Investigating the effect of phosphodiesterase inhibitors on human sperm motility and function

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Declaration

The data used in this thesis was gathered by me alone and I am the sole author of the text. I have personally cited all references and have not submitted this thesis previously for any other degree.

Name Anne Rice
Signed ........................................
Abstract

Assisted reproductive technologies (ART) have rapidly progressed through the years and it is becoming increasingly apparent that the main cause of infertility is male factor. Today, ICSI represents most treatment which itself demonstrates the severity of male infertility. This may include problems with sperm concentration, motility and/or morphology. Sperm motility defects are associated with most cases of male infertility and provide problems for sperm reaching, binding to and penetrating the oocyte therefore impacting on fertilisation success.

Improving motility of human sperm has previously been investigated using various PDE inhibitors. PDE inhibitors have been shown to enhance sperm motility and studies have associated this with predicting an increase in IVF rates. Enhancing sperm motility increases the probability of a successful result. With the use of PDE inhibitors it may also be possible to improve sperm function. This includes enabling sperm to bind to the zona-pellucida of human oocytes, a technique that is closely correlated with predicting IVF outcome.

This study investigates the effect of various PDE inhibitors on human sperm motility of samples from both fertile and sub-fertile men. This is done using CASA throughout to record motile and progressively motile cells. Experiments were carried out on various PDE inhibitors, some of which have previously been reported as having an effect on sperm motility and some which have never been investigated before. The study then goes on to investigate the effect of PDE inhibitors on sperm function of samples from sub-fertile men. This includes a sperm penetration test to
determine whether PDE inhibitors allow sperm to penetrate a viscous substance more easily, mimicking the in-vivo action of penetrating cervical mucus in the female reproductive tract. Lastly, this study explores the effect of PDE inhibitors on the ability of sperm from sub-fertile men to bind to the zona-pellucida of human oocytes. This study is a novel approach in the clinical investigation of PDE inhibitors in the human sperm-oocyte interaction stage of fertilisation.