Relevance of seminal plasma fructose concentrations to male infertility

Alaa Jaleel Hamada *, Dina T. Ali **, Usama S. ALNasiri**
*Urology Department Al-Kadhmia Teaching Hospital
**Institute of Embryo Researches and Infertility Treatment / AL-Nahrain University

Abstract:

Background

Seminal fructose is derived from the seminal vesicle and is therefore a suitable marker for its function. Fructose is the energy source for sperm and may have an importance in pathological conditions of semen, e.g. in asthenozoospermia.

Objective

To find out if there is a correlation between seminal plasma fructose level and sperm concentration and motility in infertile Iraqi men. In addition, the study assessed the reliability of using seminal fructose concentr ation as indicator of seminal vesicles function.

Patients and Methods

Forty six infertile men, free from infectious disease or endocrine disorders, were selected for the study. Control group, selected from couples with proven male fertility, were 10 fertile men. Semen samples, collected from theses fertile and infertile men, were analyzed for general seminal fluid examination and fructose concentration determination.

Results

Seminal fructose has been noticed to have significant negative correlations with sperm count, with percentage of motile sperm and with absolute number of motile sperms. These negative correlations may be due to increased rate of fructolysis with higher sperm count and motility or due to an endocrine cause related to relatively high FSH in infertile men. To use seminal plasma fructose as a marker for seminal vesicles function, a correction for the opposing factors that affect fructose level such as sperm count and motility is carried out. Corrected seminal fructose is positively correlated with the total number of motile sperm. Furthermore, a positive correlation between true corrected fructose and the percentage as well as the total number of motile sperm has been found.

Conclusion

Seminal fructose level has an inverse correlation with sperm count and percentage and number of motile sperm in the study group. Seminal fructose is a good marker of seminal vesicle function after using the correction formulae

Key Words: fructose, seminal fluid analysis, male infertility

Introduction

Secretion of the seminal vesicles constitutes the main (50%) and the last fraction of the ejaculates with an average volume of(2.5) ml and a pH in the neutral to alkaline range(1, 2) The physiologic role of the seminal vesicle is not entirely known; however, the secreted fluid is important in the motility and metabolism of ejaculated sperms. For assessment of seminal vesicles function there are several methods, one of which is measurement of seminal fructose has been used in almost all laboratories of the world as a marker of the seminal vesicular function(3.) Normal semen fructose concentrations range from 120 to 450 mg/dl (11-16 micromole/ml).The lower reference value for total fructose content is defined by WHO as 13 micromole or more per ejaculate. Causes of low fructose below 120 mg/dl are: Inflammation of the seminal vesicles, androgen deficiency, partial obstruction of the ejaculatory ducts, incomplete ejaculation may result in low fructose concentrations(4) Absent seminal fructose usually indicates congenital absence of the seminal vesicles and vas deferens(5). The present study will evaluate the seminal fructose concentrations as a marker for seminal vesicles function in face of opposing factors affecting its measurement which may jeopardize its value as representative parameter for seminal vesicles function and the correction formulae of seminal plasma fructose levels undertaken to rectify the opposing factors to retain its importance as a marker of seminal vesicles function.

PATIENTS AND METHODS

Forty six male patients aged (20 - 47) years were selected out of a total of two hundred and ten male patients during their attendance at the infertility clinic at Institute of Embryo Researches and Infertility treatment, Al-Nahrain University in Al-Kadhmia during the period from December 2007 to May 2008 .All the selected patients were found free from any infectious disease or endocrine disorder based on clinical examination and supported by various necessary blood analysis. Semen sample from each patient was collected by masturbatation at a clean dry wide mouth, screw cap glass container, after a period of 3 to 5 days of sexual abstinence. Semen specimen after being fully liquefied is transferred to another clean disposable graduated plastic tube for their volume measurement. Seminal plasma was obtained after liquefaction by centrifugation of semen sample at 3000 r.p.m. for 15 minute; the sperm free seminal plasma was then aspirated and divided into small aliquots. In plastic Khan Tubes, stored at (-20) C for future analysis. The patients were divided into three groups depending on their sperm count(3)

- Group I:10patients Normozoospermic (sperm concetration more than 20 million/ml).
- Group II:26patients Oligozoospermic (sperm count less than 20 million/ml).
- Group III:10patients Azoospermic (sperm count = zero).

The exclusion criteria include

- Seminal sample with pus cell more than 5 cells/high power field
- Samples with volume less than 1.0 ml were all excluded from the study, for technical reason.

