Chapter 4

Dietary Fibre - Relation to Endosymbiotic Actinidic Archaeal Synthesis of Digoxin from Cholesterol Regulates Cellular Function and Contributes to the Pathogenesis of Systemic Lupus Erythematosis, Multiple Sclerosis and Rheumatoid Arthritis

Introduction

There is dietary fibre deficiency and increased endosymbiotic as well as colonic archaeal growth in autoimmune disease. The endosymbiotic archaea regulates human functions and species type and depends upon the colonic archaea whose density is determined by the fibre intake. The colonic archaeal population density depends upon dietary fibre intake. Populations with low fibre intake have lesser density of colonic archaeal microflora and endosymbiotic archaea. Endosymbiotic archaea contributes to neanderthalisation of the species. Populations consuming a high saturated fat and protein diet with low fibre intake tend to get increased endosymbiotic archaeal growth and are neanderthalised. Populations with high fibre intake up to 80 g/day tend to have reduced archaeal density in the colon and reduced archaeal endosymbiosis contributing to homo sapienisation of the population. Thus fibre intake regulates the endosymbiotic archaeal density and type of human species.

Actinides like rutile, endogenous digoxin as well as organisms like phytoplasmas and viroids have been implicated in the etiology of systemic lupus erythematosis, multiple sclerosis and rheumatoid arthritis.[1-4] Endogenous digoxin has been related to the pathogenesis of systemic lupus erythematosis, multiple sclerosis and rheumatoid arthritis.[4] The possibility of endogenous digoxin synthesis by actinide based primitive organism like archaea with a mevalonate pathway and cholesterol catabolism was considered.[5-8] An actinide dependent shadow biosphere of archaea in the above mentioned disease states is described.[7, 9]

Materials and Methods

The following groups were included in the study: - systemic lupus erythematosis, multiple sclerosis and rheumatoid arthritis. 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. Plasma from fasting heparinised blood was used and the experimental protocol was as follows (I) Plasma+phosphate buffered saline, (II) same as I+cholesterol substrate, (III) same as II+rutile 0.1 mg/ml, (IV) same as II+ciprofloxacine and doxycycline each in a concentration of 1 mg/ml. Cholesterol substrate was prepared as described by Richmond.[10] Aliquots were withdrawn at zero time immediately after mixing and after incubation at 37 ℃ for 1 hour. The following estimations were carried out: - Cytochrome F420 and digoxin.[11-13] Cytochrome F420 was estimated flourimetrically (excitation wavelength 420 nm and emission wavelength 520 nm). 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

Plasma of control subjects showed increased levels of the above mentioned parameters with after incubation for 1 hour and addition of cholesterol substrate resulted in still further significant increase in these parameters. The plasma of patients showed similar results but the extent of increase was more. The addition of antibiotics to the control plasma caused a decrease in all the parameters while addition of rutile increased their levels. The addition of antibiotics to the patient’s plasma caused a decrease in all the parameters while addition of rutile increased their levels but the extent of change was more in patient’s sera as compared to controls. The results are expressed in tables 1-2 as percentage change in the parameters after 1 hour incubation as compared to the values at zero time.

Table 1. *Effect of rutile and antibiotics on cytochrome F420.*

Group	CYT F420 % (Increase with Rutile)		CYT F420 % (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD
Normal	4.48	0.15	18.24	0.66
MS	22.12	1.81	61.33	9.82
SLE	22.29	1.66	59.02	7.50
RA	22.06	1.61	57.81	6.04
F value	306.749		130.054	
P value	< 0.001		< 0.001	

Table 2. *Effect of rutile and antibiotics on digoxin.*

Group	Digoxin (ng/ml) (Increase with Rutile)		Digoxin (ng/ml) (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD
Normal	0.11	0.00	0.054	0.003
MS	0.52	0.03	0.214	0.032
SLE	0.56	0.05	0.220	0.052
RA	0.53	0.06	0.212	0.045
F value	135.116		71.706	
P value	< 0.001		< 0.001	

Discussion

Dietary Fibre Deficiency, Endosymbiotic Archaea, Cholesterol Catabolism and Autoimmune Disease

There is dietary fibre deficiency and increased endosymbiotic as well as colonic archaeal growth in autoimmune disease. There was increase in cytochrome F420 indicating archaeal growth. The archaea can synthesize and use cholesterol as a carbon and energy source.[6, 14] The archaeal origin of the enzyme activities was indicated by antibiotic induced suppression. The study indicates the presence of actinide based archaea with an alternate actinide based enzymes or metalloenzymes in the system as indicated by rutile induced increase in enzyme activities.[15, 16] The archaeal beta hydroxyl steroid dehydrogenase activity indicating digoxin synthesis was increased.[8] The archaea can undergo magnetite and calcium carbonate mineralization and can exist as calcified nanoforms.[17] This can lead to the pathogenesis of systemic lupus erythematosis, multiple sclerosis and rheumatoid arthritis.

