Original Article

The Use of Vaginal Lubricants and Ultrasound Gels Can have Deleterious Effects on Sperm Function

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Abstract

Context: Some vaginal lubricants and ultrasound gels are known to be detrimental to sperm function and therefore could negatively affect fertility. **Aims:** The aim of the current study was to develop a sperm motility index (SMI) to test the sperm toxicity of ultrasound gels and vaginal lubricants used in reproductive medicine. **Settings and Design:** Two ultrasound gels (Aquasonic® and Kefus®) and five vaginal lubricants (Vaginesil™, Velastisa®, K-Y Jelly®, Control®, and Durex®) were studied. Three different concentrations (1%, 5%, and 10%) of each lubricant were tested. **Subjects and Methods:** SMI was calculated dividing the percentage of progressively motile sperm in each tested gel by that in the control at 0.5, 1, 2, and 24 h of incubation at 5% of CO_2 and 37°C. SMI values <0.75 indicate sperm toxicity. **Statistical Analysis Used:** The main outcome measured was SMI for each concentration and time of incubation. **Results:** Only Durex® did not show any deleterious effect on sperm quality. The rest of lubricants presented different degrees of toxicity. Vaginesil™ resulted in toxic for all concentrations and incubation periods (SMI < 0.12). Control® and Velastisa® presented toxicity at 10% after 2 h, while K-Y Jelly® showed toxicity at 10% from 1 h of incubation. Regarding ultrasound gels, Aquasonic® showed toxic effects after only 0.5 h (SMI = 0.70 ± 0.15), while Kefus® showed slightly toxic effects after 2 h (SMI 0.69 ± 0.07). **Conclusions:** SMI is an accurate tool to evaluate sperm toxicity. One of the main strengths of the article is the inclusion of representative semen samples and known products used worldwide. This study has a relevant clinical translation since it highlights the importance of evaluating the possible sperm toxicity of simple products used in reproductive medicine.

Keywords: *Progressive motility, sperm survival assay, sperm toxicity, ultrasound gel, vaginal lubricant*

Introduction

Commercial gels are commonly used for oocyte recovery in transvaginal punctures, in vaginal ultrasound examinations to monitor follicle development, and before intrauterine insemination. Vaginal lubricants are used to treat vaginal dryness in dyspareunia, for recreational purposes during intercourse, for sperm collection, and to facilitate insertion of medical devices in assisted reproduction techniques (ART). Many gels contain traditionally harmless ingredients such as glycerine or propylene glycol and can change the pH and osmolality levels.[1] When mixed with human semen during intercourse or intrauterine insemination, these gels may affect sperm function decreasing its

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fertilization potential which may also decrease the chance of successful conception.[2-4] The reported toxic effects on sperm are related to dose and duration of exposure.[4-6] Previous studies have primarily used gel concentrations of 10% or higher at only 1 and 24 h of exposure, which may not reflect the levels of sperm encountered in the vagina after ejaculation.[2,3]

The toxic properties of substances used in reproductive medicine can be screened by using the sperm survival assay (SSA) that provides a sperm motility index (SMI) where values of <0.75 indicate sperm toxicity.[6,7] Therefore, this index could be an accurate tool for evaluating motility that also allows us to assess toxic effects on sperm and embryos.

The aim of this research was to test the SMI to analyze the sperm toxicity in two ultrasound gels and five nonspermicidal vaginal commercial lubricants, commonly used in ART. For this objective, low concentrations of gels were used to better reflect the proposed *in vivo* exposure.

Subjects and Methods

Patient selection and semen preparation

This study was approved by the Institutional Review Board of Hospital Universitari i Politècnic La Fe, in Valencia, Spain (2015/0574). After informed consent, semen samples from 20 normozoospermic men donors (mean age: 35.9 ± 4.3 years) were collected by masturbation after a sexual abstinence of 2–5 days. The semen sample was evaluated according to the World Health Organization criteria.[8] Sperm quality analysis was performed using a computer-assisted sperm analysis (CASA), the Integrated Sperm Analysis System for human semen (PROiSER R + D S. L., Spain). Semen samples were washed by the swim-up technique. Sperm concentration was adjusted to 20 million sperm/ml with *in vitro* fertilization (IVF) culture media (Origio Medicult, Denmark), as an effective working concentration.

