CREATINE KINASE IN THE DOG: A REVIEW

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ABSTRACT


In the dog, creatine kinase (CK) is mostly present in the skeletal muscles, myocardium, brain and intestine. The MM isoenzyme predominates in muscles and myocardium. In plasma, reference values depend on the technique used and CK-MB accounts for about 30-45% of total CK activity. Sex has no influence on plasma CK activity, which is higher in young dogs than in adults. Plasma CK is elevated after physical exercise. After its release from the cells, CK reaches the plasma mostly via the lymphatic route and then remains in the plasma compartment. It is rapidly cleared with a half-life of about 2 hours. Muscle diseases are the main source of plasma CK elevations: inherited myopathies, malignant hyperthermia, hypothyroidism, vitamin E-selenium deficiency, prolonged decubitus, intramuscular injections, surgery, etc. Plasma CK is also increased in experimental myocardial infarction, for which the dog is an interesting model, allowing quantification of the damage by measuring the total CK activity released.

Keywords: creatine kinase, dog, lymph, muscle, plasma

Abbreviations: ADP, adenosine diphosphate; ATP, adenosine triphosphate; CK, creatine kinase; DGKC, Deutsche Gesellschaft für klinische Chemie; IM, intramuscular; IV, intravenous; Kin, Michaelis constant; poly(A), polyadenylate; RNA, ribonucleic acid; mRNA, messenger RNA

Creatine kinase (CK, EC 2.7.3.2) has long been used for diagnosing and monitoring myocardial infarction in humans; this was reinforced by the introduction of the measurement of the CK-MB isoenzyme, which is specific for the myocardium in man. In animals, CK has mainly been used as a marker of skeletal muscle damage, either in nutritional myopathies or in exercise-induced muscle damage.

Interesting and fundamental investigations have been carried out using the dog as a model for cardiac ischaemia in humans. Extensive studies, which could not be performed in larger species, were carried out to elucidate the structure, metabolism and diagnostic significance of creatine kinase. Thus, the dog is an interesting model from which information can be cautiously transposed to other species. Moreover, the metabolic information which thus becomes available provides a better basis for a rational diagnostic use of this enzyme.

This review summarizes information about the activity of CK; its structure and metabolism, distribution in organs and measurement; reference values and physiological factors of variation; and variations in different diseases.
CATALYTIC ACTIVITY

CK catalyses the exchange of a phosphate moiety between ATP and creatine phosphate in Lohman's reaction (Figure 1). The equilibrium of this reaction favours the formation of creatine phosphate at a higher pH and the formation of ATP at a lower pH: the optima are 8.3 - 9.0 and 6.9 - 7.2, respectively (Hess et al., 1964; Stolle and Rick, 1976; Connett, 1985, 1987). The affinity for ADP and ATP is higher than for creatine phosphate or creatine (Table I).

![Figure 1. Lohman's reaction catalysed by creatine kinase](image)

This reaction is very important in skeletal and myocardial muscle cells, in which CK allows energy storage as creatine phosphate when demand is low. When demand increases, CK then enables rapid restoration of the intracellular pool of ATP necessary for muscle contraction (Cardinet, 1989). It may also be involved with ADP-ATP translocase in an 'energy shuttle' shifting ATP from the mitochondrial matrix to the cytoplasm (Saks et al., 1980).

<table>
<thead>
<tr>
<th>Substrate</th>
<th>MM isoenzyme</th>
<th>BB isoenzyme</th>
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<tbody>
<tr>
<td>Creatine phosphate</td>
<td>2.40 ± 0.20</td>
<td>0.90 ± 0.20</td>
</tr>
<tr>
<td>Creatine</td>
<td>22.30 ± 6.90</td>
<td>2.30 ± 0.80</td>
</tr>
<tr>
<td>Mg-ADP</td>
<td>0.09 ± 0.01</td>
<td>0.11 ± 0.02</td>
</tr>
<tr>
<td>Mg-ATP</td>
<td>0.55 ± 0.13</td>
<td>0.16 ± 0.02</td>
</tr>
</tbody>
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From Basson et al. (1985)