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Original Research Article

Vitamin D Supplementation Improves Sperm Motility in Infertile Males with Asthenozoospermia: A Prospective Observational Study

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Abstract

Background*:** Vitamin D deficiency may be associated with endocrine disturbances including male infertility. Vitamin D receptor and metabolizing enzymes are found in the male reproductive system. Expression of Vitamin D inactivating enzyme in spermatozoa may be responsible for sperm motility and vitamin D responsiveness. Vitamin D supplementation may help in improvement of asthenozoospermic infertile males who are vitamin D deficient. ***Objective*:** To evaluate the impact of Vitamin D supplementation on sperm motility in vitamin D-deficient asthenozoospermic infertile males. ***Methods*:** A total of 110 infertile males who had asthenozoospermia and vitamin D- deficiency were included in this study. Vitamin D supplementation was given 40000 IU weekly for six weeks and 2000 IU daily for another six weeks and follow up semen analysis was done after 3 months to analyze the changes in sperm motility. Statistical analyses were carried out by paired t test. ***Result: The mean age was 33.19±5.81 years (range from 25 to 45 years).The mean vitamin D level was 16.19±3.19 ng/ml before and 32.93±7.74 ng/ml after supplementation, the increase being statistically significant ($p<0.05$). There was significant ($p<0.05$) increase in sperm motility (%), 23.58±9.51 before treatment versus 35.29±14.76 after treatment. The changes in progressive motility (18.20±8.15 % vs 28.94±13.06 %) and total motile count (17.10±16.78 % vs 28.52±25.89 %) were statistically significant ($p<0.05$). ***Conclusion*:** Supplementation of vitamin D improves sperm motility in infertile males with asthenozoospermia and vitamin D-deficiency.

Keywords: Male infertility, asthenozoospermia, sperm motility, Vitamin D deficiency.

INTRODUCTION

Infertility is inability to achieve pregnancy after one year of regular unprotected intercourse or after six months if the woman is older than 35 years of age. Infertility affects an estimated 15% couples globally, amounting to 48.5 million couples. Male factor is solely responsible in 20-30% and contributes to 50% of infertility [1].

Vitamin D is synthesized mainly in the skin, where ultraviolet ray B radiation converts 7-dehydrocholesterol to Vitamin D3. Then, vitamin D3 is metabolized by the hepatic 25-hydroxylases to become

25(OH) D3. Finally, the renal 1α-hydroxylase converts 25(OH) D3 to 1, 25(OH)$_2$ D$_3$, which is the most biologically active metabolite. The actions of 1, 25(OH)$_2$ D$_3$ are mediated by binding to its high-affinity receptor, the Vitamin D Receptor (VDR). The cellular response to Vitamin D (VD) is dependent on VDR, as well as on the presence and activity of VD metabolizing enzymes [2] Vitamin D deficiency has been linked to various health disorders including bone health, cardiovascular, infectious, oncologic, musculoskeletal, neurophysiologic and reproductive disorders, as well as to overall mortality [3].

Recent studies indicate that a great variety of actions are mediated by VD/VDR, like regulation of transcription of several genes involved in mitotic activity in spermatogonia, sperm metabolism, control of estrogen synthesis in gonads, increase in intracellular Ca2+ levels and activation of different signaling pathways [4]. Vitamin D influences sperm motility by regulating intracellular Ca^{2+} content in human sperm. Sperm motility was enhanced by 25(OH)$_2$ D$_3$ and a significant dose-dependent effect on acrosin activity was observed [5]. In men vitamin D status has been associated with semen quality and sperm count, motility and morphology [6]. The vitamin D receptor has been documented in human sperm and vitamin D metabolizing enzymes are found in the male reproductive system [7]. Expression of vitamin D inactivating enzyme in spermatozoa is highly specific for infertile men as a marker for both semen quality and vitamin D responsiveness [8].

