can be prevented by a vigilant biochemist. We report a case of Rhabdomyolysis presenting with extremely low total Creatine Kinase (CK) levels which was factitious. Running the sample in dilution resulted in a very high value of total CK which could have been missed if the sample was not run in dilution and the diagnosis of Rhabdomyolysis could have been missed.

Keywords: Incorrect diagnosis, Muscle injury, Substrate depletion, Sample dilution

CASE REPORT

A 30-year-old male patient came with the history of weakness, pain and swelling of both lower limbs. General examination revealed muscular tenderness and a diagnosis of rhabdomyolysis was suspected.

Investigations showed urea value of 140mg/dl and creatinine value of 2.7mg/dl. Urine routine showed Albumin 3+, granular casts positive. His Serum Glutamic Oxaloacetic Transaminase (SGOT) value was 1110U/L and Serum Glutamic Pyruvic Transaminase (SGPT) value was 1205 U/L. He developed Congestive Cardiac Failure (CCF) and his CK-MB was 336U/L and Troponin I was positive. Since, rhabdomyolysis was suspected, Total Creatine Kinase (CK) was requested for this patient. The value obtained was zero. The sample was re-run in 1:2 dilution, 1:5 dilution and 1:10 dilution and the diluent used was normal saline. On repeating the test in dilution, the value of total CK was found to be 45,425U/L. Running sample in dilution should always be considered, if the results of diagnostic enzymes are found to be extremely low and low values do not correlate with the clinical diagnosis.

The initial value of zero was due to substrate depletion. The substrate in the above mentioned reaction is creatine phosphate. Creatine phosphate gets consumed by very high concentration of CK which is present in the serum sample before the kinetic measurement actually gets initiated. The whole substrate gets consumed within the lag phase which results in falsely low values.

DISCUSSION

Factitious biochemical reports is one of the common problems faced by the biochemist. Laboratory errors could be classified as pre-analytical, analytical and post-analytical. Pre-analytical errors include errors related to inappropriate ordering of test, wrong patient identification, haemolyzed sample, inadequate sample volume, improper transport and improper storage, inappropriate bar code labeling, errors related to centrifugation. Analytical errors are related to errors related to inappropriate test method, interferences in methods, incorrect calibration and inadequate corrective measures related to quality control outliers. Post-analytical errors are related to errors caused due to wrong result entry, inability to maintain turnaround time, inappropriate report interpretation [1]. Pre-analytical errors accounts for 32 to 75% of laboratory errors, analytical errors accounts for 13-32% of errors and post-analytical errors accounts for 13 to 40% of errors [2]. Though pre-analytical errors are more common, analytical errors have more serious consequences in patient management.

CK is an enzyme present in tissues where energy requirements are high. CK occurs in three isoforms - CK-MM (Skeletal muscle), CK-MB (cardiac muscle) and CK-BB (brain). Macro forms of CK also do exist which are expressed in certain diseases. The normal reference range for CK ranges between 46 to 171U/L in males and 34 to 145 U/L in females [3].

Total CK is measured by colorimetric method. The principle of total CK measurement is as follows: CK catalyzes the conversion of creatine phosphate and ADP to creatine and ATP. ATP liberated phosphorylates glucose to glucose-6-phosphate. Glucose-6-phosphate is oxidized to 6-phosphogluconate, reducing NADP to NADPH in presence of glucose 6-phosphate dehydrogenase. The rate of increase in NADPH absorbance at 340nm is directly proportional to the activity of CK present in serum [4].

CK and Rhabdomyolysis: Rhabdomyolysis refers to rupture of skeletal muscle which could be due to various causes like trauma, burns, malignant hyperthermia, statins, chemotherapeutic agents, anti-psychotic drugs, polymyositis, dermatomyositis [5]. The most sensitive marker of myocyte injury is Total CK (CK-NAC) levels. The CK-NAC value can go as high as 2,00,000 following rhabdomyolysis [6,7]. Within 2 to 12 hours, CK begins to rise in serum, reaches peak value by 24 to 72 hours and comes down by 7 to 10 days [8]. A 5 fold elevation of CK is considered as diagnostic of Rhabdomyolysis by majority of authors [9]. The concentration of CK is directly proportional to the extent of muscle injury [10]. Failure of CK to fall in Rhabdomyolysis is a predictor of future development of Acute Renal Failure (ARF) [11]. Bhavsar P et.al., conducted a study on biomarkers of ARF in Rhabdomyolysis and observed that on admission, CK is a better predictor of ARF in Rhabdomyolysis than Creatinine and urinary myoglobin [12]. Casares P et al., reported CK value of 14,54,952U/L in a patient with Rhabdomyolysis due to heavy work out [13]. Andrew C. Berry et al., reported a CK value of 92,803U/L in a 28-year-old male patient who developed Rhabdomyolysis with modest exercise and the patient did not develop renal failure. They also stated, any patient presenting with rhabdomyolysis with modest exercise requires further metabolic and genetic investigation to get to know the etiology of Rhabdomyolysis [14]. Yeter E et al., reported a case of Rhabdomyolysis with CK value of 3471U/L caused due to additive effect of a patient with hypothyroidism who was started on statins. They stated in any patient requiring statins, thyroid status to be checked and if found hypothyroid, thyroid status to be treated before initiating statin therapy to avoid Rhabdomyolysis [15]. This case also highlights the importance of mentioning the diagnosis while ordering the test.