Each seminal fluid sample was analyzed for:

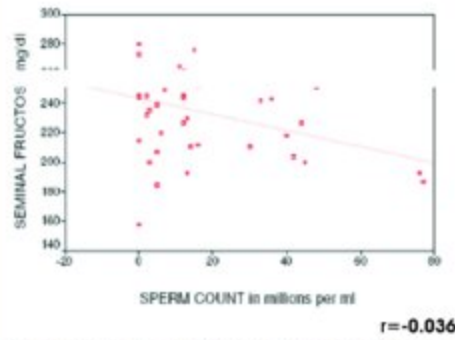
- General seminal fluid examination [appearance, color, PH, volume, Liquefaction time, sperm count, number of motile sperms, presence of RBCs, Pus cells]
- Fructose concentration according to

Resorcinol method(6 .)

- The correction formulae of seminal plasma fructose levels were undertaken to rectify the opposing factors like the sperm count and motility and to retain its importance as a marker of seminal vesicles function in form of corrected and true corrected seminal fructose as follows :
  - Corrected seminal fructose =log sperm count x seminal fructose level
  - True corrected seminal fructose = log motile sperm count x seminal fructose level

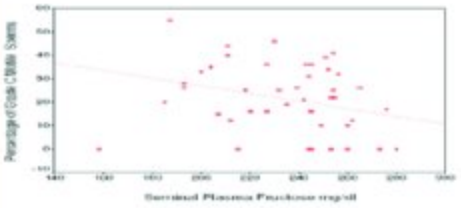
RESULTS

From the initial 46 men attended at the Al-Nahrain Infertility Institute 26 patients (56.5%) were oligospermic and 10 (21.7%) patients were azoospermic and 10 (21.7%) were with normal sperm concentration and fertile;. the average values (±SEM) found in the analysis of sperm characteristics in the study groups (normospermic ,oligospermic and azoospermic men) of seminal plasma fructose were as follows: in normal persons the average was found 217.6±22.42 mg/dl with the values range from (187-243),in oligospermic patients the result was 236.961±23.837 mg/dl with range (185-262) and in azoospermic ones the average was 246.8± 36.80 mg/dl with the range (158-280).Figure (1) represents Correlation of seminal plasma fructose to sperm count in study groups. It shows a significant inverse relationship between sperms count of men in study group and their seminal plasma fructose level. (r =-.0369), P value <0.05).In 46 study group asthenospermia was equal to 90 % even among fertile group .By assessment of sperm motility in 60 minutes it was found that grade A was very low in all sample group including the fertile ones ,while grade B >40 % in 6 persons (13%) while grade C and grade D motility had the majority of values. So, to investigate the relationship between seminal fructose and sperm motility it is wise to select the grade C motile sperms percentage and number to represent the motile sperms .An Attempt to find a correlation between seminal fructose level and percentage of motile sperms in the study group was carried out in the Figure (2) in which an inverse relationship was discovered between percentage of grade C motile sperms and seminal plasma fructose, with a statistical significance (r=-.307), P value <0.05. Since the total number of sperms is available for each patient so by substituting of number of motile sperms grade C for percentage of motile sperms grade C and again a significant negative correlation was found between seminal plasma fructose level and number of motile sperms (r = - 0.376, P value <0.0 1) paying attention for increment of the statistical significance for this correlation. In Figure (3) a plot is formulated between corrected seminal fructose and percentage of grade C motile sperms in which insignificant positive relationship is found (corrected seminal fructose = Log sperm count x seminal fructose level) r =+0.242, P value <0.36 .However, by using the total number of motile sperms Grade C instead of percentage, a significant positive correlation appeared (r = + 0.464, P value < 0.01). Figure (4) shows the positive correlation between percentage of grade C motile sperms and true corrected seminal fructose (log number of motile sperms grade C x seminal plasma fructose) with statistical significance (r =+0.637, P value <0.01) the same correlation is established between number of grade C motile sperms and true corrected seminal fructose (r = + 0.763, P value <0.01).



r=-0.0369 P<0.05

FIGURE 1 Correlation of seminal plasma fructose to sperm count



r=-0307 P value<0.05

FIGURE 2 Correlation of percentage of grade C motile sperms to seminal plasma fructose

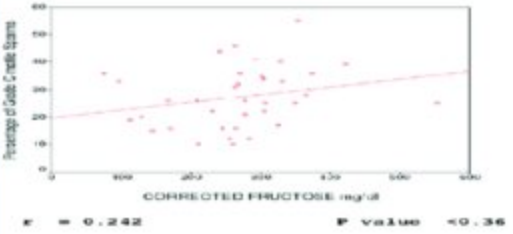


Figure 3 Correlation of percentage of grade C motile sperms to Corrected fructose

