

Study of Catsper1 Protein Levels in Unexplained and Idiopathic Infertile Men

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ABSTRACT

Catsper 1 is an important protein involved in calcium channel synthesis. These channels are essential for the hyperactivity of sperm flagellum, chemotaxis towards the egg, capacitation and acrosome reaction. Data analysis from unexplained infertility (n=50), idiopathic infertile men (Asthenozoospermia (n=50), Oligozoospermia (n=50)), and Normospermia fertile men as a control (n=26). The expression of CatSper1 protein expression in spermatozoa was reduced in unexplained infertility (mean± SD. Error 64.32±2.5 and in Asthenozoospermia 46.6±2.1 and Oligozoospermia 53.86±4.1 while significant increase was observed in Normospermia fertile men 115.19±2.3. CatSper1 protein expressions was shown to have a positive correlation between sperm concentration, Sperm Progressive motility percentage and sperm normal morphology present in idiopathic infertile men respectively (r= 0.822, r = 0.651 and r = 0.742). A positive correlation was found between CatSper1 protein expression and sperm concentration, Sperm Progressive motility percentage and sperm normal morphology present in unexplained infertile men Respectively (r= 0.845, r = 0.576 and r = 0.582). The present study shows the importance of protein catsper 1 in infertile men and its positive correlation with sperm parameters.

Keywords: Catsper 1, unexplained male infertility, idiopathic male infertility.

INTRODUCTION

Sperm functions are an important factor for successful fertility, Sperm dysfunction is the most common cause of male infertility¹. More importantly, it has been reported that sperm function is associated with the quality of the sperm genome apparatus, show high DNA fragmentation². The cation channels of sperm also known as Catsper channels or CatSper, are ion channels that are related to the two-pore channels and distantly related to Ca²⁺ channels³. The four members of this family form voltage-gated Ca²⁺ channels that seem to be specific to sperm, As sperm encounter the more alkaline environment of the female reproductive tract, Catsper channels become activated by the altered ion concentration⁴. A plethora of research has proven that the Catsper channel is essential for both human fertility, A routine semen analysis in two consanguineous families that showed autosomal-recessive male infertility discovered that both families suffer from Catsper1 gene abnormalities, In different patients, asthenoteratozoospermia was diagnosed and found to lack the Catsper2 gene^{5,6}. Furthermore, studies have also shown that all four Catsper subunits (Catsper1–4) are integral for sperm hyperactivated motility and male fertility, but lack of Catsper3 or Catsper4 has not influence spermatogenesis or initial motility of sperm⁷. Moreover, the number of sperm with progressive motility and progesterone induced acrosome reactions is significantly lower in Catsper1-suppressed groups than

that in normal groups⁸. Normal expression of the Catsper channel is associated with progressive motility and acrosome reaction, abnormal channel expression may be involved in the pathogenesis of Asthenozoospermia, Specifically, disruption of the sNHE or Catsper2 genes in mice cause male infertility, with findings of immotile spermatozoa and failed hyperactivated motility, but no other apparent abnormalities⁹. All of these results suggest that Catsper1 and Catsper2 are essential for normal male fertility in humans, Interestingly, Catsper3 and 4 play an important role in the acrosome reaction and male fertility¹⁰. Which occurs not only in the testes but also in other tissues, On the other hand, Catsper1 and Catsper2 are only detected in mammalian testes, Collectively these results suggest that Catsper1 and Catsper2 are highly specialized flagellar proteins that are more important than Catsper3 and Catsper4 in sperm¹¹. However, these mutations show an abnormal detection of Ca²⁺ currents and hyperactivated motility in spermatozoa¹².

MATERIALS AND METHODS

Semen and serum specimens were collected from infertile normospermic patients (unexplained infertile male), idiopathic infertile men include (Asthenozoospermia and Oligozoospermia) in addition to control group (Fertile Normozoospermia) that attended the fertility centre at the Al-sader hospital in Al-najaf governate. The average age of infertile patients was (32.99±32) years, the samples were collected are 521 and sample which tested are 176

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samples, the sample which obtained from control group (fertile) was 26 samples (Normozoospermia), and 50 samples from Asthenozoospermia, 50 sample from

Oligozoospermia and 50 samples from unexplained infertile male. Catsper 1 protein was measured on 176

