

Effects of sperm activity on zinc and fructose concentrations in seminal plasma

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Attempts to correlate zinc and fructose concentrations in seminal plasma with andrological parameters have produced inconsistent results. To assess further this relationship, a prospective study was performed measuring zinc and fructose concentrations in seminal plasma in 1178 patients referred for fertility treatment. Seminal analysis was performed with biochemical measurements of seminal zinc and fructose. The main outcome measures were the correlation between motile sperm concentration and seminal zinc and fructose concentrations. Zinc concentrations were not influenced by the motile sperm concentration ($r = 0.039$). Fructose concentrations were found to be negatively correlated with motile sperm concentration ($r = 0.062$). We conclude that seminal plasma zinc is an unreliable marker of spermatogenic activity. While there does appear to be a negative correlation between seminal plasma fructose concentrations and motile sperm concentration this relationship is far from linear. Due to the biochemical complexity of seminal fluid attempts to perform such simple correlations between seminal plasma components and andrological parameters are likely to produce inconsistent results and their role in the assessment of sperm function must therefore be called into question.

Key words: seminal plasma fructose/seminal plasma zinc/sperm activity

Introduction

Despite their often routine measurement in the evaluation of male fertility, attempts to correlate zinc and fructose concentrations with andrological parameters have been inconsistent. Zinc is to be found within maturing spermatozoa (Kruczynski *et al.*, 1985) but the majority of zinc within the ejaculate is derived from the prostate gland (Elliasson and Lindholmer, 1971; Srivastava and Seffy, 1985). Zinc deficiency is claimed to cause impotence (Antoniou *et al.*, 1977) and hypogonadism (Sandstead *et al.*, 1967) and zinc is thought to be important in the stabilization of sperm chromatin (Kvist *et al.*, 1990). Its high prostatic concentration is only partially

correlated with carbonic anhydrase (Vallee, 1959) for which it is a co-factor and it may have an inhibitory effect on 5 α -reductase (Wallace and Grant, 1975). Zinc has also been reported to be the primary factor responsible for the antibacterial activity of the seminal plasma (Farrell and Lyman, 1937). Various studies suggest other physiological roles for zinc but these remain to be established. Suggestions include a role in sperm production and/or viability, the prevention of spermatozoal degradation and a role in sperm membrane stabilization (Quinn, 1968; Mawhinney and Tarry, 1991).

Fructose is produced in humans mainly by the seminal vesicles with a small contribution from the ampulla of the ductus deferens and is essential for spermatozoal metabolism and motility as an energy source (Schoenfeld *et al.*, 1979). In a patient with a low volume ejaculate, the absence of fructose indicates ejaculatory duct obstruction, seminal vesicle dysfunction or hypoplasia (Aumuller and Riva, 1992).

In this study we present the results of a prospective study of seminal zinc and fructose concentrations in patients referred for routine semen analysis prior to infertility treatment. We have studied whether the motile sperm concentration influences seminal zinc and fructose concentrations.

Materials and methods

In the period between January 1, 1993 and June 30, 1995 all previously untreated patients referred for semen analysis as part of routine fertility investigations prior to fertility treatment were considered for the study. All participants were asked to produce a semen sample. Patients with azoospermia, more than 0.5×10^6 leucocytes/ml in their ejaculate or clinical evidence of a seminal infection were excluded from the study.

Semen analysis

Semen samples (one from each patient) were collected by masturbation into a sterile plastic container after 4 days of sexual abstinence, and allowed to liquefy for 30 min at room temperature. Semen volume, sperm concentration, motility and morphology were measured according to standard World Health Organization criteria (WHO, 1987). A Makler counting chamber (Sefi-Medical Instruments Ltd, Hafia, Israel) was used for concentration and motility evaluation. The total number of motile spermatozoa was assessed by a single technician. Intra-observer coefficient of variation was calculated to be 5% for both count and motility assessment.

Zinc and fructose assessment

Following semen analysis, samples were centrifuged at 1000 g for 5 min and the seminal plasma supernatant removed for measurement of zinc and fructose concentration. Zinc concentration was assessed using atomic absorption spectrophotometry (Mann, 1964). Inter-batch coefficient of variation for the assay was 8.3% at 130.7 mg/l (2 mM).

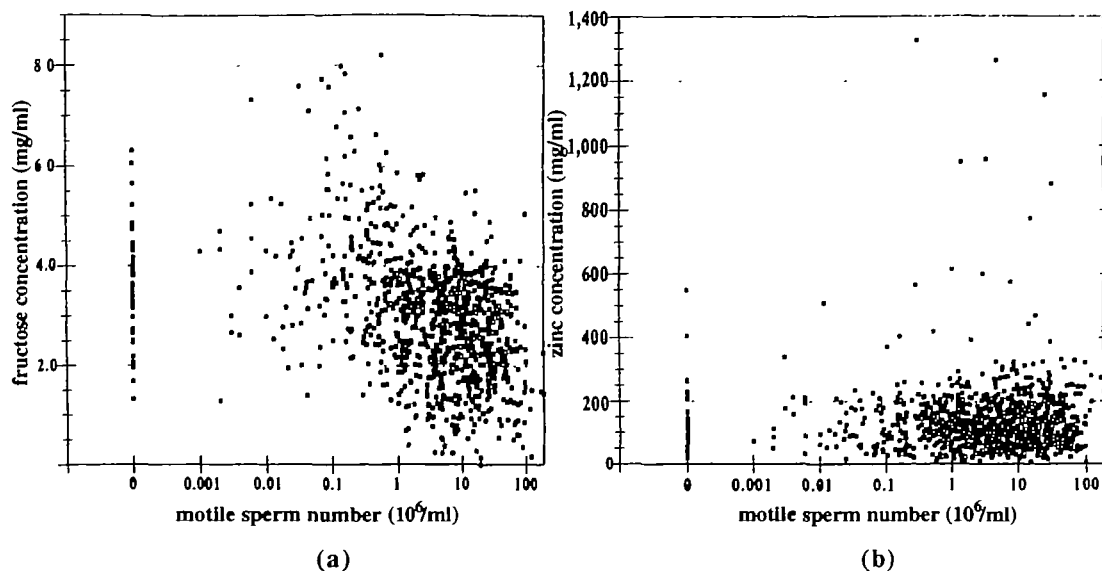


Figure 1. Relationship between the number of motile spermatozoa and (a) fructose concentration or (b) zinc concentration in seminal plasma.

