CLINICAL STUDY

Semen quality among Danish and Finnish men attempting to conceive

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Abstract

Objective: To assess differences in semen quality between similar populations from Denmark and Finland.

Design: Comparison of semen quality between 221 Finnish men (of whom 115 had no proven fertility) and 411 Danish men with no proven fertility in two follow-up studies among normal couples trying to conceive

Methods: In Finland male partners of couples without experienced infertility attempting to conceive were recruited through advertisements in local newspapers from 1984 to 1986. From 1992 to 1995 Danish men who lived with a partner and who had not attempted to achieve a pregnancy previously were recruited through their union when they discontinued birth control. All semen analyses were performed in accordance with the World Health Organization guidelines.

Results: Median sperm concentration, total sperm count and the percentage of morphologically normal spermatozoa were significantly higher among the Finnish men without proven fertility (104.0 million/ml, 304.0 million and 58% respectively) compared with the Danish men (53.0 million/ml, 140.8 million, and 41% respectively). Sperm concentration was 105.7% (95% confidence interval (CI) 58.1%-167.6%) and total sperm count was 127.4% (95% CI 71.4%-201.6%) higher among Finnish men without proven fertility than among Danish men after control for confounders. Conclusions: Some, but hardly all, of the observed difference in semen quality may be explained by differences in recruitment procedures, selection of the men and by methodological differences in semen analysis between the two countries. Also a birth cohort effect may explain some of the differences between countries as the Finnish men were recruited 11 years before the Danish men. Therefore, follow-up studies with identical recruitment and selection of men from the two countries are needed.

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Introduction

Several studies have shown declining trends in semen quality (1-3), but significant geographical differences may exist. In the United States, a study indicated higher sperm counts in New York compared with California and Minnesota (4). In France, a decline in semen quality was detected among Parisian semen donor candidates (5), whereas no change was observed in the Toulouse area (6) where the average semen quality seemed to be better than in Paris.

In the world-wide meta-analysis (2) the highest sperm count since 1956 was reported in Finland. Finnish

studies (7, 8) indicate that sperm counts in Finland have remained unchanged from 1958 to 1992 (111 million/ml vs 124 million/ml) and are higher than elsewhere in Europe. This may indicate that genetic factors play a role. Furthermore, a study comparing time to pregnancy (TTP) among English and Finnish women from three different studies found that Finnish couples had a shorter TTP (9). This may be due to differences in semen quality. It is also of interest that the incidence of testicular cancer in Finland is much lower than that in other Nordic countries (10) suggesting that these two phenomena may be related in some way.

The observed geographical differences in semen quality have been based on comparisons of different studies (mostly of semen donors). However, differences between methods in, for example, study designs, participation rates and laboratory procedures may interfere with the interpretation of data. We studied semen quality among 221 Finnish and 411 Danish men in two follow-up studies among normal couples trying to conceive in order to estimate the differences in semen quality between similar populations from Denmark and Finland.

Subjects and methods

Finnish men

In Finland 238 male partners of couples attempting to conceive during the period 1984 to 1986 were enrolled (7). These couples without experienced infertility were recruited through advertisements in the local newspapers. Most of the men were from the city of Kuopio in Eastern Finland and were aged between 22 and 47 years. Each man provided one sample for routine semen analysis performed at the Semen Laboratory of the University of Kuopio. Furthermore, information on alcohol intake, cigarette smoking, socio-economic factors and genital diseases were obtained. Four men (1.7%) had azoospermia and were excluded. Thirteen men were excluded because of missing data. Of the included 221 men 68 (30.7%) had fathered a child before. Among the women 61 (30.6%) had had earlier deliveries while 60 (30.1%) had experienced earlier spontaneous abortions or ectopic pregnancies. One hundred and fifteen couples had had no previous pregnancies.

Danish men

From 1992 to 1995 a total of 430 couples were recruited after nationwide mailing of a personal letter to $52\,255$ trade union members who were 20-35 years old, lived with a partner and had no children. Only couples without earlier pregnancies who intended to discontinue contraception in order to become pregnant were eligible for enrolment. The couples were enrolled into the study when they discontinued birth control. At enrolment both partners filled out a questionnaire on demographic, medical, reproductive, occupational and lifestyle factors. The men provided a semen sample (n=419). Eight men (1.9%) had azoospermia and were excluded (11, 12).

