The Egyptian Journal of Hospital Medicine (January 2024) Vol. 94, Page 566-570

Effect of Genital Tract Infection on Fructose Level in Semen of Infertile Men

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ABSTRACT

Background: Infertility is the inability to conceive after one year of unprotected, sexual intercourse. Most of infertility cases with signs of genital tract infections (GTI) are without manifestions. Fructose is the main sugar related to metabolism and sperm motility.

Objectives: This study aimed to evaluate the effect of GTI on the level of fructose in semen of infertile men.

Patients and methods: This study was conducted on 31 infertile male cases with pyospermia who were confirmed by semen analysis. Fructose level was measured before and after standard period of treatment of two weeks and after disappearance of infection by 3 weeks.

Results: There were highly statistically significant reductions in both serum fructose and pus cells before and after the treatment ($P<0.001$). It was concluded that fructose level was significantly reduced after pyospermia treatment, but still within the average normal value. **Conclusion:** The current study revealed that, fructose level was significantly reduced after pyospermia treatment, but still within the average normal value. However, no significant correlation was detected between both fructose level and GTI.

Keywords: Genital tract infection, Fructose, Infertile.

INTRODUCTION

Infertility is the inability to conceive after one year of unprotected sexual intercourse [(1)].

The male factor (MF) infertility has been considered a primary cause of infertility in twenty percent of cases and participates in about 50% in the remaining causes**.** There are a lot of causes for MF infertility; infections participate in about fifteen percent of such cases [(2)].

Male GTI are difficult to be detected as they are without manifestations in the majority of cases [(3)].

The number of cases searching for infertility management are increasing, as a result, the diagnosis of non-manifested GTI must gain more attention as the infectious process could be associated with asthenozoospermia [(4)].

Of note, GTI is a curable etiology of male infertility, but the resistance to the traditional antibiotics could interfere with their efficiency in management of complicated GTI or restoring fertility [(5)].

Bacteriospermia has been demonstrated to be associated with infertility by deteriorating the process of spermatogenesis, decreasing sperm motility, altering acrosome reactions, altering the shape, generation of free radicals, which ultimately ends in increased DNA fragmentations, development of antibodies against the sperms, and obstruction owing to inflammation and fibrosis [(6)]. The polymorphonuclear leukocytes is the best identified inflammatory marker in the male genital tract and has been considered as a traditional diagnostic indicator [(7)].

Seminal vesicle fluid represents 65% of the seminal fluid and the fructose in their secretions is an indispensable nutrient for sperm maturation [(8)]. In addition, it plays an essential role with regard semen coagulation, sperm motility, and inhibition of the immunological activities in the female genital tract [(9)].

Human fructose is the primary carbohydrate source in seminal plasma, which plays an important role in terms of sperm motility [(10)].

It has been demonstrated that there was a significant positive association between body mass index (BMI) and fructose levels. BMI and basal metabolic rate have a positive association with reactive oxygen species. Sperm count, morphology, and motility have negative association with reactive oxygen species [(11)]. Pearson correlation revealed significant negative association of sperm count, vitality and sperm progressive motility with fructose level [(12)].

This study aimed to assess the GTI effects on the fructose level in semen of infertile males.

PATIENTS AND METHODS

This study was conducted on 31 infertile male patients with pyospermia before and after treatment. Cases were enrolled from the Andrology Unit of Mansoura University Hospital for one year. The age of participants ranged from 21 to 45 years.

Exclusion criteria: Patients with criteria of inability to conceive less than 12 months, varicocele, cigarette smoking and drug abuser, systemic diseases and taking anti-microbial within last 3 months.

Methods

All cases were subjected to complete history taking including personal, sexual, martial history and preceding drugs. In addition, complete general and andrological examination were conducted.

Collection of semen specimens from cases was done by masturbation after 72 hours of abstinence. Prior to sampling, the cases were instructed to urinate and after that wash their glans with soapy water before drying it.

Received: 17/09/2023
Accepted: 18/11/2023

In addition, the cases were cautiously informed to evade infection of the jar by fingers. Semen analysis was performed by using computer-aided sperm analysis assessment to detect pyospermia, which mean presence of >1 million polymorph nuclear leucocytes in 1 ml of semen. Cultures were conducted in sterilized containers, then were placed on a plate with blood agar media followed by incubation at 35 ºC for two days. Then, microscopic examination was performed to detect any microbial contamination. After that, antimicrobial susceptibility testing was conducted by utilizing disc diffusion approach. After that, every patient received the proper antimicrobial treatment. Lastly, fructose test was evaluated for a second time after standard period of treatment (2 weeks) and following disappearance of infection by three weeks.

After confirmation of pyospermia by perioxidase stain, fructose was measured in semen by utilizing fructose test. This approach is based on the fact that fructose forms a pink colour when heated with resorcinol in the existence of hydrochloric acid that could be assessed by using a photometric method.

