Food intake and social habits in male patients and its relationship to intracytoplasmic sperm injection outcomes

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Objective: To investigate the influence of the male partner's lifestyle, including eating and social habits, on semen quality and intracytoplasmic sperm injection (ICSI) success.
Design: Observational study.
Setting: Private fertility clinic.
Patient(s): Two hundred fifty male patients undergoing ICSI cycles.
Intervention(s): We recorded dietary and social habits using a food frequency questionnaire adapted to meet specific study objectives. Evaluation of semen parameters and ICSI outcomes were performed.
Main Outcome Measure(s): Frequency of intake of food items and social habits were registered on a scale with five categories ranging from no consumption to repeated daily consumption.
Result(s): The sperm concentration was negatively influenced by body mass index (BMI) and alcohol consumption and was positively influenced by cereal consumption and the number of meals per day. The sperm motility was also negatively influenced by BMI, alcohol consumption, and smoking habit, whereas it was positively influenced by the consumption of fruits and cereals. The consumption of alcohol had a negative influence on the fertilization rate. The consumption of red meat as well as being on a weight loss diet had a negative impact on the implantation rate. In addition, the consumption of red meat and being on a weight loss diet had an effect on the pregnancy chance.
Conclusion(s): Couples seeking assisted reproduction treatments must be advised about the drastic effect of both the male and female lifestyle on treatment success. (Fertil Steril® 2012;97:53–9. ©2012 by American Society for Reproductive Medicine.)
Key Words: Food intake, feeding habits, male infertility, intracytoplasmic sperm injection, lifestyle

Lifestyle factors and nutritional status are known to be critical determinants of normal reproductive function (1). A combination of reduced exercise, changes in dietary composition, and increased energy intake have contributed to a growing worldwide epidemic in obesity, with serious impacts on several aspects of health, including reproductive system health (2).

The deleterious effects of obesity on reproductive health include menstrual disorders and infertility. These disorders are probably related to multiple factors, such as endocrine and metabolic functions, including the balance of sex steroids, insulin, and leptin, which, in turn, may directly or indirectly affect ovarian function, follicular growth, implantation, and the development of a clinical pregnancy (3, 4).

However, eating disorders leading to weight loss are also associated with a reduced frequency or the cessation of ovulation. Food is used as a source of energy for a variety of essential and nonessential functions. In times of deprivation, it is necessary to ration available oxidizable substrates in favor of essential functions that are required to sustain life. Reproduction is expendable at least in the short term and can be deferred until times are more favorable. For example, menstrual cycles return in some female athletes when energy expenditure is reduced such as after an injury (5).

Besides the deleterious effects of overweight and underweight status on reproductive function, it has been suggested that the consumption of specific foods and drinks and some women's social habits can affect reproductive outcomes. Alcohol and caffeine intake (6–9), as well as tobacco smoking (10, 11), could be important factors in the failure of assisted reproduction techniques (ART).

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Currently there is an increasing interest in investigating factors that can affect ART outcomes, and the impact of lifestyle on female fertility has been well documented. However, the influence of food intake and other social habits on male reproduction has been poorly investigated.

Although the success rates of intracytoplasmic sperm injection (ICSI) were thought to be independent of basic sperm parameters (12, 13), recent reports have suggested that repeated failures after ICSI may be caused by the effect of sperm-derived factors on preimplantation embryo development (14). However, whether these sperm-derived factors, referred to as paternal effects, are affected by social and eating habits is unknown. Therefore, the goal of the present study was to investigate the influence of the male partner's lifestyle, including the effects of eating and social habits on semen quality and ICSI success.

MATERIALS AND METHODS

Study Design

The study included 250 male patients undergoing ICSI cycles in a private assisted reproduction center. All patients completed a questionnaire with multiple choice questions before the beginning of the treatment. Men were asked about the frequency of consumption of many food items and were asked about their social habits.

The effects of dietary and social habits on basic sperm parameters were evaluated. In addition, the influence of dietary and social habits on fertilization, pregnancy (PR), implantation, and miscarriage rates was investigated. In addition, the female smoking habit and the female body mass index (BMI) were included in the analysis, as these variables could influence the results.