Dietary Fibre Deficiency, Endosymbiotic Archaea, Genomic Change and Autoimmune Disease

Archaeal digoxin induced redox stress can produce histone deacetylase inhibition resulting in endogenous retroviral (HERV) reverse transcriptase and integrase expression. Digoxin can cut and paste the HERV RNA by modulating RNA splicing generating RNA viroidal diversity.[18] This can also integrate the HERV RNA complementary DNA into the noncoding region of eukaryotic noncoding DNA using HERV integrase.[19] The noncoding DNA is lengthened by integrating HERV RNA complementary DNA with the integration going on as a continuing event. The archaea genome can also get integrated into human genome using integrase as has been described for trypanosomes.[20] The integrated archaea can undergo vertical transmission and can exist as genomic parasites.[19, 20] This increases the length and alters the grammar of the noncoding region producing memes or memory of acquired characters as well as eukaryotic speciation and individuality.[21] The HERV RNA complementary DNA can function as jumping genes producing a dynamic genome important in storage of synaptic information, HLA gene expression and developmental gene expression. The HERV RNA can regulate mRNA function by RNA interference.[18] The phenomena of RNA interference can modulate T cell and B cell function, insulin signalling lipid metabolism, cell growth and differentiation, apoptosis, neuronal transmission and euchromatin/heterochromatin expression. This can lead to the pathogenesis of systemic lupus erythematosis, multiple sclerosis and rheumatoid arthritis.

Dietary Fibre Deficiency, Endosymbiotic Archaea, Neuronal Transmission and Autoimmune Disease

NMDA receptors can be modulated by digoxin induced calcium oscillations resulting NMDA excitotoxicity.[4] The dipolar PAH and archaeal magnetite in the setting of digoxin induced sodium potassium ATPase inhibition can produce a pumped phonon system mediated Frohlich model superconducting state [22] inducing quantal perception with nanoarchaeal sensed gravity producing the orchestrated reduction of the quantal possibilities to the macroscopic world.[4, 22] This can lead to perception of low level EMF contributing to the pathogenesis of systemic lupus erythematosis, multiple sclerosis and rheumatoid arthritis. The higher degree of integration of the archaea into the genome produces increased digoxin synthesis producing right hemispheric dominance and lesser degree producing left hemispheric dominance.[4] Right hemispheric dominance can lead to systemic lupus erythematosis, multiple sclerosis and rheumatoid arthritis. The increased integration of archaea into the neuronal genome can produce increased digoxin mediated NMDA transmission producing systemic lupus erythematosis, multiple sclerosis and rheumatoid arthritis. Digoxin induced calcium oscillations can activate NFKB producing immune activation and cytokine secretion. The archaeal digoxin induced chronic immune activation can lead on to autoimmune disease.[23] Archaeal digoxin can induce the host AKT PI3K, AMPK, HIF alpha and NFKB producing the Warburg metabolic phenotype.[24] There is induction of glycolysis, inhibition of PDH activity and mitochondrial dysfunction resulting in inefficient energetics and insulin resistance. The archaeal digoxin generated cytokines can lead to TNF alpha induced insulin resistance. Insulin resistance can lead to systemic lupus erythematosis, multiple sclerosis and rheumatoid arthritis. Digoxin induced sodium potassium ATPase inhibition can lead to increase in HMG CoA reductase activity and increased cholesterol synthesis. The increased cholesterol substrate also leads to increased archaeal growth and digoxin synthesis due to metabolic channelling to the mevalonate pathway. Digoxin can produce sodium potassium ATPase inhibition and inward movement of plasma membrane cholesterol. This produces defective SREBP sensing, increased HMG CoA reductase activity and cholesterol synthesis. The digoxin induced inward movement of plasma membrane cholesterol can alter membrane cholesterol/sphingomyelin ratio producing modified lipid microdomains. The digoxin induced lipid microdomain modulation can regulate the GPCR couple adrenaline, noradrenaline, glucagon and neuropeptide receptors as well as protein tyrosine kinase linked insulin receptor. The digoxin mediated inhibition of nuclear membrane sodium potassium ATPase can modulate nuclear membrane lipid microdomains and steroidal/thyroxine DNA receptor function. Thus endogenous digoxin can modulate all the endocrine receptors by regulating lipid microdomains. Hyperdigoxinemia is important in the pathogenesis of systemic lupus erythematosis, multiple sclerosis and rheumatoid arthritis due to defective neuro-immuno-endocrine integration. Digoxin induced sodium potassium ATPase inhibition results in an ATP sparing effect. Eighty percent of the ATP generated is used to run the sodium potassium ATPase pump. The digoxin inhibition of the sodium potassium ATPase spares this ATP which is then used for lipid synthesis. Thus endogenous digoxin and the shadow biosphere generated Warburg phenotype can produce increased lipid synthesis and insulin resistance. Fat fuels insulin resistance by binding to the toll receptor and producing immune activation and immune infiltration of the adipose tissue.[4] Insulin resistance can lead to systemic lupus erythematosis, multiple sclerosis and rheumatoid arthritis. The digoxin mediated transcribed HERV RNA can get encapsulated in microvesicles contributing to the retroviral state. The prion protein conformation is modulated by HERV RNA binding producing prion disease. Prion proteins and HERV sequences are related to systemic lupus erythematosis, multiple sclerosis and rheumatoid arthritis. Thus the archaeal digoxin can produce neuro-immuno-metabolic-endocrine-genetic integration. The increased archaeal cholesterol catabolism and digoxin secretion can lead to diverse pathological states of systemic lupus erythematosis, multiple sclerosis and rheumatoid arthritis.

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