The detection limit was 6.6 mg/l. Concentrations of seminal fructose were measured using acid resorcinol colorimetry (Mann, 1964). Interbatch coefficient of variation for the assay was 4.6% at 3.5 mg/ml (19.6 mM). The measurement limits for the assay were 0.09 mg/ml and 7.2 mg/ml.

Statistical analysis

Data were collected and analysed using a scientific version of the Liverpool Infertility Database System infertility data-base package (LIDS RF Ltd, Liverpool, UK). In view of the large amount of data, Kendall's rank correlation coefficient was used (in preference to the more commonly used Spearman's rank correlation coefficient) to assess the strength of association between number of motile spermatozoa and concentrations of zinc and fructose in seminal plasma.

Results

A total of 1178 patients were included in the study. The average age of the study population was 32.3 years (SD = 5.8 years). There were 227 patients with azoospermia and as the aim of the study was to assess the effect of motile sperm number on zinc and fructose concentrations these patients were excluded from further analysis. No correlation between the patient's age and zinc and fructose concentration in seminal plasma was observed.

The median value for fructose was 2.8 mg/ml (15.25 mM) with a wide range of fructose concentrations (interquartile range = 10.6–20.4 mM). There was a significant negative correlation between the number of motile spermatozoa and fructose concentrations ($r = 0.062$, $P = 0.0048$) (Figure 1a). In the same population the mean concentration of zinc in patients with a detectable motile sperm population was 117.6 mg/l (1.8 mM) (interquartile range = 1.15–2.7 mM). Figure 1b shows a lack of correlation between increasing numbers of motile spermatozoa in the ejaculate and the concentration of zinc in the seminal plasma ($r = 0.0392$, $P = 0.0713$).

Discussion

This investigation, to our knowledge, is the largest prospective study correlating seminal zinc and fructose concentrations with sperm quality. Due to the nature of the study population, the patients included possessed a varying degree of fertility potential.

The issue of correlation between zinc concentration in seminal plasma and semen quality is controversial. Kvist *et al.* (1990) reported that seminal zinc concentrations were found to be lower in patients with idiopathic infertility. Saaranen *et al.* (1987) found zinc concentrations to be increased with increasing sperm numbers, as did Stankovic and Mikac-Devic (1976) who also reported increased motility in such patients. In contrast, Danscher *et al.* (1978) found a correlation between increased zinc concentrations and decreasing sperm motility. A survey by Eliasson and Lindholmes (1971) found no correlation between seminal zinc concentrations, sperm density, sperm motility, sperm morphology or age of the patient. All of the above studies are based on either very small patient numbers or on highly selected patient groups and, therefore, the value of their conclusions is limited. Results from this much larger study have demonstrated a wide range of seminal zinc concentrations within the study population with no significant correlation with either motile sperm concentration or patient's age.

Although several studies have reported that oral zinc therapy improves seminal quality in idiopathic infertility (Tikkiwal *et al.*, 1987; Kynaston *et al.*, 1988), this study suggests that such treatment is unlikely to yield any such improvements in patients with normal zinc concentrations.

The importance of seminal fructose concentration within human seminal plasma is also confusing and contradictory. Little correlation between seminal fructose concentrations and seminal activity was reported by Moon and Bunge (1968) or Matschalut and Schirren (1989). Biswas *et al.* (1987) and Schirren *et al.* (1979), however, reported decreased fructose concentrations with increasing sperm density and motility.

To test the hypothesis that sperm activity rather than sperm number causes a decrease in fructose concentration due to increased metabolic utilization, we compared the total number of progressively motile spermatozoa with fructose concentration and found a significant negative correlation between those two parameters. There were, however, considerable inconsistencies in the relationship. Figure 1a shows that the seminal plasma fructose concentration for patients with a motile sperm count of $0 \times 10^6/\text{ml}$ varied widely from just over 1.5 mg/ml to >6 mg/ml. Further analysis of Figure 1a shows that the majority of samples had a motile sperm concentration of $1-100 \times 10^6/\text{ml}$ and seminal plasma fructose concentrations of 1–4 mg/ml. The cluster of values in this area of the graph shows no observable trend. For clarity of presentation the motile sperm concentration was plotted on a log scale which has compressed the data and made the relationship appear more striking. A linear scale would make the relationship appear much less apparent.

These inconsistencies in the findings exemplify the complex relationship between the biochemical constituents of seminal plasma and parameters of sperm function. Even with the large numbers of patients involved in this study a consistent relationship between seminal plasma fructose concentrations and motile sperm concentration has not been shown. These findings suggest that the measurement of zinc and fructose in seminal plasma has little or no use in assessing sperm function. Their main role lies in identifying patients with seminal vesicle dysfunction (low seminal fructose) and patients with zinc deficiency, either dietary or metabolic.

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Received on May 20, 1996, accepted on September 17, 1996