Cross sectional studies have shown a positive correlation of vitamin D levels with serum androgen levels in men [9]. Abbasihormozi *et al*., [10] revealed that the levels of serum vitamin D in oligozoospermia, oligoasthenozoospermia and azoospermia patients were significantly lower than those in normal fertile men. Ozdemir *et al*., [11] observed that there was positive correlation between vitamin D and pre / post wash sperm count. There are favorable effects of vitamin D supplementation on semen quality, testosterone concentrations and fertility outcomes [12]. A recent randomized clinical trial showed that vitamin D treatment in a subgroup of oligoasthenozoospermic men increased the chance for a live birth compared to a placebo [13]. Oligozoospermia or asthenozoospermia accompanied with vitamin D deficiency may be treated by vitamin D supplementation which improves the count as well as motility of the sperm [14].

Accumulating evidences suggest that vitamin D deficiency may be a causal factor in the pathogenesis of oligozoospermia and asthenozoospermia. Vitamin D supplementation may be a novel therapeutic opportunity in the treatment of infertile males with VD deficiency. We hypothesized that Vitamin D supplementation improves the sperm motility in asthenozoospermic vitamin D- deficient infertile males. Our study aimed at evaluating the impact of vitamin D supplementation on sperm motility in vitamin D-deficient asthenozoospermic infertile males.

METHODS

The prospective observational study was carried out in the Department of Reproductive Endocrinology and Infertility, Bangabandhu Sheikh Mujib Medical University, Dhaka from January 2019 to December 2019. The study participants were a total of 110 infertile males, age: 25 to 45 years, diagnosed as asthenozoospermia according to WHO criteria 2010, deficient in vitamin D (Serum vitamin D levels < 20 ng/ml).Exclusion criteria were systemic and chronic disease like diabetes, hypothyroidism, renal and liver disease, infections like sexually transmitted diseases and tuberculosis, alcohol, smoking, drugs (antipsychotics, antihypertensive, antiepileptic, Dopamine antagonist etc) including vitamin D supplementation in previous six months.

Approval was taken from Institutional Review Board. The patients were briefed in detail regarding the objective, rationality, potential benefit of the study and informed written consent was taken. Semen analysis was done after three to five days of sexual abstinence and two samples four weeks apart in case of any abnormality. Makler chamber was used for semen analysis. Semen analysis parameters were based on WHO criteria 2010. Less than 40% sperm with forward progression or less than 32% with rapid progression was categorized as asthenozoospermia. Vitamin D was measured using a commercially available kit (Diasorin Corporate Headquarter, Saluggia, Italy). Those with vitamin D levels less than 20 ng/ml were regarded vitamin D deficient. A total of 110 infertile males who fulfilled the inclusion and exclusion criteria were administered vitamin D 40000 IU weekly for 6 weeks, and then 2000 IU daily for another 6 weeks. Follow up semen analysis was done at pre fixed schedule after 3 months to analyze the changes that were achieved. Then pre-treatment and post-treatment semen parameters, including sperm concentration, sperm motility, sperm morphology, was assessed. The total motile sperm count (TMC= ejaculate volume sperm concentration motile fraction) was calculated. The side effects and the spontaneous pregnancies were also recorded.

Statistical analyses were carried out by using the Statistical Package for Social Sciences version 20.0 for Windows (SPSS Inc., Chicago, Illinois, USA). The mean values were calculated for continuous variables. The qualitative observations were indicated by frequencies and percentages. Paired t-test was used for continuous variables. P values <0.05 was considered as statistically significant.

RESULTS

A total of 110 men with asthenozoospermia and vitamin D deficiency were included in analysis. The mean age was 33.19±5.81 years (range 25-45 years). Table 1 summarizes the demographic and clinical characteristics of the participants.

