In vitro Effects of Propranolol on Human Sperm Motility

Ahmadi R, Hajighorbani M*, and Masaeemanesh M.B.

Abstract---Sperms are haploid cells when fertilize an oocyte the egg is formed and a new life is started. Nowadays, infertility coming from incapability of male system, particularly from sperm disorder is very common. Some types of sperm disorders may result from the medications used by human. The main aim of this was to investigate the in vitro effects of propranolol on human sperm motility. Different concentration of propranolol were prepared and human semen samples were exposed to propranolol solution and the sperm count and motility was examined using routine laboratory method. The results showed that propranolol caused decreased motility of sperms with dose dependent pattern, i.e., the more concentration of propranolol applied, the more decrease in sperm motility occurred. In conclusion, propranolol has a potential to impair sperm count and motility, so, this aspect of the drug should be considered in patients using propranolol.

Keywords--- Propranolol, Human Sperm, Motility.

I. INTRODUCTION

Spermatozoa were first described by Leeuwenhoek in the 17th century but it was not until 1928 that the sperm count was found to be associated with fertility potential [1]. The mammalian sperm cell consists of a head, a midpiece and a tail. The midpiece has a central filamentous core with many mitochondria spiralled around it, used for ATP production for the journey through the female cervix, uterus and uterine tubes. The tail or "flagellum" executes the lashing movements that propel the spermatocyte The tail or "flagellum" executes the lashing movements that propel the spermatocyte. During fertilization, the sperm provides three essential parts to the oocyte: (1) a signalling or activating factor, which causes the metabolically dormant oocyte to activate; (2) the haploid paternal genome; (3) the centrosome, which is responsible for maintaining the microtubule system. [2]. Sperm cells are carried out of the male body in a fluid known as semen. Normal values of semen parameters issued by the World Health Organisation (WHO) in 1992 are generally used as reference values. (Standard tests- volume: 2.0 ml or more, pH: 7.2-8.0, sperm concentration: 20x106 spermatozoa/ml or more, total sperm count: 40x106 spermatozoa per ejaculate or more, motility: 50% or more with forward progression (categories a and b) or 25% or more with rapid progression (category a) within 60 minutes of ejaculation, morphology: 30% or more with normal forms, vitality: 75% or more live, i.e., excluding dye, white blood cells: fewer than 1x106/ml, immunobead test: fewer than 20% spermatozoa with adherent particles, MAR test: fewer than 10% spermatozoa with adherent particles). (Optional tests—Glucosidase. neutral.: 20 mU or more per ejaculate, zinc total.: 2.4 mol or more per ejaculate, citric acid total.: 52 mol or more per ejaculate, acid phosphatase total.: 200 U or more per ejaculate fructose total.: 13 mol or more per ejaculate)

Normal semen is an admixture of spermatozoa suspended in secretions from the testis and epididymus which are mixed at the time of ejaculation with secretions from the prostate, seminal vesicles, and bulbourethral glands. The final composition is a viscous fluid that comprises the ejaculate [3]. Sperm motility describes the ability of sperm to move properly through the female reproductive tract (internal fertilization) or through water (external fertilization) to reach the egg. Sperm motility can also be thought of as the quality, which is a factor in successful conception. Sperm movement is activated by changes in intracellular ion concentration. The changes in ion concentration that provoke motility are different among species. The change in cell volume which alters intracellular ion concentration can also contribute to the activation of sperm motility:

1) a central skeleton constructed of 11 microtubules collectively termed the axoneme and similar to the equivalent structure found in cilia
2) a thin cell membrane covering the axoneme
3) mitochondria arranged spirally around it the axoneme
have classified sperm motility under two categories only:

a) progressive motility (PR)
b) non progressive motility (NP) [4]