Lubricant and ultrasound gel preparation

Five vaginal lubricants were analyzed: Durex® (Reckitt Benckiser Healthcare, UK), Control® (Tecnilatex S. A., Spain), Velastisa® (ISDIN S. A., Spain), K-Y Jelly® (Johnson and Johnson S. A., Spain), and Vaginesil™ (Combe Europa, Spain). Considering the observations of other published studies that analyzed the damaging effects on sperm function in the range (v/v) of 1%–30%,[2,4,9] prewarmed (37°C) coital lubricants were adjusted to 1%, 5%, and 10% concentration with IVF medium as follows: With the help of an insulin syringe, the volume of lubricant desired was selected. To achieve a concentration of 1%, 0.1 ml of the lubricant was aspirated and then diluted in 9.9 ml of IVF by vortexing. In the case of the 5% concentration, 0.5 ml of the gel was aspirated and thoroughly mixed it with 9.5 ml of IVF. The 10% concentration was obtained by aspirating 1 ml of the gel and subsequently dissolving it with 9 ml of IVF. After that, the gels were incubated at the same conditions of sperm incubation (5% of CO_2 and 37°C). Subsequently, an aliquot of 50 µl of each lubricant was mixed volume by volume (v/v) with 50 µl of postwashed semen and kept in the incubator until the toxicity was measured.

The two commercial ultrasound gels studied were Kefus® (Kefus Cosmetics S. L., Spain) and Aquasonic® (Parker Laboratories, USA). In this case, to simulate real vaginal environment after the ultrasound examinations, only 10% gel concentration was tested, more accurately reflecting the amount of gel remaining in the vagina. An untreated aliquot of IVF sperm suspension served as control.

Sperm survival assay

Sperm toxicity was determined using the SMI, calculated by dividing the percentage of progressively motile sperm (fast progressive motility and slow progressive motility) in each test solution by that in the control at 0.5, 1, 2, and 24 h of incubation at 5% of CO_2 and 37°C. An aliquot of 10 µl of each test solution and control was placed in a Makler counting chamber and analyzed with the CASA system. SMI values of <0.75 indicated sperm toxicity.[7]

Statistical analysis

Statistics were performed using the Statgraphics® Plus version 5.1 (Statpoint Technologies, USA) software package. For lubricants, a tetra factorial ANOVA including the three factors of interest (lubricant, concentration, and time) and a blocking factor (sample) were performed. In the ultrasound gels, a tri-factorial ANOVA was performed. ANOVAs were followed by *post hoc* Tukey analysis to determine the variance between groups. SMI results were shown as 95% Tukey honestly significant difference (HSD) intervals over the mean, and individual SMI effect was plotted as mean ± standard error of the mean. By statistical analysis, $P < 0.05$ was considered significant.

Results

Vaginal lubricants

The tetra factorial ANOVA performed clearly showed a strong interaction between the lubricant and time factors ($P = 0.000$). This interaction was a consequence of different behaviors between lubricants in the last stage

of the incubation period (2–24 h). While Vaginesil™ and K-Y Jelly® showed no change in the average value of SMI in the last time interval, Velastisa® and Control® showed a significant increase, which was even more pronounced in Durex®. A second ANOVA eliminating the last time interval (2–24 h) showed significant results for lubricant and concentration (P = 0.000) and for time and lubricant (P = 0.001) too.

The average values for SMI with their respective Tukey HSD intervals for each lubricant are presented in Figure 1. Three clear groups of lubricants going from lower to higher SMI average values were found. The lower group corresponds to Vaginesil™ with an SMI average of 0.02 (95% confidence interval [CI]: 0.00–0.04). In the middle group, there were three lubricants, with no statistically significant differences between them: Control® (SMI mean value = 0.88, 95% CI: 0.86–0.90), K-Y Jelly® (SMI mean value = 0.83, 95% CI: 0.81–0.86), and Velastisa® (SMI mean value = 0.85, 95% CI: 0.83–0.87). The higher group corresponds to Durex®, with an average value of SMI of 0.98 (95% CI: 0.96–1.00).

A decrease in the SMI average with increasing lubricant concentration could be observed: SMI mean value with 1% gel concentration = 0.76 (95% CI: 0.74–0.77), SMI mean value with 5% lubricant concentration = 0.74 (95% CI: 0.72–0.75), and SMI mean value (with 10% lubricant concentration) =0.65 (95% CI: 0.63–0.66).