Pregnancy was defined as the presence of fetal heart activity by ultrasound at 6–7 weeks of gestation, and implantation was defined as the presence of a gestational sac visualized on ultrasound at 4–6 weeks after ET. Miscarriage was considered when the spontaneous loss of a pregnancy occurred before 24 weeks of gestation.

A written informed consent was obtained from those patients who agreed to share the outcomes of their own cycles for research purposes. The study was approved by the local Institute Review Board.

Food Consumption and Social Habits Frequency Questionnaire

All patients were interviewed face-to-face by the same professional before the beginning of the treatment. The modified validated questionnaire (15) contained multiple choice questions about the average frequency of consumption of food items during the past year.

The food categories investigated in the present study were cereals, vegetables, legumes, fruits, red and pork meat, chicken, fish, dairy products, sweet foods, alcoholic drinks, caffeine-containing soft drinks, and coffee. The frequency of food consumption was registered on a scale with five values, ranging from no consumption to repeated daily consumption. The specific categories were: 1) never or less than once a month, 2) 1–3 times per month, 3) once per week, 4) 2–4 times/week, and 5) every day.

The questionnaires were completed by the same interviewer, and a different questionnaire recorded information on exercising, weight loss diet, number of meals per day, and smoking habit. In addition the BMI was measured.

Exercising was recorded in a scale of: 1) less than 1 hour per week, 2) 1 hour per week, 3) 2 hours per week, 4) 3 hours per week, 5) 4 hours per week, 6) 5 hours per week or more. The smoking habit was recorded as the number of cigarette smoked per day and the BMI was measured by the weight/height^2 and expressed as kilograms per meter squared.

Semen Preparation

All semen samples were collected in the laboratory after 5 days of ejaculatory abstinence. After liquefaction for 30 minutes at room temperature, the semen samples were evaluated according to the threshold values established by the World Health Organization in 1999 (16) (concentration $\geq 20 \times 10^6$/mL, total count $\geq 40 \times 10^6$, and progressive motility $>50\%$) using a Makler counting chamber. Typical morphology was evaluated according to Kruger criteria (17).

Density gradient centrifugation technique was used for sperm preparation. All procedures were conducted under sterile conditions. Using a sterile pipette 1.0 mL of the "lower layer" (90% isolate; Irvine Scientific) was transferred into a conical centrifuge tube. Using a new sterile pipette 1.0 mL of the "upper layer" (50% isolate; Irvine Scientific) was gently dispensed on top of the lower layer. A liquefied 2.0-mL semen sample was then placed on top of the upper layer and the tube was centrifuged for 20 minutes at $330 \times g$ and this process was repeated using additional tubes until the whole ejaculated sample was processed. The upper and lower layers were carefully aspirated without disturbing the pellet. Using a transfer pipette, 1.0 mL of *N*-2-hydroxyethylpiperazine-*N*′-2-ethanesulfonic acid (HEPES)-buffered modified human tubal fluid (HTF; Irvine Scientific) medium was added and the resuspended pellet was centrifuged for 7 minutes at $330 \times g$. The washing procedure was repeated. The supernatant was then removed and the pellet suspended in a volume of 0.5 mL of modified HTF medium. Sperm count and motility were estimated in the recovered fractions.

Controlled Ovarian Hyperstimulation and Laboratory Procedures

Controlled ovarian hyperstimulation (COH) was achieved by long-term pituitary down-regulation using a GnRH agonist (Lupron Kit; Abbott S.A. Societé Française des Laboratoires). This was followed by ovarian stimulation with recombinant FSH (Gonal-F; Serono).

Follicular dynamics were followed by transvaginal ultrasound examination to follow the follicular growth, starting on day 4 of gonadotropin administration. When adequate follicular growth and serum E_2 levels were observed, recombinant hCG (Ovidrel; Serono) was administered to trigger final follicular maturation. Oocytes were collected 35 hours after hCG administration by transvaginal ultrasound ovum pick-up.