Table 1: Demographic and clinical characteristics of the participants (n=110)

Parameters	Number	Percentage
Residence		
Urban	73	66.4
Rural	37	33.6
Education		
Less than 12 years	62	56.3
More than 12 years	48	43.4
Monthly income		
Less than 300 $	78	70.9
More than 300 $	34	29.1
Religion		
Islam	98	89.1
Others	12	10.9
Type of infertility		
Primary infertility	86	78.2
Secondary infertility	24	21.8
Body mass index		
Less than 24 kg/m^2	71	64.6
24 and above kg/m^2	39	35.4

The mean vitamin D level was significantly increased after 3 months of supplementation (Table 2).There was statistically significant (<0.05) increase in sperm concentration over 3 months. The increase in total sperm motility, progressive motility and total motile sperm count was highly significant (<0.005).

Table 2: Serum vitamin D levels before and after supplementation (n=110)

Vitamin D (ng/ml)	Pre treatment	Post treatment	P value
Mean±SD	16.19±3.19	32.93±7.74	0.001^s
Range (min-max)	4.50-20.0	18.10-55.6	

s=significant

Table 3: Changes in semen parameters after 3 months of vitamin D supplementation (n=110)

Semen parameters mean±SD	Pre treatment	Post treatment	P value
Semen volume (ml)	2.03±0.57	2.0±0.32	0.649^{ns}
Sperm concentration(million/ml)	41.76±26.30	46.11±28.29	0.025^s
Sperm motility (%)	23.58±9.51	35.29±14.76	0.001^s
Progressive motility (%)	18.20±8.15	28.94±13.06	0.001^s
Total motile count(million)	17.10±16.78	28.52±25.89	0.001^s

ns=not significant
s=significant

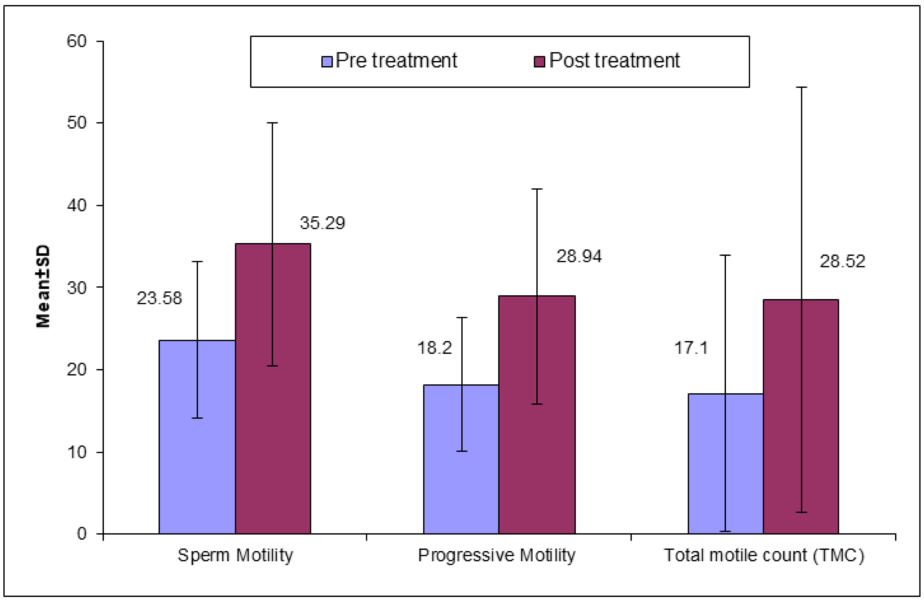

Figure 1: Bar diagram showing improvement of sperm motility, progressive motility and total motile count (TMC)

DISCUSSION

Our study explored the impact of vitamin D supplementation on sperm motility in Vitamin D deficient asthenozoospermic infertile males. With increase in serum vitamin D levels over three months of supplementation there was significant increase in sperm concentration as well as in total sperm motility, progressive motility and total motile sperm count.