Semen analysis

Finland Semen samples were obtained by masturbation except for 13 samples collected by coitus interruptus. An abstinence time of 3–5 days was recommended. The ejaculates were collected directly into a container and examined within the first two hours. The semen analysis was performed in accordance with the World Health Organization's 1980

guidelines (13), but sperm concentration was measured in a Bürker-Türk chamber. The semen volume was measured in a graded tube with 0.1 ml accuracy. An appropriate dilution was determined after a preliminary examination of the undiluted sample. Counting was undertaken using a phase-contrast microscope at a magnification of 200. Sperm morphology was scored by assessing 100 sperms in a smear stained by Papanicolaou's method. Almost all Finnish semen samples were analysed in the same laboratory by the same technician during the whole study period.

Denmark Semen samples were obtained by masturbation and were collected at the home residence. We encouraged sampling following three days of abstinence, but emphasised that samples obtained outside this time window would still be useful. Semen samples were analysed in two different laboratories by three different technicians. The ejaculates were collected directly into a 50 ml polyethylene container and 93.8% were examined within the first two hours (no difference between laboratories). The semen analysis was performed in accordance with the World Health Organization's 1992 guidelines (14), but sperm concentration was measured in a Makler chamber in one laboratory and in a Bürger-Türk chamber in the other. After complete liquefaction the sample was kept in a heated chamber at 37 °C until analysis. The semen volume was measured in a graded tube with 0.1 ml accuracy. An appropriate dilution was determined after a preliminary examination of the undiluted sample. Counting was undertaken using a phase-contrast microscope at a magnification of 200. The sample was counted twice, and if there was more than 10% difference between the two counts, the sample dilution was remixed, and the counting procedure was repeated. One technician from one laboratory performed all the morphological evaluations. Variation in sperm count between the two Danish laboratories was checked by comparison of 28 samples from each centre and no significant variation was found (P = 0.82).

In a previously performed evaluation study, technicians from different European countries (including Denmark and Finland) analysed the same 26 semen samples (15). The inter-laboratory variation in sperm count was tested and no systematic difference was found (inter-laboratory coefficient 0.96, paired t-test = 0.23, P=0.82). Large inter-laboratory variation regarding assessment of motility and morphology parameters existed.

Statistics

Frequency distributions of the various semen parameters were highly skewed and a non-parametric test (Mann-Whitney test) was used to test differences in parameters between the countries. The distributions of residuals of semen parameters were tested for normality and logarithmically transformed to obtain normality of the residuals. Multiple linear regression

analysis with the logarithmically transformed semen parameters as dependent variables and potentially confounding variables was finally performed. The following confounding variables were included: length of abstinence (logarithmically transformed and entered as a continuous variable), age (below or above 30 years), season at delivery of the sample (September-February (winter)/March-August (summer)), smoking (yes/no), cryptorchidism (yes/no), orchitis in adulthood (yes/no), sexually transmitted diseases (yes/no) or urinary tract infections and genital disorders (yes/no).

Results

Subjects

Table 1 shows the distribution of some of the variables related to semen quality among the 411 Danish men, among all 221 Finnish men and among the 115 Finnish men without previous proven fertility. One (0.6%) of the Finnish men and ten (2.5%) of the Danish men had a history of cryptorchidism, and 23 (13.8%) and 58 (14.2%) respectively had experienced some other type of genital disorder such as varicoceles or inguinal hernia. Thirty-four (20.3%) of the Finnish men had experienced sexually transmitted diseases (gonorrhoea or chlamydia) or urinary tract infection compared with seventy-seven (19.4%) of the Danish men. Thirteen (7.7%) of the men in Finland and twelve (3.0%) of the men in Denmark had had orchitis in adulthood.

The mean age of the 221 Finnish men (30.4 years) and of the subgroup of 115 men without proven fertility (28.8 years) was significantly higher than the mean age of the 411 Danish men (27.7 years) (Table 2). Among the 221 Finnish men, 18.4% were smokers compared with 32.4% of the Danish men. More Danish (84.3%) than Finnish (42.5%) men delivered their semen sample from September to February.

Semen parameters

Table 2 shows the age and the values of the most

important semen parameters among the 411 Danish men and the 221 and 115 Finnish men with and without proven fertility respectively. Sperm concentration, semen volume, total sperm count and the percentages of normal spermatozoa were all significantly higher among the Finnish men than among the Danish men. Among the Danish men, 17.1% and 20.4% had sperm counts below 20 million/ml and above 100 million/ml respectively. Among the Finnish men the proportions were 4.5% and 48.9% (Fig. 1).

