Evaluation of Creatine Kinase as a Diagnostic Tool for Thyroid Function

KMDS Panag*, Gitanjali*, Sudeep Goyal**

ABSTRACT

Thyroid disorders are very commonly affecting the general population, even the persons residing in non goitrous areas are no exception. Currently used tests for the assessment of thyroid functions (thyroid-stimulating hormone [TSH], tri-iodothyronine [T3] and thyroxine [T4]) are not sometimes sufficient to clearly make out the diagnosis as T3 and T4 levels are affected by so many other nonspecific conditions. The present study was done to evaluate the role of alternative biochemical parameter creatine kinase (CK) in diagnosing thyroid disorders. Sixty hypothyroid and 40 hyperthyroid patients were compared with 50 age, sex and socioeconomic status matched healthy controls. FT3, FT4 and TSH levels were measured by ELISA method and CK levels were measured by modified IFCC method. In hypothyroid patients, significant increase in CK levels was found as compared to control group (190 ± 40 IU/l in hypothyroid patients and 100 ± 70 IU/l in control group). A negative correlation was also found between FT3 and CK (r = –0.51; p < 0.005). In patients of hyperthyroidism, the levels of CK were found to be on the lower side. It was concluded that CK measurements may be useful as alternative diagnostic tool for the diagnosis of thyroid function disorders, which may be not only because of prevalence of muscular dystrophies in thyroid disorders but also due to role of FT3 in gene expression.

Keywords: Thyroid disorders, creatine kinase, diagnostic tool

Thyroid gland is located in the neck, anterior to trachea. It consists of two lobes that are connected by an isthmus. The gland produces hormones which play a great role in control of basal metabolic rate (BMR), general body metabolism, growth, development and tissue differentiation. Thyroid dysfunction is one of the most common endocrinological disorders. Consequently, abnormalities of these hormones frequently involve many organ systems producing diverse clinical signs and symptoms which are generally nonspecific. Thus confirmation of a provisional diagnosis of thyroid disorder rests largely upon biochemical parameters.¹

The commonly used parameters for assessment of thyroid function are estimation of thyroid stimulating hormone (TSH), total tri-iodothyronine (T3), total thyroxine (T4), free T3 (FT3) and free T4 (FT4). Out of these TSH has been accepted as the initial screening test. This is because serum level of TSH has been documented to reflect the integrative action of thyroid hormone on the tissue most sensitive to circulating thyroid hormones, the pituitary.²

However, the abnormal TSH level necessitates the use of other indicators of thyroid status including total and FT3 and T4. None of these parameters have proven to be ideal as their measured levels tend to vary in conditions like pregnancy, use of oral contraceptives, protein wasting diseases, liver disease, certain drugs and heparin, etc.³ The inherent limitations of these parameters necessitate the establishment of alternate markers and enzymes like transaminases, lactate dehydrogenase (LDH) and creatine kinase (CK). Among these, CK has shown promising results as a diagnostic tool for thyroid disease.

Serum CK was first used as a diagnostic aid in progressive muscular dystrophy.⁴ It has since then become important clinical marker for muscle damage. The serum CK levels in healthy individuals depend on age, race, lean body mass and physical activity.⁴-⁶ Musculoskeletal disorders often accompany thyroid dysfunction. In addition to well-known observation that musculoskeletal disorders are common in patients with hypothyroidism, they are also observed in thyrotoxicosis and level of CK is altered in both these conditions.⁷ In recent years, studies have been conducted...
to establish a relationship of CK levels in thyroid diseases. Skeletal muscle is affected by hypothyroidism more profoundly in cases of overt hypothyroidism and less so when subclinical hypothyroidism is present.

Thus, it follows that assay of CK activity in serum may prove to be valuable in screening of thyroid disorders and in the present study, we tried to evaluate the role of CK as an alternative diagnostic tool in patients of thyroid disorder.

MATERIAL AND METHODS

The study was done at GGS Govt. Medical College, Faridkot, Punjab. The study group comprised of 100 patients randomly selected from patients coming for thyroid function tests in the biochemistry diagnostic laboratory. There were 60 hypothyroid cases and 40 hyperthyroid cases. Fifty age, sex and socioeconomic status matched persons were taken as controls. Exclusion criteria was taken to rule out other diseases which can alter the results of study like cardiovascular, neuromuscular involvements, recent cerebral stroke, gross hepatic or renal dysfunction and pulmonary infarction. All patients were screened for any drug history, especially drugs which can affect CK or thyroid hormone levels. Recent history of intramuscular injections, strenuous exercise was ruled out. Informed written consent was obtained for venipuncture. Venous blood was withdrawn for investigations taking all aseptic precautions. Serum was separated and investigated either immediately or it was preserved at 2-8°C for upto three days for CK measurement.