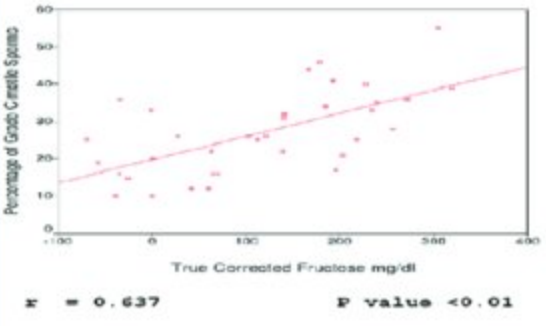


Figure 4 Correlation of percentage of grade C motile sperms to true Corrected fructose

Discussion

Semen contains fructose, presumably as a source of energy for spermatozoa(7) at the average of (12.4 micromole/ml). The metabolic end products of the anaerobic fructolysis are pyruvate and lactate(8)Several studies have indicated that seminal fructose level is different between fertile and infertile men. One of them reported a significant increase in seminal plasma fructose of non-obstructive azoospermic as well as of severe oligospermic patients when compared to normospermic men(9) Similar observations have been found by Soufir-JC(10), Patel *et al* (11), George T.(12), Coppens(13), and Rocha-FI(14)The present study demonstrates the mean values , standard deviations, and ranges expressed as mg/dl, and statistical significance of seminal plasma fructose levels of infertile non-obstructive azoospermic patients (246.8±36.80 mg/dl with the range (158-280), oligospermic (236.96± 23.84) mg/dl with range (187-262) and fertile men (217.6±22.42) mg/dl with the values range from (187-249).

It is shown obviously that the mean of seminal fructose level is higher in non-obstructive azoospermic and oligospermic men in comparison with normospermic men in the study group ,with statistical significance P value <0.05. It is perhaps worthwhile to consider that in polyzoospemic semen, ise., those with sperm density >250 x 10 /ml, the lowest values of seminal fructose can be present due to the increase in fructolysis process(15.) The present study findings are in concordance with previous reports (9,12,14,16) as a statistical significant elevation (P <0.05) in seminal plasma fructose levels are observed in non-obstructive azoospermic and oligospermic when compared to that of normosperic men, while insignificant elevation (p > 0.05) of fructose were observed in seminal

plasma non-obstructive azoospermic patients when compared to oligospermic patients .However, this study disagrees with the findings of Nun et al(17)Wetterour -U(18), Ando et al(19) Ferwardeen(20) and Zopfgen(21) that reported similar levels of seminal plasma fructose in both fertile and infertile subjects .Moreover, the present results are in disagreement with Dickerman(22) findings that the concentration of fructose in semen was generally higher in specimens of high volumes than those of low volumes, including semen devoid of sperm. In figure (1) it was demonstrated clearly a negative significant correlation between sperm count and seminal plasma fructose level ($r = -0.0369$, $P<0.05$).The possible reason of this study findings is increment of utilization of fructose by higher sperm count leading to fall in seminal plasma fructose . Certain objections to this explanation have been reported ,firstly ;as increased fructolysis should result in an increase lactic acid production(23) Schirren(24) found no such increase in semen of normospermic men;secondly the amount of fructose in semen available for spermatozoa is in excess of their utilization for energy requirement (25)thirdly fructose is not the sole source of energy spermatozoa nutrition .Another possible reason for above finding is related to dependence of seminal vesicle function on FSH and androgen .Although not measured in sample study group but finding of high FSH is common in azoospermic or oligospermic patients ,so finding of high seminal plasma fructose concentration in infertile patients may be due to increased production from seminal vesicles attributed to feedback mechanism of low spermatogenesis which causes an increase in pituitary gonadotrophin FSH ;which stimulates testosterone production which induces seminal vesicles function to raise fructose production (26) Since fructose is good energy source for spermatozoa while staying in semen a correlation between seminal plasma fructose level and percentage of grade C motile sperms is demonstrated in Figure (2) showing significant negative relationship between them ($r =0.0307$ p value < 0.05) .Besides plotting the relationship and exchanging the number of motile sperms grade C for the percentage of grade C motile sperms significant negative relationship is found ($r = -0.376$, P value <0.01).The explanation may be due utilization of fructose by the motile spermatozoa as mentioned above . Gustavo F. Gonzales demonstrated that the value of the measurement of seminal fructose concentration or corrected seminal fructose concentration as markers of the function of the seminal vesicles in cases of semen samples with poor sperm motility may be non-significant (27) Other studies demonstrated that the corrected seminal fructose has been shown to be a better marker of seminal vesicle function than simple measurement of the seminal fructose concentration28- 34. Low levels of corrected seminal fructose have been observed in men with hypofuction of seminal vesicles(10,11) and this has been related to male infertility .Subjects with hypofuction of seminal vesicles have low sperm motility which may cause infertility(28)(29).Corrected fructose is correlated with he sperm motility in men with normal sperm motility whereas seminal fructose is not, However, in asthenozoospermic samples, unable to observe a relationship between the sperm motility and the corrected fructose value(33). Thus the corrected fructose value is not a good marker of the seminal vesicle function in infertile men35. In the present study a graph is formulated between corrected seminal fructose level and percentage of grade C motile sperms in the first one and the number of motile sperms Grade C in the second one the first graph number (3) demonstrates