We administered 40,000 IU of vitamin D weekly for 6 weeks followed by 2000 IU daily for 6 weeks. Wadwa *et al*., [15] enrolled infertile males with oligoasthenozoospermia who had vitamin D levels below 30 ng/ml. Weekly 60,000 IU cholecalciferol along with calcium was administered over 6 months. Deng *et al*., [16] randomized 86 Chinese infertile men with idiopathic oligoasthenozoospermia, to a experimental group given vitamin D 2000 IU/day and calcium and a control group of equal number given vitamin C and E for three months. Alzoubi *et al*., [17] provided vitamin D supplementation of 5,000 IU/day to 117 Jordanian men with idiopathic infertility with low vitamin D. The mean vitamin D level was significantly increased after supplementation in our study as in other studies [15, 16]. There was also significant improvement in sperm count and motility (total and progressive motility) in all studies [15-17].

In our study, no statistical significant (p>0.05) difference was found between pre treatment and post treatment semen volume. The finding is consistent with that of Yang et al. [14] and Ramlau-Hansen *et al*., [18] who found no significant association of semen volume with vitamin D status.

The effect of vitamin D supplementation on sperm count and motility can be explained by different studies on association of sperm quality with serum vitamin D levels. Zhu *et al*., [13] found that serum 1, 25-dihydroxyvitamin D_3 level was positively correlated with progressive motility and total sperm number in infertile men. Ozdemir *et al*., [11] on evaluation of post wash semen found a positive correlation between serum vitamin D (VD) levels and progressively motile sperm count. Abbasihormozi *et al*., [10] showed a positive correlation of sperm motility with vitamin D in oligoasthenoteratozoospermic men. Blomberg-Jensen *et al*., [19] suggested that infertile men with lower vitamin D levels had decreased sperm motility. Tirabassi *et al*., [20] showed in a multivariate analysis a positive association of progressive sperm motility with vitamin D after adjusting for age, BMI, PTH, and varicocele. A review of the publications by Grzechocinska *et al*., [21] concluded that both low (<20 ng/ml) and high (>50 ng/ml) serum concentration of vitamin D negatively affect sperm concentration, their progressive movement and morphology. Supplementation is required when vitamin D concentration is below 20 ng/ml (up to 50 nmol/l), especially in men with oligo- and asthenozoospermia. Seminal plasma vitamin D may be involved in regulating sperm motility. Vitamin D may enhance sperm motility by promoting the synthesis of ATP both through the cAMP/PKA pathway and the increase in intracellular calcium ions [22].

Jensen *et al*., [23] assessed the effect of vitamin D and calcium supplementation levels ≤50 nmol/L on 330 men by a placebo controlled trial. Vitamin D supplementation was not associated with changes in semen parameters, although spontaneous pregnancies tended to be higher in couples in which the men were in the treatment group (7.3% vs 2.4%). The effect may not be apparent at higher levels of vitamin D or there may be additional effects on fertility besides the change in sperm parameters. Rubal *et al*., [24] had a small study of 20 men. The sperm motility was similar between the deficient, insufficient, and replete groups (48% vs 42% vs 55%). The lack of significant difference may be due to small sample size. Ramlau-Hansen *et al*., [18] revealed that no significant association exists between vitamin D levels and sperm motility.

The right treatment of male infertility is a relatively costly procedure. In our country, due to ignorance of the patients, lack of sharp cut technology in every level sometimes people are misguided by various types of treatment procedures. Maximum people of our country live below the standard level economical parameters. Vitamin D supplementation to improve abnormal semen parameters will help our people to save their hard earnings and also help the infertility service providers in low resource settings.

Limitations of the study include study population selected from one center that may not favor generalization of findings. The study was conducted with a relatively small sample size over a very short period of time. Only one sample of semen analysis was done post treatment.

CONCLUSION

Supplementation of Vitamin D in deficient asthenozoospermic infertile male improves the sperm quality, mainly sperm motility.

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Conflict of interest: nil

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