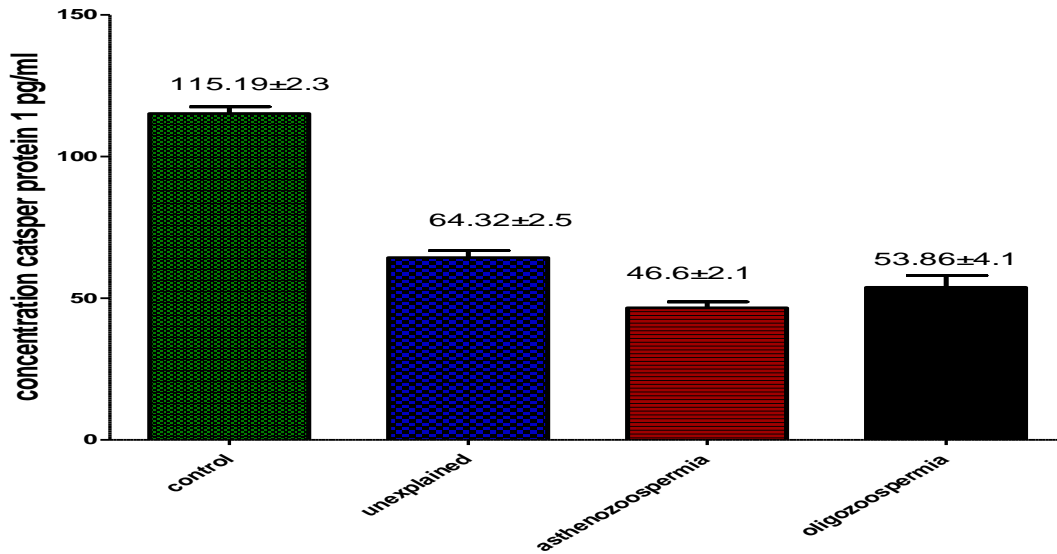


Figure 1: The comparison of catsper 1 protein concentration in the serum between Asthenozoospermia, Oligozoospermia, Unexplained infertile men with fertile men (control). b. This mean significant decrease ($p < 0.05$)

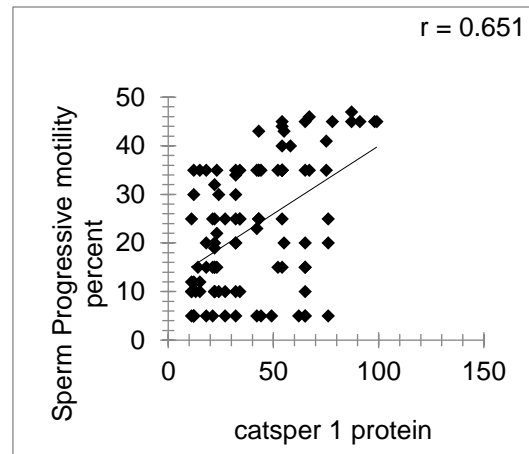
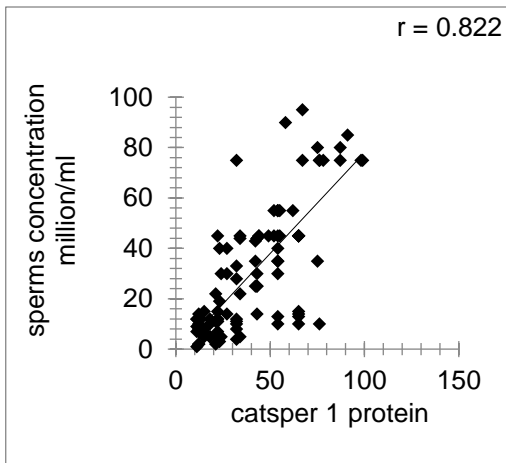


Figure 2: The correlation between catsper1 proteins with sperm concentration in idiopathic infertile male. Figure 3: The correlation between catsper1 proteins with Sperm Progressive motility in idiopathic infertile male.

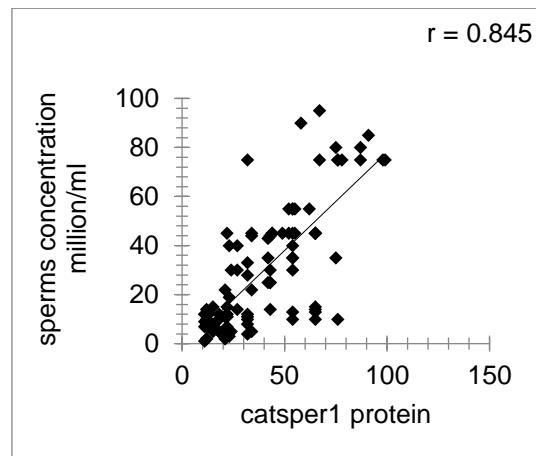
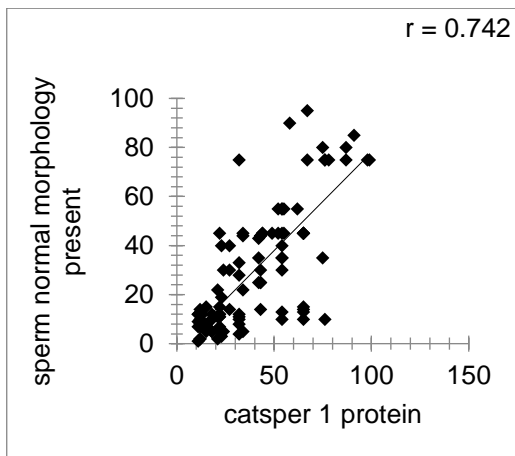