insignificant positive correlation between corrected fructose and percentage (r= 0.242 ,P<0.36) while substituting the No. of motile sperms for percentage of motile sperms grade C a significant negative correlation between corrected fructose level and no. of motile sperms. (r = + 0.464, P value < 0.01). Gonzales et al. demonstrated that True corrected seminal fructose seems to be truly related to sperm motility (27) Testing this hypothesis in this study demonstrates a significant positive correlation between True corrected fructose and percentage of Grade C motile sperms as in figure (4) (r =+ 0.637 P value < 0.01) and a more significant significant positive correlation between True corrected fructose and number of grade C motile sperms (r = +0.763 P value <0.01).This may raise the possibility of using the True corrected fructose as the best indicator of seminal vesicles function. Rajalakshmi et al. had demonstrated that fructolysis is very low when spermatozoa have poor motility(37) This suggests that fructose is used mainly by motile spermatozoa. Therefore correction for fructose should be carried out for the concentration of motile sperms (true corrected fructose) rather than with respect to motile plus immotile sperm concentration as used before (corrected fructose). An important question is how to assess seminal vesicle function reliably in infertile men by choosing simple and reproducible means of measurement of its products?, that raises the value of choosing seminal fructose level as indicator of seminal vesicle function because its measurement is simple and reproducible. Since the complex interpreting factors related to sperm count or motility that affect the exact measurement of seminal fructose so the advice is to use true corrected fructose level as indicator of seminal vesicles function.

Conclusions

It was made explicit that seminal fructose level has an inverse correlation with total sperm count and number and percentage of motile sperms in patients studied, that raises its value as a good marker of seminal vesicle function after using the correction formulae

References

1.Higgins SJ, Burchell JM. Effects of testosterone on messenger ribonucleic acid and protein synthesis in rat seminal vesicle. Biochem J 1978; 174: 543-51.

2.Lieber MM, Barham SS, Veneziale CM. In vitro propagation of seminal vesicle epithelial cells. Invest Urol 1980; 17: 348.

3.WHO Laboratory Manual for the Examination of Human Semen and Sperm-Cervical Mucus Interaction.4 ed. Madrid: Médica Panamericana; 2001. p 35.

4.Campbell-Walsh urology.-9th ed. / editor-in-chief, Alan J. Wein; editors, Louis R. Kavoussi, Andrew C. Novick, Alan W. Partin, Craig A. Peters, Chapter 19 , JAY I. SANDLOW et al,2007,PP 1483.

5.Fouad R. Kandell, Ronal S. Swerdloff, John Pryor, Male Reproductive Dysfunction Pathophysiology and Treatment, 2007, pp 268.

6.Mann T. The biochemistry of semen and of male reproductive tract London: Methuen and Co .LTD. 1964.

7.Amnon, Marker: Modern Methods in Semen Analysis Evaluation in Infertility, Philadelphia, W.B.Saunders: 1988, 633-661.

8.Mann T and Lutwak-Mann C. Male Reproductive Function and Semen, 1981, pp. 196-202.Springer-Verlag, Berlin, Heidelberg, New York.

9.Biswas S, Ferguson K, Stedronska J, Boffoe G, Mansfield M, Koskab N. Fructose and hormone levels in semen: their correlation with sperm counts and motility. Fertil Steril 1978; 30: 200-4.

10.Soufir JC. Azoospermia, astheno zoospermia, oligospemia and seminal biochemistry.Ann. . Biol. Clin.Paris, 1985, 43(1):67-70.

11.Patel SM, Skandhan KP, Mehta YB. Seminal plasma fructose and glucose in normal and pathological conditions. Acta Eur. Fertil. 1988 ,19(6): 329-332

12.George T. Biochemical parameters changes in the seminal fluid of infertile men with its relations to sperm count .University of Baghdad, College of Medicine , 1990

13.Coppens L. Diagnosis and treatment of obstructive seminal vesicle pathology. Acta Urol Belg 1997; 65:11-9.