Ethical approval: Mansoura Faculty of Medicine Medical Ethics Committee gave its approval to this study. All participants gave written consents after receiving all information. The Helsinki Declaration was followed throughout the study's conduct.

Statistical analysis

The obtained data were coded, processed, and analysed with SPSS version 22 for Windows®. Shapiro Walk test was used to determine if the data followed a normal distribution. Qualitative data was provided as frequencies and relative percentages. The Chi square test (χ^2) was used to compare qualitative characteristics across many groups. Quantitative data were presented as mean ± SD. The independent samples t-test was used to compare two sets of regularly distributed variables (parametric data). A significant p-value was defined as one that is equal to or less than 0.05.

RESULTS

Table (1) demonstrated that the mean age of the studied cases was 29.90 ± 5.65 ranging from 18 to 44 years.

Table (1): Age of the studied cases

	Mean ±SD (min-max)
Age / years	29.90 ± 5.65 (18-44)

Table (2) demonstrated comparison of semen fructose and pus cells change between pre- and post-treatment. There were highly statistically significant reductions in both semen fructose and pus cells before and after the treatment (P<0.001).

Table (2): Occupation and residence of the studied cases

			N (31)	
Occupation	**Doctor**	**N, %**	6	19.4
	Nurse	**N, %**	6	19.4
	Student	**N, %**	7	22.6
	Carpenter	**N, %**	6	19.4
	Farmer	**N, %**	6	19.4
Residence	**Rural**	**N, %**	13	41.9
	Urban	**N, %**	18	58.1

SD, standard deviation

Table (3) showed that among studied cases, 19.4% were doctors, 19.4% were nurses, 22.6% were students, 19.4% were carpenters, 19.4% were farmers. Residence was rural in 41.9% and urban in 58.1%.

Table (3): Comparison of semen fructose and pus cells change between pre- and post-treatment.

	Pre-treatment	**Post - treatment**	**Test of significance**	**% of change**
Semen fructose Mean ±SD (min-max)	207.03± 64.95 (85-309)	173.61± 55.12 (50-285)	t=3.69 p=0.001*	16.14%
Pus cells Median (min-max)	2.0 (1.0-10.0)	0.9 (0.7-1.8)	Z=4.52 P<0.001*	60.9%

t: Paired t test, Z: Wilcoxon signed rank test, *statistically significant.

Table (4) demonstrated comparison of organism results by culture between pre- and post-treatment. There was a statistically significant improvement of results before and after treatment.

Table (4): Comparison of organism results by culture between pre and post treatment

	Pre-treatment N(%)	**Post - treatment N(%)**	**Test of significance**
Organism			
No organism	17(54.8)	23(74.2)	
Staphylococcal SPP	2(6.5) 8(25.8)	3(9.7) 3(9.7)	SM=2.12
Staphylococcus aureus	3(9.7)	1(3.2)	P=0.03*
G-ve bacilli E-coli	1(3.2)	1(3.2)	

SM: Stewart Maxwell test, *statistically significant.

Table (5) revealed a relation between organism results and semen fructose pre-treatment. There was no statistically significant relation between organism results and semen fructose pre-treatment (P>0.05).

Table (5): Relation between organism results and serum fructose pre-treatment

	Semen fructose Pre-treatment	**Test of significance**
Organism	Median (min-ma	
No organism	210(95-309)	KW=2.62
Staphylococcal SPP	160(85-235)	P=0.622
Staphylococcus aureus	217.5 (90-300)	
G-ve bacilli	190(115-285)	
E-coli	288(288-288)	

Table (6) revealed relation between organism results and semen fructose pretreatment. There was no statistically significant relation between organism results and semen fructose post-treatment (P>0.05).

Table (6): Relation between organism results and semen fructose post- treatment

	Semen fructose post- treatment	**Test of significance**
Organism	Median (min-max)	
No organism	190(50-285)	KW=8.06
Staphylococcal SPP	111(71-160)	P=0.08
Staphylococcus aureus	130 (100-183)	
G-ve bacilli	260(260-260)	
E-coli	200(200-200)	

KW: Kruskal Wallis test

Table (7) demonstrated correlation between semen fructose and pus cells for pre-treatment and post-treatment values. There was no statistically significant correlation between semen fructose and pus cells for pre-treatment and post-treatment values (P>0.05).

Table (7): Correlation between semen fructose and pus cells for pre and post treatment values

	Pre- treatment		**Posttreatment**	
Semen fructose & pus cells	r=-0.187	p=0.315	r=0.072	p=0.701

r: Spearman correlation coefficient.

DISCUSSION

Infertility is inability to conceive after twelve months of unprotected, sexual intercourse. Worldwide, 180 million subjects complain of infertility. Male infertility has been considered as one of the primary etiologies of infertility. Essentially, twenty percent of infertility cases are owing to MF infertility. Since sexual intercourse involves both sexes, male and female etiologies are occasionally co-existing, as a result, it is of great importance that the two partners are assessed for infertility and managed together. In general, the MF is responsible for fifty percent of all cases of infertility either alone or in association with different causes [(13)].