FT₃ and FT₄ were measured by competitive enzyme-linked immunosorbent assay (ELISA). TSH was measured by quantitative ELISA using Monobind kits. CK was measured by modified International Federation of Clinical Chemistry (IFCC) method based on the principle that ATP formed by reaction of CK on creatine phosphate and ADP reacts with glucose to form glucose 6 phosphate, which reduces NADP to NADPH. The rate of reduction of NADP to NADPH is measured at 340 nm.

RESULTS

The present study was conducted to evaluate the levels of CK in hypothyroid and hyperthyroid patients. The study and control groups were compared according to age, sex distribution and routine investigations were done which showed insignificant results. Table 1 shows the levels of the four parameters TSH, FT₃, FT₄ and CK in control and study groups.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control</th>
<th>Hypothyroid</th>
<th>Hyperthyroid</th>
</tr>
</thead>
<tbody>
<tr>
<td>FT₃ (pg/dl)</td>
<td>2.8 ± 0.64</td>
<td>1.4 ± 0.41</td>
<td>5.82 ± 2.39</td>
</tr>
<tr>
<td>FT₄ (ng/ml)</td>
<td>1.30 ± 0.17</td>
<td>0.82 ± 0.20</td>
<td>3.5 ± 1.8</td>
</tr>
<tr>
<td>TSH (mIU/l)</td>
<td>2.50 ± 0.80</td>
<td>20.11 ± 13.57</td>
<td>0.18 ± 0.18</td>
</tr>
<tr>
<td>CK (IU/l)</td>
<td>100 ± 70</td>
<td>190 ± 40</td>
<td>60 ± 30</td>
</tr>
</tbody>
</table>

The mean values of FT₃ and FT₄ in hypothyroid patients were 1.4 ± 0.41 pg/dl and 0.82 ± 0.20 ng/ml respectively. TSH levels were 20.11 ± 13.57 mIU/l. The mean values of FT₃ and FT₄ in hyperthyroid patients were 5.82 ± 2.39 pg/dl and 3.5 ± 1.80 ng/ml respectively. TSH level was 0.18 ± 0.18 mIU/l. The mean value of FT₃ and FT₄ in control patients was 2.8 ± 0.64 pg/dl and 1.3 ± 0.17 ng/ml, respectively. TSH level was 2.50 ± 0.80 mIU/l.

The CK values in the three groups were 190 ± 40, 60 ± 30 and 100 ± 70 IU/l in hypothyroid, hyperthyroid and normal individuals, respectively.

DISCUSSION

The study was done to evaluate the role of CK as a supportive parameter for diagnosing hypothyroid or hyperthyroid individuals. The levels of CK are found to be significantly higher in patients of hypothyroidism as compared to normal individuals which may be because of skeletal muscle involvement in thyroid disorders. Hekimsoy et al in a study conducted in 2005, found that skeletal muscle is affected by hypothyroidism more profoundly in cases of overt hypothyroidism as compared to subclinical hypothyroidism. Also, there was positive correlation between CK and TSH (r = 0.432; p = 0.04), a negative correlation was found between FT₃ and CK (r = –0.556; p = 0.002). Giampietro et al in 1984, found myoglobin and CK to be the best indicators of hypothyroid myopathy, since they are sensitive for the early detection of muscle involvement due to metabolic disorder and are closely correlated to the metabolic condition of patients.

Scott et al in a study conducted in 2002 showed that thyroid hormone replacement therapy resulted in resolution of clinical symptoms and a marked reduction in CK levels in a patient with progressive proximal weakness and serum CK level of over 29,000 IU/l. Such a high serum CK level in a patient with hypothyroidism underscores the importance of assessing thyroid function in patients with weakness, regardless of serum CK levels, even when systemic symptoms and signs of hypothyroidism are minimal or absent. In case studies, patients with hypothyroidism solely presented...
with symptoms of myositis and very high levels of CK which resolved after treatment for hypothyroidism and in a patient of Grave’s disease, patient developed myalgia with high level of CK after total thyroidectomy, the features were normalized after treatment and again reappeared after treatment was stopped. These studies clearly show that muscular involvement was there in thyroid disorders. In hypothyroid patients with decrease in serum T3, there is significant increase in CK and this may be in fact used as a parameter for screening hypothyroid patients.

In the present study, similar results were found showing increased levels of CK in hypothyroid patients and decreased CK in hyperthyroidism. Also, there was a negative correlation between FT3 and TSH. Some authors suggest direct role of T3 at the regulation of gene expression. It has been shown to induce or repress production of different proteins by increasing or decreasing transcription. Authors have studied thyroid hormone-dependent gene expression in differentiated embryonic stem cells which were induced or repressed in response to T3. Very high levels of FT3 have been documented to inhibit protein synthesis.

It is concluded from these findings that measurement of CK may act as a good tool to diagnose hypothyroidism not only because of well-documented muscular dystrophy in thyroid patients but also because of negative correlation between FT3 and CK possibly mediated at the level of gene expression.

REFERENCES