14.Anrade-Rocha FT. Seminal fructose levels in male infertility: relationship with sperm characteristics. International Journal of Urology and Nephrology 1999, 31, 107-111.

15.Fraser LR, Quinn PJ. A glycolytic product is obligatory for initiation of the sperm acrosome reaction and whiplash motility required for fertilization in the mouse. J Reprod Fertil. 1981; 61:25-35.

16.Breznik R and Barko E. Zinc and other markers in the seminal plasma of infertile men. Jugosl. Ginekol. Perinatal. 1986, 26 (1-2): 23-27.

17.Nun S, Musacchio I and Epstien JA. Variations in seminal plasma constituents from fertile, subfertile and vasectomized azoospermic men .Fert.Steril. 1972,

23(5):357-360.
18.Wetterauer U. Recommended biochemical parameters for routine semen analysis. Urol.Res. 1986, 14(5):241-246.
19. Ando S, Carpino A, Buffore Ivt and IYfaggiolini. [VI. Sisci, D.: The evaluation of L-carnitine, zinc and fructose in seminal plasma of patients with varicocele and nonazospermia. Andrologia. 1989 , 21(2) : 155-160
20. Forwardin T. Biochemical parameters changes in the seminal fluid of subfertile men .University of Baghdad, College of sciences. 1989.
21. Zopfgen A, Priem F , Sudhoff F , Jung K , Lenk S , Loening SA and Sinha P. Relationship between semen quality and the seminal plasma components ; carnitine, alpha glucosidase,fructose, citrate, granulocyte elastase in infertile men compared with a normal population. Hum. Reprod. 2000 , 15(4): 840-845
22.Dickerman Z , Sagiv M , Savion Lvi , Allalouf D , Levinski H and Singer R. Andrological parameters in human semen of high (greater than 6 ml) and low (less than or equal to 1 ml volume Andrologia. 1989, 21(4): 353-362.
23.Andrade - Rocha F T. Fructose in the semen and its relation with the sperm count. Reproducao, 1993, 8, 16.
24.Schirren C. Relation between' fructose content of semen and fertility in man. J.Reprod. F ertil. 1963, 5: 347.
25.Pererson RN and Freund . Factors affecting fructose utilization and lactic acid formation by human semen, the role of glucose and pyruvic acid. Fertil. Steril. 1971, 22: 639.
26.Moon K , Osborn RB , Yannone ME et al. Relationship of testosteron to human seminal fructose. Invest. Urol. 1970, 7: 478.
27.Gustavo F. Gonzales and Arturo Villena: True corrected seminal fructose level: a better marker of the function of seminal vesicles in infertile men, international journal of andrology, 2001, 24:255-260.
28.Gonzales GF. Functional structure and ultrastructure of seminal vesicles.Arch Androl 1989; 22: 1-13.
29.Gonzales GF, Garc?a-Hjarles M, Napuri R. Corrected seminal fructose levels: an index of the secretory activity of the seminal vesicles. Arch Androl. 1988; 21: 135-42.
30.Gonzales GF, Garc-a-Hjarles M, Gutierrez R, Guerra-Garc-a R. The secretory activity of the seminal vesicles and its relationship with sperm motility: Effects of the infections in the male reproductive tract. Inter J Androl 1989; 12: 286-94.
31.Gonzales GF. Corrected seminal fructose test. Arch Androl 1994; 33: 17-22.
32.Gonzales GF, Villena A. Influence of low corrected seminal fructose levels on sperm chromatin stability in semen from men attending an infertility service. Fertil Steril 1997; 67: 763-8.
33.Gustavo F. Gonzales. Function of seminal vesicles and their role on male fertility Asian J Androl 2001 Dec; 3: 251-258
34.Gonzales GF,Kortebani G and Mazzolli AB. Leukocytospermia and function of the seminal vesicles on seminal quality. Fertil Steril 1992; 57: 1058-65.
35.Fabiani R, Johansson L, Lundkvist O and Ronquist G. Prolongation and improvement of prostasome promotive effect on sperm forward motility. Eur J Obstet Gynecol Reprod Biol 1995; 58: 191-8.
36.Ford WCL and Rees JM. The bioenergetics of mammalian sperm motility. In: Gagnon C, ed. Controls of Sperm Motility: Biological and ClinicalAspects.Boca Raton, Fla: CRC Press; 1990:175-202.
37.Rajalakshmi M , Sharma RS , David GF and Kapur fyf.NL. Seminal fructose in normal and infertile men. Contraception, 1989 ,39(3): 299-306