

Creatine Kinase High in Children: A Practical Approach

Jorge Sales Marques*

Pediatric Department, Centro Hospitalar Conde S. Januário, Macau, China

***Corresponding Author:** Jorge Sales Marques, Pediatric Department, Centro Hospitalar Conde S. Januário, Macau, China.

Received: February 05, 2017; **Published:** February 18, 2017

Creatine kinase (CK) is the most sensitive indicator and the best way to evaluate the evolution of muscle injury.

About 20% of the “normal” individuals present elevated plasma CK values.

CK-dimer, has 3 isoforms: MM, MB, BB. They are different electrophoretically- Muscle tissue: 99% MM; Cardiac tissue: 20% MB and Brain tissue: 90% BB.

The concentration of CK-MB in muscle tissue increases in cases of muscular dystrophy, motor neuron diseases, inflammatory, infectious, metabolic, congenital and endocrine myopathy.

We need to exclude elevation of CK in non-neurological causes such as exercises, some drugs like statins, zidovudine and clofibrates, rhabdomyolysis secondary to infections and prolonged seizures, iatrogenic procedures like muscle biopsy or major surgery. The CK level, mostly is not too high and in 48 - 72 hours return to normal range.

In neuromuscular causes, the CK in Duchenne and Becker muscular dystrophy increased from birth, with peak about 2 years of age, with progressive decline as the muscle is replaced by fat and fibrosis. CK value is from 15,000 up to 35,000 IU / L. The child showed progressive proximal muscle weakness. At birth they are rarely symptomatic or showed mild hypotonia. They usually sit and walk within the expected age or a little later. Gowers sign is evident after 3 years old. In female carriers of Duchenne and Becker, the CK levels usually are up to 3x normal.

In pelvic and scapular waists dystrophy, there is a variable elevation of CK with proximal muscle weakness.

In fascioscapulohumeral dystrophy, the CK is slightly increased and the muscle weakness is predominantly at the shoulders and face.

In Steinert's disease, the CK is normal or slightly increased. The newborn showed hypotonia since birth, with delayed psychomotor development, muscle myotomy after the age of 5 years.

In inflammatory myopathies (polymyositis and dermatomyositis), the child presented with muscle weakness, abnormal EMG, changes in muscle biopsy and CK value can increase about 100x about the normal range.

Other inflammatory diseases associated with CK elevation are:

- rheumatoid arthritis, SLE, Sjogren's disease, scleroderma, systemic vasculitis, Behçet's disease and sarcoidosis.

Infectious myopathy can be caused by virus, bacteria, fungus, parasites, mycobacteria and spirochetes.

Most common metabolic myopathies are McArdle's disease or muscle phosphorylase deficiency: is an autosomic recessive disorder with intolerance to recurrent exercise in childhood and recurrent episodes of cramps, fatigue and myoglobinuria in adolescence. CK levels do not normalize in the intercritical periods. Another disease is Carnitine palmitoyltransferase deficiency with CK levels normal in intercritical period.

Mitochondrial cytopathies can cause also CK high but are associated with unrelated clinical findings and more systemic involvement.

Pompe disease or alpha glucosidase deficiency is also a recessive inheritance with heterogeneous clinical manifestations: generalized fatigue, myalgias, involvement of the pelvic girdle muscles and cardiomyopathy, respiratory failure, with increase of CK up to 15x.

Malignant hyperthermia can cause fever, generalized muscle contraction and stiffness, metabolic acidosis and rhabdomyolysis, it usually occurs after the use of inhaled anesthetic drugs in susceptible individuals. CK may rise markedly during one episode and remain elevated after recovery. It can occur sporadically or in a familiar way. Individuals with central core disease are susceptible to malignant hyperthermia.

Periodic paralysis (related to K) is an unpredictable recurrent episode of muscle weakness for a few hours to a few days and then resolve spontaneously. CK values increase during one episode and remain slightly elevated at intervals.

Endocrine myopathy are caused by hypothyroidism with myalgias, easy fatigue, slight muscle weakness, mild to moderate elevation of muscle enzymes. Rhabdomyolysis and myoglobinuria may occur after vigorous exercise. The values of muscle enzymes return to normal after 1 to 2 months of thyroid hormone replacement therapy.

In hyperthyroidism, muscle enzymes are usually normal, but episodes of rhabdomyolysis and acute renal failure may occur.

In acromegaly, progressive proximal muscle weakness may occur. Muscle biopsy may produce mild myopathic changes and slight elevation of muscle enzymes.

In nemaline myopathy, CK is normal or slightly increased. Muscle atrophy, hypotonia, and muscle weakness.

In Central Core Disease, CK is normal except in bouts of malignant hyperthermia.

In myofibrillar myopathy, affect older children and adolescents and cause nonspecific proximal and distal weakness.

In motor neuron disease, CK is elevated in 75% of amyotrophic lateral sclerosis.

In spinal muscular atrophies, CK may be normal, but it is usually high in the hundreds, ROTs decreased and we can find fasciculation. There are 3 types:

- Type 1 or Werdnig-Hoffman disease – the child showed severe hypotonia, generalized weakness, poor muscle mass, absent ROTs and eating difficulties.
- Type 2 - slower and more progressive – the patient has progressive muscle weakness and many can survive to school age but in a wheelchair.
- Type 3 or Kugelberg-Welander disease – is a milder form with progressive muscle weakness, especially involving the shoulders.

What is important for the diagnosis?

The patient history is very important: complain of muscle weakness (eg. climbing stairs or combing hair), asthenia, muscle pain, cramps, exercise intolerance and is important to ask for family history of same symptoms.

On physical examination, we need to do a complete neurological check up using the Medical Research Council scale (MRC) that consist in:

- 5 = muscle strength
- 4 + = submaximal movement against resistance
- 4 = moderate movement against resistance
- 4- = slight movement against resistance
- 3 = movement against gravity but not against resistance
- 2 = motion with gravity removed
- 1 = "flicker" - small movements
- 0 = no movement

The osteotendinous reflexes are decreased in muscle and motor neuron diseases. We can observe fasciculation in the case of motor neuron disease and Gowers sign.

Generalized muscle weakness can appear in periodic paralysis or myasthenia gravis. Distal muscle weakness can be found in motor neuron disease, like peripheral neuropathy and myasthenia gravis.

Proximal muscle weakness is possible in myopathies such as Duchenne muscular dystrophy and myasthenia gravis.

CK are very high in: Duchenne and Becker dystrophy, dystrophy of the waists, Pompe disease ,chronic acquired changes, inflammatory myopathies, hypothyroidism, acute muscle injury, rhabdomyolysis, trauma and injections.

CK are low to moderate high in: hypothyroidism and hypoparathyroidism, drugs, exercise, muscle trauma, metabolic myopathies, congenital myopathies, inflammatory myopathies and motor neuron disease.

If we found CK high in a patient, first of all we need to see is 1.5 above normal range and repeat the blood test after one week or in the period of one month. If confirm, need to do EMG in case of myopathy and the muscle biopsy will probably confirm the diagnosis. The muscle biopsy should be performed only in patients with abnormal EMG (myopathic), CK > 3x normal and exercise intolerance or pain induce by exercise (Flow chart of CK high – figure 1).