TABLE 1

Description of the average of basic semen parameters, frequency of consumption of food and social habits, and ICSI outcomes among the studied population.

Variable	Unit	Value
Sperm concentration	106/mL	68.9 ± 46.9
Sperm motility	% motile cells	54.3 ± 26.5
Sperm morphology	% Kruger normal cells	4.9 ± 0.9
Cereals	Frequency	0.377 ± 0.6
Vegetables	Frequency	2.75 ± 0.7
Legumes	Frequency	2.63 ± 0.57
Fruits	Frequency	2.33 ± 0.73
Meat	Frequency	2.96 ± 2.41
Fish	Frequency	1.23 ± 0.43
Dairy products	Frequency	3.8 ± 2.3
Sweet foods	Frequency	0.45 ± 0.4
Alcoholic drinks	Frequency	1.71 ± 3.6
Soft drinks	Frequency	1.6 ± 1.2
Coffee	Frequency	2.76 ± 0.9
Exercising	Frequency	1.55 ± 2.2
Weight loss diet	Yes/no	Yes: 53.2%; no: 46.8%
Smoking	Cigarettes/d	0.8 ± 3.4
Meals/d	Number	3.3 ± 1.2
BMI	kg/m^2	26.9 ± 4.39
Fertilization rate	% fertilized oocyte	75.8%
Implantation rate	% gestational sacs	25.4%
Pregnancy rate	% of pregnant women	38.0%
Miscarriage rate	% of fetal loss	29.4%

Note: Values expressed as percentage or average ± SD. BMI = body mass index; ICSI = intracytoplasmic sperm injection.

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The recovered oocytes were assessed for their nuclear status. The oocytes in metaphase II were submitted to ICSI following routine procedures (18).

Sperm samples were collected by masturbation within 3–5 days of ejaculatory abstinence. Before semen preparation for sperm injection, the sperm concentration, sperm motility, and sperm morphology according to Kruger strict criteria (17) were recorded. Normal fertilization, which was indicated by the presence of two clearly distinct pronuclei, was assessed 18 hours after ICSI. After 3 days in culture, 1–3 embryos were transferred per patient.

Statistical Analysis

To study the influence of social and eating habits on pregnancy and miscarriage outcomes, binary logistic regressions were performed. To study the influence of social and eating habits on sperm concentration, percentage of motile spermatozoa, sperm morphology, fertilization rate, and implantation rate, linear logistic regressions were conducted. All regression analysis was adjusted for maternal and paternal age, the number of retrieved oocytes, number of transferred embryos and endometrium thickness and FSH dose, maternal smoking, and female BMI, as these variables would be considered potential confounders of the association between the factor evaluated and the ICSI outcomes.

The results were expressed as odds ratios (OR) with a 95% confidential interval (CI) or regression coefficients (RC) and a *P* value. The results were considered to be significant at the 5% critical level ($P<.05$). Data analysis was carried out using the Minitab (version 14) Statistical Program.

RESULTS

Demographic Characteristics

The patients' characteristics are as follows (mean ± SD): maternal age, 32.3 ± 4.4 years; paternal age, 38.4 ± 9.3 years; total dose of FSH administered for ovarian stimulation, 2,230 ± 712 UI; number of aspirated follicles, 13.4 ± 9.3; number of retrieved oocytes, 9.8 ± 3.4. The patients' ethnicity is as follows: white (82.0%), Asian (5.2%), Hispanic (2.0%), black (4.0%), other or mixed (2.8%), and unknown or not stated (4.0%). The average of basic semen parameters, frequency of consumption of food and social habits, and ICSI outcomes among the studied population are described in Table 1.

Influence of Food Intake and Social Habits on Basic Sperm Parameters

The sperm concentration was negatively influenced by BMI and alcohol consumption and was positively influenced by cereal consumption and number of meals per day. The sperm motility was also negatively influenced by BMI, alcohol consumption, and smoking habit, whereas sperm motility was positively influenced by the consumption of fruits and cereals. The sperm morphology was not affected by any food consumption or social habit (Table 2).

