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Membrane Sodium Potassium ATPase Inhibition Mediated ATP Synthesis Induced by Digoxin, Photoinduction and Electromagnetic Fields

Introduction

Endogenous digoxin, exposure to sunlight and electromagnetic fields can produce membrane sodium potassium ATPase inhibition. Membrane sodium potassium ATPase in the setting of digoxin, photic and electromagnetic field induced inhibition can synthesize ATP. The cellular membrane sodium potassium ATPase mediated synthesis of ATP in response to sunlight, electromagnetic fields and endogenous digoxin induced sodium potassium ATPase inhibition can serve as a nonmitochondrial source of ATP for the purpose of cellular metabolism. The membrane sodium potassium ATPase mediated ATP synthesis can serve as a source for cellular energetics.¹ This was studied and reported in this paper.

Materials and Methods

The following groups were included in the study: - meditation group, endomyocardial fibrosis, Alzheimer's disease, multiple sclerosis, non-Hodgkin's lymphoma, metabolic syndrome x with cerebrovascular thrombosis and coronary artery disease, schizophrenia, autism, seizure disorder, Creutzfeldt Jakob's disease and acquired immunodeficiency syndrome. There were 10 patients in each group and each patient had an age and sex matched healthy control selected randomly from the general population. The blood samples were drawn in the fasting state before treatment was initiated.

The experimental protocol for the study of membrane sodium potassium ATPase mediated ATP synthesis was as follows.

Reagents:

Phosphate buffer:

A) NaH_2PO_4 0.15 M

B) K_2HPO_4 0.15 M

Reagent C) Mix 24ml of A + 76ml B. Adjust the pH to 7.2

Reagent D) Mix equal volume of reagent C + normal saline

MgSO_4 0.0138 M

ADP Na salt 0.0125 M

Procedure: Citrated blood 5 ml. Separate the RBC by centrifugation at 1300 rpm at 4 °C. Wash with normal saline till supernatant is clear. Suspend the RBC in normal saline. Incubate the suspension at 37 °C for 4 hours. Centrifuge and remove the supernatant and suspend the RBC in solution D containing MgSO_4 + ADP.

Reaction mixture:

1. Mix well allows the system to attain 37 °C in a thermostatic water bath
2. Withdraw an aliquot and deprotenise immediately with 0.8N perchloric acid and neutralize with 1N KOH and estimate the ATP in the supernatant
3. Incubate the remaining mixture at 37 °C for 1hr. Withdraw another aliquot and deprotenise immediately with 0.8 N perchloric acid and neutralize with 1 N KOH and estimate the ATP in the supernatant. Difference in the ATP content is the measure of ATP synthase activity.

Three sets of protocols were used (1) Addition of digoxin at a concentration of 1 mg/ml, (2) exposure to sunlight of the experimental setup for 1 hour, (3) exposure to low intensity electromagnetic field for 1 hour. ATP was estimated by the method described before.²⁻⁴

Informed consent of the subjects and the approval of the ethics committee were obtained for the study. The statistical analysis was done by ANOVA.

Results

The results of the study showed increased ATP synthesis by RBC membrane sodium potassium ATPase in the presence of added digoxin, exposure to sunlight and low intensity electromagnetic fields. The added digoxin, exposure to sunlight and low intensity electromagnetic fields produce sodium potassium ATPase inhibition. Membrane sodium potassium ATPase in its inhibited state can synthesize ATP. The results are expressed in table 1 as percentage change in the parameters after 1 hour incubation as compared to the values at zero time. There was RBC membrane sodium potassium ATPase mediated ATP synthesis in the patients with schizophrenia, malignancy, metabolic syndrome x, autoimmune disease and neuronal degeneration in the presence of added digoxin, exposure to sunlight and low intensity electromagnetic fields.

Table 1. Sodium potassium ATPase inhibition mediated membrane ATP synthesis.

Group	Digoxin induced ATP synthesis % change		Photoinduction induced ATP synthesis % change		EMF induced ATP synthesis % change	
	Mean	±SD	Mean	±SD	Mean	±SD
Normal	4.40	0.11	4.34	0.15	4.48	0.15
Schizo	23.67	1.42	23.81	1.49	22.06	1.61
Seizure	23.09	1.90	22.79	2.20	21.68	1.90
AD	23.58	2.08	22.82	1.56	22.70	1.87
MS	23.52	1.76	23.09	1.81	23.12	2.00
NHL	24.01	1.17	21.93	2.29	22.12	1.81
DM	23.72	1.73	23.02	1.65	23.24	2.01
Meditation	23.15	1.62	22.13	2.14	23.46	1.87
CJD	23.00	1.64	23.12	1.71	22.79	2.13
Autism	22.60	1.64	22.73	2.46	22.59	1.86
EMF	23.37	1.31	22.98	1.50	22.29	1.66
F value	449.503		348.867		306.749	
P value	< 0.001		< 0.001		< 0.001	

Discussion

Membrane sodium potassium ATPase primarily is involved in the generation of the membrane resting potential and the paroxysmal depolarization shift. Membrane sodium potassium ATPase when inhibited can serve as an enzyme mediating ATP synthesis. The membrane sodium potassium ATPase is also inhibited by digoxin, photoexposure and low intensity electromagnetic fields. The study demonstrates that digoxin induced membrane sodium potassium ATPase inhibition can induce membrane sodium potassium ATPase mediated ATP synthesis. Photic and electromagnetic induction of membrane sodium potassium ATPase mediated ATP synthesis is also demonstrated in the study in normal individuals as well as in pathological states.

