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Research paper

Mobile phones electromagnetic radiation and NAD$^+$-dependent isocitrate dehydrogenase as a mitochondrial marker in asthenozoospermia

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Abstract

NAD$^+$-dependent Isocitrate Dehydrogenase (NAD$^+$-IDH) could be one of the cell phone radiation targets. Enzyme activity alteration may lead to decline in sperm motility during radio-frequency electromagnetic waves (RF-EMW) exposure. The current case control study aimed to investigate the possible relationship between mitochondrial NAD$^+$-IDH activity in human seminal plasma and sperm motility among asthenozoospermic cellular phone users. A total number of ninety idiopathic infertile males referred from the Department of Dermatology and Andrology, were enrolled in this study. NAD$^+$-IDH activity was measured in human seminal plasma by spectrophotometer. Computer-aided sperm analysis (CASA) following WHO criteria has been used for semen analyses. The results showed that IDH activity was increased in patients with prolonged cell phone daily use ≥4 h/day. Its level, correlated negatively with either the motility ratio percentages ($r = -0.46$, $p < 0.001$) or the progressive motility percentages ($r = -0.50$, $p < 0.001$) in the study groups. The current study suggests that NAD$^+$-IDH in human seminal plasma could be one of seminal plasma biomarkers reflecting the mitochondrial function of spermatozoa. Alteration of its level could reflect the defective motility of sperms among some cases of cellular phone users.

Keywords: Mobile phone electromagnetic radiations; Isocitrate dehydrogenase; Human; Sperm parameters

1. Introduction

The growing popularity of mobile usage is associated with increased concern regarding its radiation (RF-EMW; radio-frequency electromagnetic waves) harmful effects on human health, brain and fertility among others [1–3].

RF-EMW exposure effects on male fertility has been studied and evaluated in many animal and human studies but the results are inconsistent. The main semen parameter that the majority of studies have shown to be significantly affected is the motility [1,4–11].

Spermatozoa are highly specialized cells, offering utilities for studying several basic aspects of metabolic control such as the role of ATP (adenosine triphosphate) homeostasis for cell function [12]. As the energy metabolism of mitochondria is a main factor supporting multiple functions of the sperm, they harbor significant metabolic pathways during germ cell development and fertilization [13]. However, the most important aspect of mitochondria function in all cell types is ATP production, which can be used in the case of spermatozoa for maintaining motility of the sperms that represents one of the main determinants of male fertility. Consequently, the presence of structural and functional alterations in mitochondria from asthenozoospermic (i.e. percentage of progressively motile spermatozoa <32%; fifth percentile relative to the average fertile male) [14] subjects supports the vital role played by these organelles in sperm motility energy maintenance [15].

Krebs cycle (tricarboxylic acid cycle; TCA, citric acid cycle), is a group of enzyme-catalyzed chemical reactions

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(Fig. 1A) of key importance in all living cells that use oxygen as part of cellular respiration. In eukaryotes, it occurs in the mitochondrial matrix as a part of a metabolic pathway involved in the chemical conversion of carbohydrates, lipids and proteins into carbon dioxide and water generating a form of usable energy. The metabolic step in this cycle catalyzed by isocitrate dehydrogenase, occupies a central position in the intermediary metabolism, links multiple synthetic and catabolic pathways and could be rate limiting [16].

Isocitrate dehydrogenase (IDH) is a large, ubiquitous, and very ancient protein sub-family member playing key roles in energy metabolism. IDHs can be divided into two main groups according to coenzyme specificity: NAD^+-specific IDHs (EC 1.1.1.41, NAD^+-IDH) and $NADP^+$-specific IDHs (EC 1.1.1.42, NADP-IDH) [17]. Eukaryotic NAD^+-IDHs are heterotetramer (Fig. 2A); localized in the mitochondria (Fig. 2B), regulating the metabolic fluxes and the generation of ATP in the TCA cycle. This later isoenzyme catalyzes allosterically the oxidative NAD^+-dependent decarboxylation of isocitrate to α-ketoglutarate (α-KG) and CO_2 while converts NAD^+ to NADH in the presence of Mn^{2+} or Mg^{2+}. This is a two-step process involves oxidation of isocitrate to oxalosuccinate, followed by the decarboxylation of the β-carboxyl group to form the α-ketoglutarate (Fig. 1B).

