Creatine Supplementation in Endurance Sports

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1. INTRODUCTION

Creatine (Cr) is a compound that is synthesized endogenously in the kidneys, liver, and pancreas by the transamidination and subsequent transmethylation of three constituent amino acids: glycine, agrinine, and methionine (1). As a result of its amino acid origin, Cr can also be manufactured and consumed as a nutritional supplement. Consequently, Cr is currently regarded as a true ergogenic aid, owing to many well-controlled clinical trials that have demonstrated increases in muscle strength, power output, and muscle mass in response to exogenous Cr consumption (1-6). In fact, aside from the potential ergogenic benefits of caffeine, Cr is the most widely marketed nutritional supplement in the world.

Cr was first discovered as an organic constituent of meat by a French scientist, Chevreul, in 1835. Later, Cr was characterized as an essential intermediate in skeletal muscle metabolism in the early 20th century (7). However, because the majority of scientific literature on Cr supplementation as an ergogenic aid has been published since 1992, the beneficial effects of Cr on human performance are relatively new. The paper by Harris et al. (8) is perhaps regarded as a landmark study, as it was the first to demonstrate that 20 g/d of oral Cr supplementation for three or more days increased total muscle-Cr stores, which was further augmented by exercise. Since then, a plethora of studies have examined the effects of Cr supplementation on exercise performance tasks that rely heavily on the Cr phosphate (CrP) energy system (5).
It is well known that short-duration (10–20 s) high-intensity (90–100%) exercise relies on ATP resynthesis through the Cr kinase (CK) reaction:

\[
\text{CrP} + \text{ADP} + H^+ \xrightarrow{\text{creatinkinase}} \text{ATP} + \text{Cr}
\] (1)

The CK reaction resynthesizes ATP from ADP very rapidly, but is limited in capacity, owing to the exhaustible stores of CrP in the muscle. This concept is supported by the findings of Tesch et al. (9) who reported that fast-twitch fibers have greater CrP stores than slow-twitch fibers. In addition, fast-twitch fibers had lower CrP concentrations following 30 s of maximal exercise than slow-twitch fibers, which suggested that fast-twitch fibers rely heavily on CrP-mediated ATP resynthesis (9). However, with 5 d of Cr supplementation, Greenhaff and colleagues (10) have demonstrated 20–25% increases in total muscle-Cr stores, 20% of which is available as CrP. Therefore, it is not surprising that Cr supplementation augments short-duration high-intensity exercise, which is driven largely by CrP energy system favored by fast-twitch muscle fibers (11). Why, then, would Cr supplementation improve endurance performance, which is most often associated with slow-twitch muscle fibers and their oxidative capacity? The answer to this question may lie in the mechanisms of action of Cr and CrP.

Four primary mechanisms have been suggested to explain the ergogenic benefits of Cr supplementation (6):

1. Increases in total muscle-Cr concentrations will provide more CrP for the CK reaction (Eq. 1). Energy is released by the hydrolysis of ATP to facilitate muscle contraction as a result of the following reaction:

\[
\text{ATP} + \text{H}_2\text{O} \xrightarrow{\text{ATPase}} \text{ADP} + \text{P}_i + \text{energy}
\] (2)

During high-intensity exercise, the rapid hydrolysis of ATP will increase the concentration of ADP, which will drive the CK reaction to the right, because of the Law of Mass Action. The law of mass action or the mass action effect is a property of near-equilibrium, reversible reactions that will drive the direction of the reaction based on the concentration of the reactants (12). For example, when the concentration of ADP increases, the CK reaction will proceed to the right to yield more ATP and free-Cr. This is beneficial when a rapid supply of ATP is needed during anaerobic, short-duration high-intensity muscle contractions. Therefore, the higher the concentration of CrP in the muscle, the longer the CK reaction can resynthesize ATP, which translates into