Influence of Food Intake and Social Habits on ICSI Outcomes

The male consumption of alcohol and coffee and the female smoking habit had a negative influence on the fertilization

TABLE 2

Linear regression analysis of eating and social habits that may affect the sperm concentration, sperm motility, and sperm morphology.

Response variable	Predictor variable	RC	*P* value
Sperm concentration	Cereals	15.293	< .01
	Vegetables	5.380	.104
	Legumes	7.983	.035
	Fruits	5.541	.129
	Meat	−7.776	.310
	Fish	2.764	.441
	Dairy products	2.834	.440
	Sweet foods	−4.046	.089
	Alcoholic drinks	−5.003	< .01
	Soft drinks	−0.233	.897
	Coffee	2.749	.138
	Exercising	7.888	.074
	Weight loss diet	9.487	.045
	Smoking	−0.238	.945
	Meals/d	5.836	.046
	BMI	−2.3331	< .01
Sperm motility	Cereals	10.974	< .01
	Vegetables	9.602	.436
	Legumes	2.861	.444
	Fruits	7.453	.028
	Meat	−0.078	.991
	Fish	4.091	.217
	Dairy products	2.579	.445
	Sweet foods	2.568	.239
	Alcoholic drinks	−8.5592	< .01
	Soft drinks	0.595	.721
	Coffee	−0.109	.949
	Exercising	2.861	.444
	Weight loss diet	−3.848	.374
	Smoking	−8.003	.013
	Meals/d	4.295	.110
	BMI	−2.7780	< .01
Sperm morphology	Cereals	0.749	.327
	Vegetables	6.029	.643
	Legumes	6.823	.326
	Fruits	5.760	.609
	Meat	−5.829	.878
	Fish	6.456	.564
	Dairy products	3.765	.604
	Sweet foods	1.963	.421
	Alcoholic drinks	−8.865	.974
	Soft drinks	0.934	.612
	Coffee	−0.312	.906
	Exercising	3.164	.231
	Weight loss diet	−2.484	.984
	Smoking	−8.003	.567
	Meals/d	3.457	.476
	BMI	−0.876	.573

Note: BMI = body mass index; RC = regression coefficient.

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rate (Table 3). The consumption of red meat and female BMI had a negative impact on the implantation rate. Being on a weight loss diet had also a negative influence on the implantation rate; however, it was noted that this result was dependent on the female BMI (Table 3).

In addition, the consumption of red meat and female BMI had an effect on the chance of pregnancy, and being on a weight loss diet had also a negative influence on the implantation rate; however, it was again dependent on the female BMI (Table 4). The miscarriage outcome was not influenced by any food consumption or social habit (Table 4).

DISCUSSION

The main challenge for the success of ICSI is to produce viable embryos that have high implantation potential. Implantation and early postimplantation development are conditioned by the viability of each embryo transferred, which, in turn, depends on the biological quality of the oocyte and the spermatozoon at the given embryo's origin. Consequences of the actions of sperm-derived factors on preimplantation embryo development, referred to as paternal effects, have been shown to be responsible for repeated failures of assisted reproduction attempts (14).

However, although there is an increasing interest in investigating social and eating habits that may affect reproduction outcomes in women, the influence of such habits in male reproduction is still poorly understood. The present study investigated whether the consumption of specific foods and social habits may influence semen quality and ICSI outcomes. Our data suggest that both semen quality and ICSI outcomes may be influenced by specific food intake and social habits.

Smoking habits and alcohol consumption were shown to be involved in sperm quality and fertilization function impairment. Several studies have suggested that human semen quality and fertility have been declining during the past decades (17, 19, 20). Deterioration in seminal samples has been related to environmental and occupational pollutants, changes in lifestyles, exposure to toxins, and dietary habits (1, 21, 22). Concerning lifestyle, smoking habits may be associated with decreased levels of seminal plasma antioxidants, which places their sperm at additional risk of oxidative damage (23, 24), whereas excessive alcohol consumption may cause an increase in systemic oxidative stress (25).