CONCLUSION

Samples for CK estimation should be run in dilution in cases of Rhabdomyolysis to avoid error in its reporting.

REFERENCES

[1] Plebani M. The detection and prevention of errors in laboratory medicine. *Ann Clin Biochem*. 2010;47:101-10.
[2] Sharma P. Preanalytical variables and laboratory performance. *Indian Journal of Clinical Biochemistry*. 2009;24:109-10.
[3] Roberts WL, McMillin GA, Burtis CA. Reference Information for the Clinical Laboratory In: Burtis CA, Ashwood ER, Bruns DE editors. Tietz text book of clinical chemistry and molecular diagnostics 5th edn: Philadelphia: Saunders;2012:2131-88.
[4] Panteghini M, Bais R. Serum Enzymes In: Burtis CA, Ashwood ER, Bruns DE editors. Tietz text book of clinical chemistry and molecular diagnostics 5th edn: Philadelphia: Saunders; 2012:565-98.
[5] Guis S, Mattei JP, Cozzone P J, Bendahan D. Pathophysiology and clinical presentations of rhabdomyolysis. *Joint Bone Spine*. 2005;72:382-91.
[6] Criddle L. Rhabdomyoysis. Pathophysiology, recognision and management. *Critical Care Nurse*. 2003;23:14-32.
[7] Russell T. Acute renal failure related to rhabdomyolysis: pathophysiology, diagnosis, and collaborative management. *Nephr Nurs J*. 2005;32:409-17.
[8] Brancaccio P, Lippi G, Maffulli N. Biochemical markers of muscular damage. *Clin Chem Lab Med*. 2010;48:757-67.
[9] Keltz E, Khan FY, Mann G. Rhabdomyolysis. The role of diagnostic and prognostic factors. *Muscles, Ligaments and Tendons Journal*. 2013;3:303-12.
[10] Hunter JD, Gregg K, Damani Z. Rhabdomyolysis *Continuing Education in Anaesthesia, Critical Care & Pain*. 2006;6:141-43.
[11] Subramanian A, Sukheeja D, Trikha V, Pandey AK, Albert V, Pandey RM. Evaluation of serum creatine kinase and urinary myoglobin as markers in detecting development of Acute Renal Failure in severely injured trauma patients. *ISRN Emergency Medicine*. 2013:1-8.
[12] Bhavsar P, Rathod KJ, Rathod D, Chamania CS. Utility of serum creatinine, creatine kinase and urinary myoglobin in detecting Acute Renal Failure due to Rhabdomyolysis in trauma and electrical burns patients. *Indian J Surg*. 2013;75:17–21.
[13] Casares P, Marull J. Over a millon creatine kinase due to a heavy work-out: A case report. *Cases Journal*. 2008:173.
[14] Berry AC, Lenchus JD, Avalos D, Caplan A, Berry BB, Monzel MJ. Exertional Rhabdomyolysis: A case of markedly elevated creatine kinase without acute kidney injury. *Journal of Medical Cases*. 2014;5:483-85.
[15] Yeter E, Keles T, Durmaz T, Bozkurt E. Rhabdomyolysis due to the additive effect of statin therapy and hypothyroidism: a case report. *Journal of Medical Case Reports*. 2007;1:130.

PARTICULARS OF CONTRIBUTORS:
1. Professor, Department of Biochemistry, Pondicherry Institute of Medical Sciences, Pondicherry, India.
2. Tutor, Department of Biochemistry, Pondicherry Institute of Medical Sciences, Pondicherry, India.
3. Associate Professor, Department of Biochemistry, Pondicherry Institute of Medical Sciences, Pondicherry, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Sunil Kumar Nanda,
Professor, Department of Biochemistry, Pondicherry Institute of Medical Sciences, Pondicherry, India.
E-mail: drsknanda1@gmail.com

FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: **Jun 27, 2016**
Date of Peer Review: **Aug 06, 2016**
Date of Acceptance: **Aug 17, 2016**
Date of Publishing: **Oct 01, 2016**