Regarding the individually analyzed sperm toxicity of the different vaginal lubricants according to the concentration and incubation time, we observed that with only 0.5 h of incubation, Vaginesil™ was toxic at all concentrations (SMI at 1% lubricant concentration = 0.12 ± 0.09; SMI at 5% lubricant concentration = 0.00 ± 0.00; SMI at 10% lubricant concentration = 0.00 ± 0.00). After 1-h incubation, sperm toxicity was only observed in K-Y Jelly® at 10% concentration (SMI = 0.69 ± 0.10). However, at 2 h of incubation, most of lubricants exhibited sperm toxicity with a concentration of 10% (SMI Durex® =1.00 ± 0.10; SMI Vaginesil™ =0.00 ± 0.00; SMI Control® =0.74 ± 0.21; SMI Velastisa® =0.71 ± 0.08; SMI K-Y Jelly® =0.68 ± 0.25). Conversely, Durex® had no toxicity at any point during the incubation period.

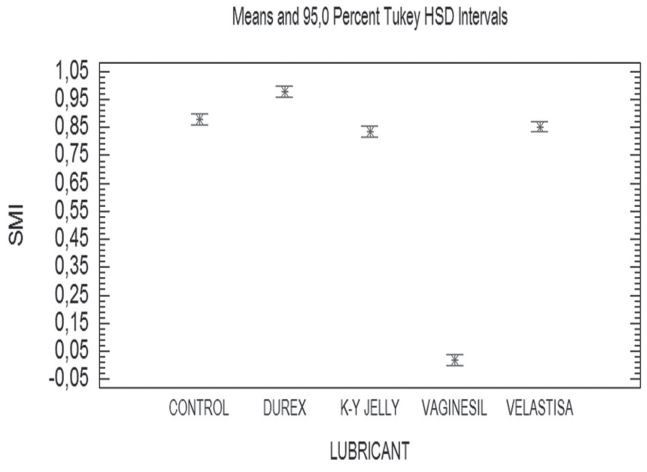

Figure 1: Graphical representation of mean values of Sperm Motility Index (SMI), with their respective Tukey HSD intervals for each lubricant. Asterisks show the mean value for each SMI and the lines are the lower and upper confidence intervals (95% CI).

Ultrasound gels

The ANOVA results clearly showed significant effects on the interaction between gel and time (P = 0.003). There were different behaviors between gels from 2 to 24 h of incubation proving that Aquasonic® did not change its SMI average, while Kefus® showed a high increase in SMI average.

To analyze the gel behavior more accurately, the focus was on an analysis time of 2 h or less. The ANOVA results showed again significance in the interaction (P = 0.000). Aquasonic® was significantly more toxic than Kefus® (P = 0.000). In addition, this difference in toxicity increased significantly as exposure time also increases [Figure 2]. The average value of SMI for exposure times of 0.5–2 h was 0.48 for Aquasonic® (95% CI: 0.41–0.55) and 0.74 for Kefus® (95% CI: 0.67–0.81).

An individual analysis of sperm toxicity showed that Aquasonic® was toxic at all incubation periods (SMI at 0.5 h = 0.70 ± 0.15; SMI at 1 h = 0.52 ± 0.21; SMI at 2 h = 0.39 ± 0.27; SMI at 24 h = 0.22 ± 0.17). However, Kefus® showed slightly toxic effects only after 2 h of exposure (SMI = 0.69 ± 0.07).

Discussion

Sperm motility is the most important predictor of sperm transport and subsequent fertilization. Therefore, the toxic properties of ultrasound gels and vaginal lubricants used in reproductive medicine can be screened by using the SSA through the SMI.[6,7] Several studies have reported a deleterious effect of various commercially available lubricants such as K-Y Jelly®, Astroglide®, and Replens® on sperm function and motility.[9-12] Vargas *et al*.[6] showed the toxic effect of glycerine which penetrates across sperm membranes and can disrupt cell function and motility even at low concentrations. Their results showed that both Replens® and Felis® contain glycerine and they were found to be toxic. Aquasonic® does not list ingredients and was also toxic. On the other hand, Pre-seed® which was known to not contain glycerine was not toxic.

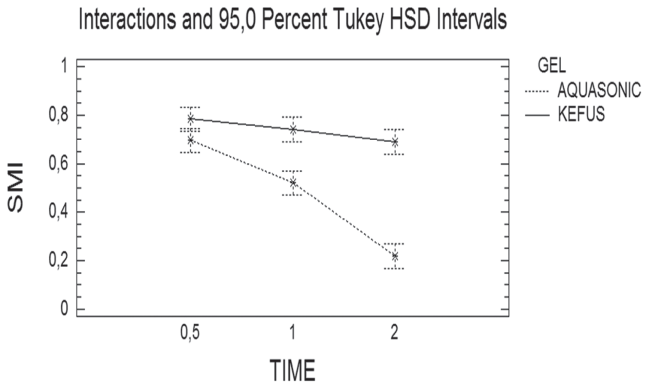

Figure 2: Interaction plot between Sperm Motility Index (SMI), incubation times (0.5 to 2 hours) and ultrasound gels, with their respective Tukey HSD intervals for each incubation times. Asterisks show the mean value for each incubation time and the lines are the lower and upper confidence intervals (95% CI).