Figure 4: The correlation between catsper1 proteins with sperm normal morphology in unexplained infertile male. Figure 5: The correlation between catsper1 Proteins with sperm concentration in idiopathic infertile male.

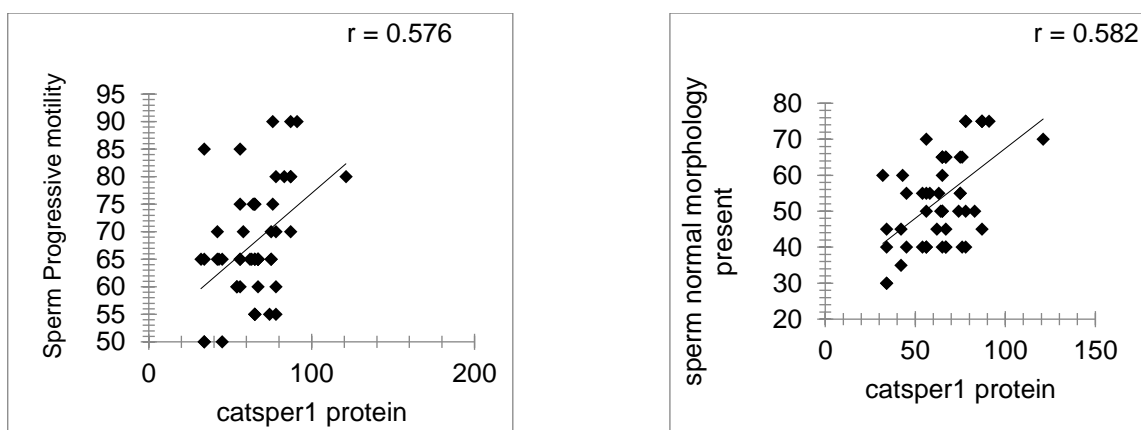


Figure 6: The correlation between catsper1 proteins with sperm progressive motility in unexplained infertile male. Figure 7: The correlation between catsper1 proteins with sperm normal morphology in percent in unexplained infertile male.

samples using ELISA (Enzyme-Linked-Immuno-Sorbent-Assay) by using ELISA reader (Huma Germany origin). All specimens and reagents should reach room temperature before use. All reagents must be mixed softly without foaming. Once the procedure has started, all steps must be completed without interruption, and biochemical tests were conducted in the laboratories of Biology Department/ faculty of Sciences/ University of Kufa. The ELISA kits used in this study was (catsper1) (MBS7217719) Elabscience company USA).

RESULTS

The result showed a significant CatSper1 protein expression in spermatozoa was reduced in unexplained infertility (mean± Std. Error 64.32±2.5 also reduced in Asthenozoospermia 46.6±2.1 and Oligozoospermia 53.86±4.1 while significant increase was observed in Normospermia fertile men 115.19±2.3).

A positive correlation was found between CatSper1 protein expressions, And the sperms concentration, Sperm Progressive motility percent and sperm normal morphology present in idiopathic infertile men respectively ($r = 0.822$, $r = 0.651$ and $r = 0.742$). And A positive correlation was found between CatSper1 protein expression and the sperms concentration, Sperm Progressive motility percent and sperm normal morphology present in unexplained infertile men respectively ($r = 0.845$, $r = 0.576$ and $r = 0.582$).

DISCUSSION

The present study Shows CatSper1 protein expression in spermatozoa was significantly reduced in unexplained infertility, Asthenozoospermia and Oligozoospermia compared with Normospermia fertile men may be due to there is a defect in the Protein synthesis that come from defect in the gene that responsible for the protein synthesis¹³. The present study also shows that CatSper1 protein expression in spermatozoa had a positive correlation between CatSper1 protein, sperms concentration, Sperm Progressive motility and sperm normal morphology in idiopathic and unexplained infertile men. Our result agree with several studies that

show positive correlation found between CatSper1 protein, with sperms concentration, Sperm Progressive motility and sperm normal morphology¹⁴. Protein synthesis that effect by accompanying with spermatogenesis cause by increase free radicals^{15,16}.

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