Multiple linear regression analysis was performed with the logarithmically transformed semen parameters as dependent variables and parameters seen in Table 1 as explanatory variables including age and period of abstinence. Sperm concentration was 114.9% (95% confidence interval (CI) 70.0%-163.2%, P < 0.0001), total sperm count was 135.8% (95% CI 87.1%-197.1%, P < 0.0001) and the percentage of morphologically normal spermatozoa was 42.6% (95% CI 34.5%-51.2%, P < 0.0001) higher among Finnish men than among Danish men after control for length of abstinence, age, season at delivery of the sample, smoking, cryptorchidism, orchitis in adulthood, sexually transmitted diseases or urinary tract infections and genital disorders. In the sub-group of Finnish men without proven fertility sperm concentration was 105.7% (95% CI 58.1%–167.6%, P < 0.0001), total sperm count was 127.4% (95% CI 71.4%-201.6%, P < 0.0001) and the percentage of morphologically normal spermatozoa was 42.8% (95% CI 32.8%-53.5%, P < 0.0001) higher after control for confounders.

Discussion

In two follow-up studies of Danish and Finnish couples trying to conceive, we found that Finnish men had a significantly higher sperm concentration, total sperm count and a higher percentage of morphologically normal spermatozoa than Danish men. Differences in sampling and recruitment procedures may explain some of the contrast between the countries. Also, a part of the observed difference in sperm count could

Table 1 The distribution of lifestyle factors and diseases in reproductive organs among Danish men and all Finnish men and Finnish men without proven fertility.

Variable	Danish men (n=411)	All Finnish men (n=221)	Finnish couples without proven fertility (n = 115)
Smokers (%)	32.4	18.4	17.1
Cryptorchidism (%)	2.5	0.6	1.1
Varicoceles, inguinal hernia or genital malformations (%)	14.2	13.8	16.7
Parotitis as adult*	3.0	7.7	8.9
Urinary tract infections or sexually transmitted diseases (%) Season for delivery of the sample	19.4	20.3	20.1
Percent delivered during winter (September–February) (%)	84.3	42.5	52.2

^{*} No information on orchitis was available from the Finnish men.

Table 2 Mean (and standard deviation s.p.) and median (and 5 and 95 percentiles, 5–95%) age, period of abstinence and semen parameters among Danish men and all Finnish men and Finnish men without proven fertility.

Variable	Danish men (n=411)	All Finnish men (n=221)	Finnish couples without proven fertility (n=115)	P values*
Age (years) Mean (s.p.) Median (5-95%)	27.7 (3.0) 27.0 (23.0–33.0)	30.4 (4.7) 30.0 (24.0–39.1)	28.8 (3.8) 28.0 (23.7–36.0)	<0.0001/0.02
Period of abstinence (days) Mean (s.p.) Median (5-95%)	3.7 (2.3) 3.0 (1.0–9.0)	3.9 (1.1) 4.0 (3.0–6.0)	3.8 (1.0) 4.0 (3.0–6.0)	<0.0001/0.001
Sperm concentration (million/ml) Mean (s.p.) Median (5-95%)	68.5 (61.0) 53.0 (6.0–202.8)	136.9 (126.5) 100.0 (20.0–379.4)	126.8 (118.0) 104.0 (13.6–354.4)	<0.0001/<0.0001
Seminal volume (ml) Mean (s.p.) Median (5-95%)	3.0 (1.5) 2.8 (1.0–5.7)	3.4 (1.6) 3.1 (1.4–6.6)	3.4 (1.6) 3.1 (1.5–6.1)	0.01/0.04
Total sperm count (million) Mean (s.p.) Median (5–95%)	198.6 (189.5) 140.8 (10.5–578.4)	380.9 (277.9) 310.8 (50.3–999.9)	358.0 (252.7) 304.0 (47.8–904.0)	<0.0001/<0.0001
Morphologically normal spermatozoa (%) Mean (s.p.) Median (5–95%)	39 (11) 41 (19–55)	57 (11) 59 (38–72)	57 (12) 58 (36–72)	<0.0001/<0.0001

^{*}Mann-Whitney U-test. P value for differences between Danish and all Finnish men/P value for differences between Danish men and Finnish couples with no previous abortions or births.

be explained by methodological differences in semen analysis between the two countries.

In an evaluation study (15), the inter-laboratory variation in sperm count was around 15%. However, significant inter-individual differences were found and may hamper the interpretation of the morphology data. Only one of the technicians performing the semen analyses in the two countries participated in the evaluation study and the inter-individual variation between the others (not tested technicians) may indeed be higher.