Many previous studies reported that RF-EMW emitted from commercially available cell phones have no thermal effect [18]. However, several views were proposed to elucidate the disruption of metabolic pathways by this type of waves. Some of these views are based on experimental evidences and some on hypothetical models. NAD^+-specific IDH

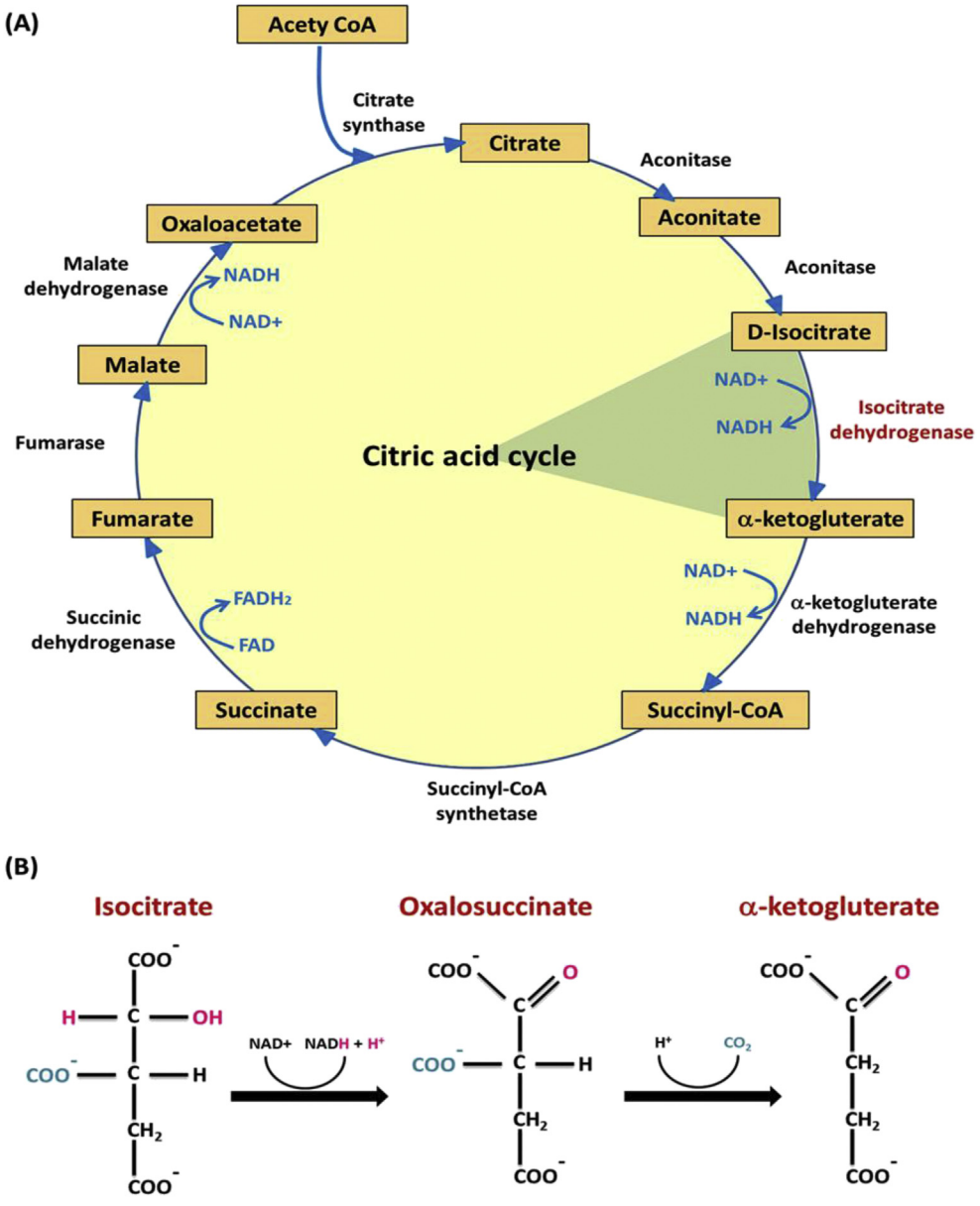

Fig. 1. Citric acid cycle and NAD^+-dependent IDH action. (A) The rate-limiting step of the citric acid cycle catalyzed by isocitrate dehydrogenase, is one of the irreversible reactions in the citric acid cycle due to its large −ΔG (negative free energy change) (B) The two-step process of isocitrate dehydrogenase action.