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Diabetes & its Complications

Polyamine Metabolism in Sperm Cell

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ABSTRACT

Polyamines putrescine, spermidine and spermine are natural constituents of living organisms. In mammals they are present in tissues and fluids. Since they are basic molecules interact with a variety of polyanions such as nucleic acids. Deoxyribonucleic acid is stabilized by polyamines. Recently, attention has been focused to understand their role in diabetes mellitus and reproductive abnormalities not only in male but also in female reproduction. Several investigations have demonstrated that in un-controlled diabetic men, sperm deoxyribonucleic acid is glycated and fragmented, which has relevance in human reproduction. In our laboratory we show that polyamines prevent both processes. This paper provides information on polyamine synthesis, interconversion and physiological effects in sperm cell with emphasis in human sperm cell.

Keywords

Polyamines Putrescine, Spermidine, Spermine, Synthesis, Interconversion, Human Sperm, Metabolism, Human Reproduction.

Introduction

Polyamines are a group of small basic molecules whose characteristic is to possess two or more amino groups in their structure. Although several molecules with these characteristics exist in nature, three of them have been the most studied, since there is a close relationship in their biosynthesis and interconversion in the organism. These molecules are putrescine, spermidine and spermine. Polyamines are natural constituents of most living organisms. They are present in tissues and body fluids such as blood, human milk, amniotic fluid, and semen [1]. Since their discovering in the human semen through the formation of crystals [2], several studies have been conducted using samples obtained from humans and from experimental models to understand two aspects; first, their metabolism and second, their role in reproductive physiology in health and disease. Recently, attention has been focused to understand their role in diabetes mellitus and reproductive abnormalities not only in male but also in female reproduction, but their relation to cancer and other diseases has been widely studied.

Biosynthesis in mammals

In mammals, biosynthesis of polyamines is carried out from ornithine [3,4] and therefore, the route leading to the formation of putrescine is through the enzyme ornithine decarboxylase which is regulated by polyamines at the levels of transcription, translation and protein stability [4]. The ornithine available for this reaction comes from plasma and can be formed inside cells by the action of arginase, an enzyme that is also present in extrahepatic tissues apart of the urea cycle. Spermidine and spermine are formed from putrescine and involve other enzymes; S-adenosylmethionine decarboxylase and spermidine and spermine synthases which incorporate propylamine groups derived from S-adenosylmethionine to form spermidine and spermine, respectively. Several enzymes are involved in the reversal of the aminopropyl transferase reactions such as N^1-spermine/spermidine acetyltransferase and acetylpolyamine oxidase. Acetylpolyamine oxidase acts on N^1-acetylspermine to form spermidine, but this enzyme also converts N^1-acetylspermidine into putrescine plus N-acetyl-3-aminopropanaldehyde [4]. Diamine oxidase is another enzyme involved in polyamine metabolism.

Biosynthesis in sperm cell

Activity of ornithine decarboxylase was reported in human spermatozoa [1], later activity of arginase was demonstrated in

ram epididymal/eyaculated spermatozoa [5], and its distribution in sperm cell was studied during epididymal maturation [6]. In addition to this, although very low or almost undetectable activities of S-adenosylmethionine decarboxylase and spermidine synthase these enzymes are present in human sperm cells. Demonstration of diamine oxidase in human spermatozoa has been definitive [1]. S-adenosylmethionine decarboxylase and spermidine synthase, were invariably found in seminal plasma, which was also found an exceptionally rich source of diamine oxidase activity [7]. On the other hand, spermine synthase activity was demonstrated using preparations from the rat ventral prostate in the presence of S-adenosylmethionine and spermidine [8], but information on its activity in human semen is scarce.

It is known that normal human semen contains spermine in concentrations of 5 to 15 mM [9,10], and smaller amounts of spermidine are present in human seminal fluid [11], which also contains putrescine and other amines such as 1, 3-diaminopropane and 1, 5, diaminopentane (cadaverine) synthesized by other metabolic pathways not discussed here. The molar ratio of spermine to spermidine in human semen is greater than 12 [12].

Physiological effects

Evidence has been obtained by *in vitro* studies that spermine enhances the activity of seminal maltase, which is involved in the degradation of glycogen, and which increases glucose utilization by sperm, at the same time reducing fructose utilization [13], Additions of physiological amounts of spermine to spermatozoa suspensions caused a significant increase in 3′, 5′- cyclic adenosine monophophate levels [13], a nucleotide that induces capacitation in human spermatozoa [14], the effect of spermine on 3′, 5′- cyclic adenosine monophophate levels may be explained by the fact that this polyamine inhibits phosphodiesterase activity of 3′, 5′- cyclic adenosine monophophate, besides activating adenylate cyclase activity [15]. It has also known that the effect of spermine on 3′, 5′- cyclic adenosine monophophate levels could be further enhanced by prostaglandin E_2 and has been demonstrated that prostaglandin E_2 produces stimulation of ornithine decarboxylase [16].

A positive correlation between concentrations of spermidine and spermine and motility of ejaculated spermatozoa has also been demonstrated in rams [17]. The effect appears direct because addition of polyamines or L-arginine to human spermatozoa with reduced or no motility increased sperm motility [18]. Both polyamines; spermidine and spermine have been associated with improvement in *in vitro* fertilization and pregnancy in mice [19] and humans [20].

Conclusion

In conclusion, information has shown that polyamines are essential regulators of cell growth and gene expression. In male reproduction, polyamine expression correlates with stages of spermatogenesis [21]. Since *in vitro* studies have shown a close association of polyamines with nucleic acids [22-24], the role of polyamines on the deoxyribonucleic acid in hyperglycemia conditions is being investigated.

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