The advantage of our study was that the two populations were comparable as they both included

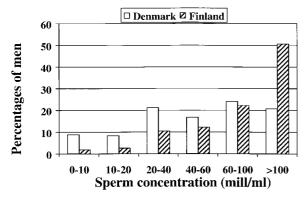


Figure 1 The percentage of Finnish and Danish men with a sperm concentration of 0–10 million/ml, 10–20 million/ml, 20–40 million/ml, 60–100 million/ml and above 100 million/ml.

couples with no known infertility problems who discontinued contraception in order to become pregnant. However, some differences existed as Danish couples were recruited through their union by a personal letter whereas Finnish couples were recruited through advertisements in newspapers. This may cause differences in participation rates and selection of couples between the two countries. This could explain some, but hardly all, of the observed difference in semen quality between the two countries. The inclusion criteria also differed among couples from the two countries: the Danish couples were enrolled from the day they discontinued the use of birth control in order to become pregnant for the first time whereas the Finnish couples were enrolled after a period of trying to conceive of varying length. This may have increased the proportion of subfertile couples and probably also the proportion of men with poor semen quality in the Finnish study, as the very fertile couples may already have conceived before they were enrolled in the study. This would have tended to underestimate the differences in semen quality between the two countries. Furthermore, 48% of the Finnish couples had either previous abortions or births. However, a similar difference in semen quality was found among the couples without proven fertility in Finland and the Danish couples. Also, the Finnish men were recruited from a single location (Kuopio) in Finland whereas the Danish men were recruited nationwide. Therefore, the Finnish men may not be representative of the whole Finnish population. On the other hand Finnish studies (7, 8)

indicate that sperm counts in Finland in the same time period are in the same range as among the men from Kuopio (mean 111–124 million/ml vs 137 million/ml).

Differences in the distribution of risk factors between men from Denmark and Finland do not appear to explain our findings. More Danish men had cryptorchidism, but more Finnish men experienced orchitis in adulthood and urinary tract infections or sexually transmitted diseases. We controlled for these differences in the multiple regression analyses, which did not change the reported associations.

More men from Denmark than from Finland smoked. We controlled for the effect of smoking in the multiple regression analyses, which did not affect the reported differences. Furthermore, non-smoking Finnish men had a significantly better semen quality than non-smoking Danish men. We could not reliably compare the alcohol intake among men from the two countries as the questionnaires regarding alcohol consumption differed. No information on the intake of caffeine was present in the Finnish study. However, the results regarding the influence of lifestyle factors such as smoking, alcohol and caffeine intake on semen quality are contradictory (16–22) and we do not believe that differences in lifestyle factors can explain our findings.

More men from Denmark delivered their semen sample from September to February when the sperm concentration has been reported to be slightly higher than during the summer season (23–26). This would result in a higher true difference than that reported. The Finnish men had a slightly longer period of abstinence but comparing men with an abstinence period of three days gave identical results. Thirteen Finnish men delivered their sample by coitus interruptus, but exclusion of these did not change the median values of the semen parameters or the reported differences found by multiple regression analyses.

The Finnish men's mean age was 3 years older than the mean age of the Danish men. Furthermore, the Finnish study was conducted 11 years before the Danish study. Semen quality has been reported to decline with increasing year of birth (3, 5). This may explain some of the observed differences between the men recruited in Denmark and Finland. No decline in semen quality was observed among 5481 infertile Finnish men in the same age group between 1967–1994 (7, 8). However, some increase in spermatogenic disorders over calendar time among middle-aged Finnish men has been reported in a necropsy study (27).

We cannot explain the differences in semen quality between the Finnish and Danish men. It is known that the Finnish population differs genetically from that of the other Nordic countries in many respects. There are, for instance, several genetic diseases typical of the Finnish people (28). Testicular cancer incidence is much lower in Finland than in Denmark and the other Nordic countries (10). Furthermore, testicular cancer incidence is higher among the white than the

black population in the USA (29, 30). This suggests that genetic factors have an impact on testicular function. On the other hand, it has been speculated that the adverse changes are attributable to altered exposures to estrogenic and other endocrine disrupting agents during fetal development (31). According to this hypothesis exposure to these chemicals should be lower in Finland than in Denmark. Indeed, some of the suspected chemicals are used in much larger quantities in Denmark than in Finland (32).

In conclusion, we found that Finnish men had a better semen quality than Danish men. Some, but hardly all, of the observed difference in semen quality may be explained by differences in recruitment procedures, selection of the men and by methodological differences in semen analysis between the two countries. A birth cohort effect may also explain some of the differences, as the Finnish men were recruited 11 years before the Danish men. Therefore, follow-up studies with identical recruitment and selection of men from the two countries are needed.

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