An identification of factors, which participate in MF infertility could be associated with better management [(14)]. Fructose, synthesized in seminal vesicles, is important for both metabolism and motility of sperms [(15)]. Zinc (Zn) and citrate are secreted by the prostate glands. Zn is vital for gonadal development and function [(16)]. Citrate is required for the processing of semen components, and regulation of sperm motility [(12)]. On the other hand, the contribution of biochemical markers in semen is still a matter of debate and treatment to enhance semen quality, which is associated with a relatively unreliable outcomes [(14)].

The actual role of GTI in the context of infertile males isn't totally identified. Leukocytospermia is considered as a predictor of GTI in males and it is associated with deficient semen parameters [(17, 18)].

This study was conducted on 31 infertile male cases with pyospermia before and after treatment who were enrolled from Andrology Unit at Mansoura University Hospitals for one year to evaluate the effect of GTI on the level of fructose in semen of infertile males. Our study demonstrated that there were highly significant reductions in both semen fructose and pus cells before and after the treatment. In contrast, there was no significant correlation between semen fructose and pus cells for pre-treatment and post-treatment. Also, there was no statistically significant relation between organism results and semen fructose before and after the treatment (P>0.05). The first evidence that infection of the sex glands may alter the excretory functions was declared in 1960 [(19)]. About fifty percent of white blood cells (WBCs) present in the seminal fluid arise from infection of the accessory glands, which has been demonstrated to be accompanied by increased number of WBCs in the ejaculate [(17)].

The actual explanation of reduced fructose level after treatment of GTI could due to the fact that fructose value reduces as the sperm concentration increases as supported by **Toragall *et al.*** [(12)] who revealed that there was a significant negative relationship between fructose level and sperm concentration as when fructose value diminishes, the sperm concentration increases. Also, **Trang *et al.*** [(20)] analyzed the semen specimens of sixty males with normal sperm characters versus sixty males with oligozoospermia and likewise recorded that fructose value was greater in the second group. Such association demonstrates the utilization of fructose by sperm. The increased fructose level in cases with teratozoospermia could be defined by its limited usage by spermatozoa with morphologic deficits [(15)]. From their results we concluded that fructose level was affected mainly by sperm concentration not by infection as revealed by the current study. In the current study we did not give a comment on sperm count, which could affect fructose level than infection. **Gudeloglu and Parekattil** [(21)] demonstrated that 89% of cases with azoospermia group, had fructose within normal values.

Essentially, fructose values are high in nonobstructive azoospermia and significantly reduced in obstructive azoospermia [20]. Also, **Zheng *et al.*** [22] displayed that no statistic difference was noticed in seminal plasma fructose between the Ureaplasma urealyticum infection groups and the controls. In contrast, **Djordjevic *et al.*** [17] displayed that the values of acid-phosphatase, fructose and gamma-glutamyl transpeptidase were significantly reduced in infertile males with leukocytospermia in comparison with free ones. In addition, **Gonzales *et al.*** [23] demonstrated that positive semen cultures were accompanied by lowered corrected fructose values and asthenozoospermia when there was evidence of GTI. It has been demonstrated that GTI could produce an obstruction of the seminal duct obstruction, as a result decreasing their secretion into seminal plasma**.** Also, **Ludwig *et al.*** [24] revealed that the amount of fructose/ejaculate was significantly reduced in cases with leukocytospermia compared to controls ($P<0.05$). No significant difference was recorded between the inflammatory patients, or between chronic prostatitis and control group.

Of note, GTI could interfere with semen quality and have been demonstrated to be accompanied by deteriorated spermatogenesis and impaired sperm functions [25, 26]. Although, this condition remains under controversy, a potent correlation was recorded between infection of semen and the existence of WBCs in semen and male infertility [27, 28]. Impaired regulation of spermatogenesis owing to the existence of microbes and stimulation of seminal WBCs could affect semen quality. Proinflammatory cytokines which include IL-1α & IL-6 or IL-8 released by WBCs could be accompanied by an inflammatory response consequently affecting semen quality [25, 28, 29].

The discrepancies between our study and the preceding studies may be owing to the fact that all the previous studies compared between infected cases and normal cases, however in the current study we evaluated only one group before and after the antibiotic regimens. That's why, we build our explanation on the fact that fructose was utilized for sperm motility after infection treatment, which in turn improves sperm parameters. Another important note to be considered was the fact that increased fructose level after therapy was within the normal range that doesn't affect the infertility at all.

CONCLUSION

The current study revealed that, fructose level was significantly reduced after pyospermia treatment, but still within the average normal value. However, no significant correlation was detected between both fructose level and GTI.

RECOMMENDATIONS

Further studies on this subject with larger samples size are required. Further studies to assess the secretory functions of the epididymis, seminal vesicles and the prostate, by utilizing alpha-glucosidase, fructose and Zn as parameters, in cases with chronic epididymitis, and, chronic urethritis are required.

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