British scientist James W. Black successfully developed propranolol in the 1960[5]. Propranolol is a sympatholytic nonselective beta blocker. sympatholytics are used to treat hypertension, anxiety, and panic. It was the first successful beta blocker developed[6]. Propranolol is available in generic form as propranolol hydrochloride. It is on the World Health Organization's List of Essential Medicines, a list of the most important medications needed in a basic health system [7]. Propranolol is a nonselective beta blocker, that is, it blocks the action of epinephrine and norepinephrine on both β1- and β2-adrenergic receptors. It has little intrinsic sympathomimetic activity, but has strong membrane stabilizing activity (only at high blood concentrations, e.g. overdosage). Propranolol has
inhibitory effects on the norepinephrine transporter and/or stimulates norepinephrine release (the concentration of norepinephrine is increased in the synapse)[8]. Since propranolol blocks β-adrenergceptors, the increase in synaptic norepinephrine only results in α-adrenergic activation, with the α1-adrenerceptor being particularly important for effects observed in animal models. Therefore, it can be looked upon as an indirect α agonist, as well as a β antagonist. Probably owing to the effect at the α1-adrenerceptor, the racemic and the individual enantiomers of propranolol have been shown to substitute for cocaine in rats, with the most potent enantiomer being S-(−)-propranolol. In addition, some evidence suggests propranolol may function as a partial agonist at one or more serotonin receptors (possibly 5-HT1B). Both enantiomers of the drug have a local anesthetic (topical) effect, which is normally mediated by blockade of voltage-gated sodium channels. Few studies have demonstrated propranolol’s ability to block cardiac, neuronal, and skeletal voltage-gated sodium channels, accounting for its known "membrane stabilizing effect" and antiarrhythmic and other central nervous system effects[9]-[11]. The main aim of this study was to determine in vitro effects of propranolol on human sperm count and motility.

II. MATERIAL AND METHODS

In this experimental laboratory investigation, we used propranolol solution (propranolol powder dissolved in serum physiologic solution) to determine the effects of propranolol on sperm motility. We prepared 4 samples as following:

Group 1: 1 cc normal semen + 0.1mg/dl propranolol
Group 2: 1 cc normal semen + 0.01 mg/dl propranolol
Group 3: 1 cc normal semen + 0.001 mg/dl propranolol
Group 4 (control group): 1 cc normal semen+ serum physiologic solution (50 lambda)

10 minutes after adding propranolol to semen sperm count and motility was examined using routine laboratory method.

III. RESULTS

In all experimental groups, sperm count 10 minutes after addition of propranolol was 150.000.000/ ml. There was no significant difference between sperm count of experimental groups and control group which consist of 150.000.000/ ml sperm cell.

Table I shows the sperm motility in semen solution without added drug or serum physiologic solution. Sperm count in this solution was 150.000.000/ml.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Motility (%)</th>
<th>Class A(%)</th>
<th>Class B(%)</th>
<th>Class C(%)</th>
<th>Class D(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal semen</td>
<td>60</td>
<td>10</td>
<td>40</td>
<td>10</td>
<td>40</td>
</tr>
</tbody>
</table>

Table II shows the motility and the classes of sperms in control and experimental groups.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Motility (%)</th>
<th>Class A(%)</th>
<th>Class B(%)</th>
<th>Class C(%)</th>
<th>Class D(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>60</td>
<td>10</td>
<td>25</td>
<td>25</td>
<td>-</td>
</tr>
<tr>
<td>0.001 mg/dl propranolol</td>
<td>50</td>
<td>10</td>
<td>20</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>0.01 mg/dl propranolol</td>
<td>40</td>
<td>20</td>
<td>20</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>0.1 mg/dl propranolol</td>
<td>5</td>
<td>5</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Our findings show that propranolol has inhibitory effects on sperm motility with dose dependent pattern; that is, the more concentration of propranolol applied, the more decrease in sperm motility occurred.

IV. DISCUSSION

We have shown that propranolol has inhibitory effects on sperm motility. In line with our finding, there are other studies indicating that propranolol has inhibitory effects on sperm motility [12]. Both α and β-adrenergic receptors which are targets of propranolol have been identified on human sperms[13], [14]. It has been demonstrated that drugs able to block β-adrenergic receptors interfere with sperm motility[15]. Adrenergic monoamines possibly modulate sperm motility by both a calciumdependent and a cyclic nucleotide-dependent mechanism. Effect of β-adrenergic antagonists on fish sperms indicate that propranolol affects fish sperm motility and causes vesicle formation in sperms[16]. Propranolol is a β-blocker that is used to treat tremors, angina, hypertension, heart rhythm disorders, etc.[17]. The D-isomer has the β-blocking activity while the L-isomer has membrane stabilizing effect. Propranolol also possesses local anesthetic activity of short latency and fairly long duration. It is known to inhibit sperm function/motility and sexual dysfunction[18]. These properties make it an ideal candidate for development as a potential novel spermicidal agent [19].

V. CONCLUSION

We have shown that propranolol inhibit sperm motility in a dose dependent manner. This property may make it a candidate for development as a potential novel spermicidal agent.

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REFERENCES