ATP synthesis is usually a mitochondrial function and is subserved by mitochondrial oxidative phosphorylation. ATP synthesis is also mediated by anaerobic glycolysis. These are the two major recognized sources of ATP synthesis. Membrane sodium potassium ATPase is a ubiquitous enzyme and is present in all cell membranes. Membrane sodium potassium ATPase is also seen in organelle membranes especially nuclear membrane and endoplasmic reticular membranes. Membrane sodium potassium ATPase inhibition adds a new dimension to the enzymes function. Membrane sodium potassium ATPase is inhibited by endogenous digoxin, neurotransmitters like glutamate, sunlight, electric fields, magnetic fields and adrenergic hormones. Membrane sodium potassium ATPase when inhibited can catalyse ATP synthesis.

Membrane sodium potassium ATPase mediated ATP synthesis in the presence of digoxin, sunlight and electric fields induced inhibition can be a major source of ATP and cellular energetics. The human body can use photoinduction of membrane sodium potassium ATPase inhibition mediated membrane ATP synthesis as a means of garnering solar energy for cellular metabolism. The electromagnetic fields induced membrane sodium potassium ATPase inhibition mediated ATP synthesis is a mechanism by which the human body can utilize electric and magnetic fields for cellular metabolism.

The membrane sodium potassium ATPase inhibition mediated ATP synthesis may serve as a major source of cellular energetics. The sunlight induced photic induction of membrane sodium potassium ATPase inhibition mediated ATP synthesis may be a primitive source of cellular energy before the evolution of mitochondrial oxidative phosphorylation. The electromagnetic induction of membrane sodium potassium ATPase inhibition mediated ATP synthesis may also be a similar primitive source of cellular energy. The photic and electromagnetic induction of membrane sodium potassium ATPase inhibition

related ATP synthesis still serves as a major source of cellular energetics despite the presence of mitochondrial oxidative phosphorylation and anaerobic glycolysis.

The membrane sodium potassium ATPase inhibition mediated ATP synthesis is increased in pathological states like endomyocardial fibrosis, Alzheimer's disease, multiple sclerosis, non-Hodgkin's lymphoma, metabolic syndrome x with cerebrovascular thrombosis and coronary artery disease, schizophrenia, autism, seizure disorder, Creutzfeldt Jakob's disease and acquired immunodeficiency syndrome. This is due to the increased endogenous digoxin synthesis in these disease states. The endogenous digoxin is produced by symbiotic actinidic archaea having a mevalonate pathway. The archaeal digoxin induced membrane sodium potassium ATPase inhibition mediated ATP synthesis may serve as a source of ATP for primitive endosymbiotic cellular archaeal cellular metabolism. This may be the major source of cellular energy for endosymbiotic actinidic archaea.

Extracellular ATP produces immune activation, cell proliferation, excitatory neurotransmission and cell death contributing to pathological states. ATP is a neurotransmitter in the central and sympathetic nervous system. ATP is stored in and released from synaptic nerve terminals and is known to act postsynaptically via P2X receptors. It promotes calcium signalling. ATP is a co-transmitter at noradrenaline, acetyl choline and GABA synapse. Extracellular ATP can inhibit glutamate transmission. It can thus regulate the NMDA/GABA thalamo-cortico-thalamic pathway mediating conscious perception. ATP functions as a fast excitatory neurotransmitter and is involved in the pathogenesis of schizophrenia. It also plays a role in the pathogenesis of depression. Purinergic receptors regulate cell proliferation and cell differentiation. They also play a role in organ development and regeneration.

Thus extracellular ATP may play a role in oncogenesis. Extra cellular ATP and purinergic receptors can mediate cell death. They can initiate neurodegenerative process. They are important in the pathogenesis of Alzheimer's disease and Parkinson's disease. Extracellular ATP and purinergic receptors are involved in immune activation and can initiate autoimmune disease. 5'AMP is immunosuppressive, inhibits NFkB and reduces cytokine secretion. ATP is immunostimulatory, activates NFkB and promotes cytokine secretion. Thus the ectoATPases can regulate the 5'AMP/ATP ratio and regulate immune signalling. Extracellular ATP can modulate the response to bacterial and viral infection. Extracellular ATP is involved in the signaling pathway of HIV infection and are important cell fusion and HIV replication. Extracellular ATP and purinergic receptors are also involved in lipopolysaccharide signalling. The ectoATPase acts upon ATP to generate 5'AMP. 5'AMP activates 5'AMP activated protein kinase. 5'AMP-activated protein kinase or AMPK or 5' adenosine monophosphate-activated protein kinase is an enzyme that plays a role in cellular energy homeostasis. It is expressed in a number of tissues, including the liver, brain, and skeletal muscle. The net effect of AMPK activation is stimulation of hepatic fatty acid oxidation and ketogenesis, inhibition of cholesterol synthesis, lipogenesis, and triglyceride synthesis, inhibition of adipocyte lipolysis and lipogenesis, stimulation of skeletal muscle fatty acid oxidation and muscle glucose uptake, and modulation of insulin secretion by pancreatic beta-cells. The *C. elegans* homologue of AMPK, *aak-2*, has been shown by Ristow and colleagues to be required for extension of life span in states of glucose restriction mediating a process named mitohormesis. 5'AMP can reversibly inhibit mitochondrial oxidative phosphorylation and produce cell hibernation. Purinergic receptors are involved in regulating pancreatic insulin and glucagon secretion. Extracellular ATP may play a role in the development of metabolic syndrome x.⁵⁻¹³

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