In recent years, oxidative stress and the role of reactive oxygen species in the pathophysiology of human sperm function and male infertility have been explored intensively. Spermatozoa, from the moment that they are produced in the testes to when they are ejaculated into the female reproductive tract, are constantly exposed to oxidizing environments, and oxidative stress has been recognized as one of the most important causes of male infertility (26).

We also demonstrated that the consumption of grains and fruits and the number of meals per day are positively related to sperm quality. These findings are consistent with a higher intake of minerals, essential amino acids, and antioxidant vitamins, which would lead to the maintenance or improvement of semen quality (27).

The consumption of coffee was also related to decreased fertilization capacity. Caffeine, a psychotropic drug (28), is present naturally and is an additive in many foods and drugs. It has been reported that 80% of pregnant women consume caffeinated beverages (29), which may have detrimental effects on reproductive biology. In fact, caffeine has been implicated as a risk factor for delayed conception (30, 31).

Klonoff-Cohen et al. (7) showed a significant association between female but not male caffeine consumption and live births. Likewise, although a significant effect of caffeine intake on fertilization rates has been observed in the present study, the pregnancy, implantation and miscarriage rates

TABLE 3

Linear regression analysis of eating and social habits that may affect the fertilization and implantation rates.

Response variable	Predictor variable	RC	*P* value
Fertilization rate	Cereals	1.151	.646
	Vegetables	3.539	.246
	Legumes	1.483	.601
	Fruits	1.201	.657
	Meat	−8.096	.152
	Fish	5.028	.164
	Dairy products	0.715	.792
	Sweet foods	−1.727	.339
	Alcoholic drinks	−3.958	.007
	Soft drinks	−1.471	.115
	Coffee	−3.963	.007
	Exercising	0.681	.801
	Weight loss diet	−18.046	.019
	Smoking	−3.540	.018
	Meals/d	0.313	.887
	BMI	0.2620	.542
	Female smoking	−4.352	.043
	Female BMI	0.575	.398
Implantation rate	Cereals	6.555	.292
	Vegetables	11.081	.072
	Legumes	5.733	.320
	Fruits	7.234	.213
	Meat	−36.2	.003
	Fish	4.507	.446
	Dairy products	3.061	.602
	Sweet foods	3.031	.428
	Alcoholic drinks	−3.100	.314
	Soft drinks	−0.541	.861
	Coffee	−1.269	.690
	Exercising	3.833	.568
	Weight loss diet	−17.43	.028
	Smoking	−0.713	.896
	Meals/d	4.513	.347
	BMI	0.8011	.380
	Female smoking	−2.984	.543
	Female BMI	−12.43	.035

Note: BMI = body mass index; RC = regression coefficient.

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TABLE 4

Binary regression analysis of eating and social habits that may affect the pregnancy and miscarriage outcome.

Response variable	Predictor variable	OR	95% CI	*P* value
Pregnancy	Cereals	1.59	0.73–2.48	.259
	Vegetables	1.67	0.87–4.32	.398
	Legumes	1.93	0.33–2.47	.107
	Fruits	0.62	0.28–1.35	.230
	Meat	0.06	0.06–0.7	.042
	Fish	0.81	0.36–1.81	.605
	Dairy products	0.71	0.33–1.55	.393
	Sweet foods	1.06	0.63–1.77	.838
	Alcoholic drinks	1.02	0.69–1.50	.936
	Soft drinks	0.93	0.62–1.39	.737
	Coffee	0.83	0.54–1.26	.380
	Exercising	1.69	0.86–2.70	.341
	Weight loss diet	0.21	0.01–1.19	.011
	Smoking	0.86	0.38–1.93	.706
	Meals/d	1.23	0.64–2.35	.540
	BMI	1.04	0.92–1.17	.579
	Female smoking	1.02	0.88–2.02	.484
	Female BMI	0.43	0.25–1.13	.027
Miscarriage	Cereals	1.02	0.91–1.12	.674
	Vegetables	1.43	0.83–1.84	.763
	Legumes	0.89	0.63–1.16	.549
	Fruits	1.23	0.87–2.24	.976
	Meat	0.85	0.43–1.16	.267
	Fish	1.21	0.68–1.48	.293
	Dairy products	1.09	0.97–1.16	.653
	Sweet foods	0.78	0.65–1.18	.784
	Alcoholic drinks	0.98	0.89–1.12	.736
	Soft drinks	1.02	0.97–1.24	.540
	Coffee	1.01	0.89–1.12	.182
	Exercising	1.08	0.97–1.21	.943
	Weight loss diet	0.98	0.78–1.32	.432
	Smoking	0.85	0.65–1.74	.273
	Meals/d	1.23	0.56–1.98	.187
	BMI	1.13	0.93–1.65	.298
	Female smoking	1.02	0.96–1.67	.476
	Female BMI	0.96	0.79–1.34	.354