Most of the gels investigated in this study have not been previously examined. Aquasonic® showed toxic effects at only 30 min of exposure (SMI = 0.70 ± 0.15) and significantly decreased SMI after 1 h (SMI = 0.52 ± 0.21) and 2 h (SMI = 0.39 ± 0.27). In contrast, Kefus® showed slightly toxic effects only after 2 h exposure (SMI = 0.69 ± 0.07). Claassens *et al*.[7] demonstrate that an SMI with values of >0.75 was an accurate predictor for lack of embryo toxicity as soon as 2 h after preparation. Therefore, Kefus® could be considered as a convenient ultrasound gel at 10% concentration as it did not present toxicity. This might be due to the presence of nontoxic ingredients. These results coincided with those obtained by Vargas *et al*.,[6] which demonstrate that during the 24-h assay, Aquasonic®, Felis®, and Replens® caused declines in mean percentage of motile sperm, resulting in SMI values of <0.75 and a designation of sperm toxic effects even at 0.83% concentration ($P < 0.05$). Aquasonic® gel is commonly used for vaginal ultrasound examination to monitor follicle development before intercourse or insemination. Based on sperm toxicity found in this study and others,[1-6] this gel should not be used for transvaginal procedures in patients.

Regarding the sperm toxicity for vaginal lubricants, Sandhu *et al*.[4] found that all commercial lubricants except Pre-seed® impaired sperm motility. The K-Y Jelly® lubricants were the most detrimental to sperm. The negative effect on sperm motility has been attributed to the presence of toxic chemicals, low pH, and elevated osmolality of commercial coital lubricants.[13,14]

In this study, SMI showed that Vaginesil™ was toxic at all concentrations and incubation periods (SMI <0.12). Control® and Velastisa® only presented toxicity at 10% and 2 h incubation period and K-Y Jelly® showed toxicity at 10% and 1-h incubation. In contrast, exposure to Durex® initiated hyperactive motility and the sperm remained hyperactive during the entire incubation period without showing any decline in motility. Therefore, Durex® improved sperm motility and obtained an SMI of >1. Sandhu *et al*.[4] obtained similar results with Mustard® oil, indicating that this might be due to the activation of transient receptor potential channels. Their presence in human sperm and their involvement in flagellar activity have been previously described.[15]

The effects of vaginal lubricants and ultrasound gels have been studied mainly by comparing sperm motility, vitality, DNA fragmentation, and recently, by SMI. SMI considers progressive motility in both test and control samples for each incubation time, it can therefore be considered more accurate when assessing the toxicity of gels. Motility, vitality, and DNA fragmentation provide little to no statistically significant information and hence are not as effective when predicting sperm and embryo toxicity. SMI can provide an effective IVF quality control system for material and culture media such as the gels and lubricants used in ART programs.

These data confirm that even gels labeled as nonspermicidal can significantly impair sperm motility even at lower concentrations than previously reported (1%). Vaginesil™ was toxic in all concentrations and incubation periods. Therefore, this lubricant should be avoided when treating vaginal dryness in dyspareunia, for sperm collection, and when facilitating insertion of medical devices in fertility patients. Nevertheless, it should not be considered an effective contraceptive.

This study has several strengths. All semen samples used were representative of semen samples intended for the intrauterine insemination technique. Hence, we were able to simulate to perfection the possible sperm toxicity that exists in vaginal lubricants and ultrasound gels. Moreover, we tested products used worldwide and prescribed by most specialists. The main study limitation was that it cannot be perfectly reflected what would happen *in vivo* because it was an *in vitro* study.

Among the ultrasound gels evaluated by SMI in this study, only Kefus® did not show any sperm toxicity after 2 h exposure, so its use in ART procedures would be recommended. Regarding vaginal lubricants, Durex® may be a promising treatment for vaginal dryness in infertile couples who are trying to conceive; however, large-scale *in vivo* trials are needed to support our findings.

Further research is needed to investigate the toxic effects of all the ingredients listed in ultrasound gels and vaginal lubricants, paying special attention to glycerine. Listing every ingredient should be mandatory for all gels that are available.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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