Note: BMI = body mass index; CI = confidence interval; OR = odds ratio.

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were not affected, suggesting that if there is a harmful effect of caffeine on sperm fertilization potential, once fertilized, the embryo development is not impaired.

However, not only the fertilization but also the pregnancy and implantation rates were negatively affected in patients who reported being on a weight loss diet. It is well known that the reproductive system is extremely sensitive to influences from the external environment and the mechanisms responsible for the adjustment of reproductive function involve the availability of calories (32, 33).

Women with anovulation associated with strenuous exercise or who are underweight have low levels of leptin, LH, and E_2. The frequency of gonadotropin pulses is too low to sustain development of antral follicles to the point of ovulation (34). However, whether the mechanism by which reproductive function is impaired in men with food deprivation also involves the endocrinologic system is still unknown. In the present study the effect of being on a weight loss diet on implantation rate and PR were dependent on the female BMI, and it could be argued that partners usually share the same habits. Therefore if one partner is undergoing a weight loss diet, it is likely that the other is also experiencing food deprivation, especially when they are overweight and the decreased chance of assisted fertilization treatment success in these couples is due to the diminished quality oocyte rather than the sperm.

Although undernutrition is the dominant factor regulating reproductive activity under natural conditions, obesity is an important cause of subfertility in many modern societies (35). Recently, Martini et al. (36) suggested a deleterious effect of obesity on seminal quality, probably by alterations in the function of the epididymis. This is consistent with our findings that demonstrated a negative influence of BMI on sperm quality. However, in a recent systematic review with meta-analysis, MacDonald and colleagues (37) failed to demonstrate any evidence of an association between increased BMI and semen parameters.

Our evidence also suggests that successful pregnancy and implantation outcomes are decreased in patients reporting a more frequent intake of meat. This finding is consistent with poor semen quality associated with a higher intake of-products that may incorporate xenobiotics, mainly

xenoestrogens or certain anabolic steroids (17, 38, 39). The use of these compounds in the food industry results in an increased total level of xenoestrogens and sex steroids in processed foods, such as meat or milk, whose intake contributes significantly to daily exposures.

Xenoestrogens are highly lipophilic substances that can accumulate in fat-rich foods, such as meat, and may be suspected as partially responsible for the decline in semen quality. In a recent study by Mendiola and colleagues (40), an association with poor semen quality was observed in foods with processed meat available to consumers (sausages and others). In this study, the control group had a significantly higher intake of skimmed milk and a lower intake of dairy products, and consequently, a possibly lower intake of products containing lipophilic substances such as xenoestrogens.

Other food items were associated with an increased ICSI success. Intake of vegetables lead to a higher implantation chance, and as discussed, this is consistent with a higher intake of antioxidants and micronutrients, which would have a positive influence on sperm quality.

In summary, our study demonstrated that semen quality and ICSI outcomes may be influenced by food intake and social habits. Smoking habits and alcohol consumption were shown to be involved in sperm quality and fertilization impairment, whereas other items, such as fruits, cereals and vegetables, were positively related to sperm quality and implantation rate. Meat intake, as well as food deprivation or high BMI, were negatively correlated with ICSI success. Therefore, our evidence suggests that couples seeking ART must be advised about the adverse effects of both the male and female lifestyles on treatment success.

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