Chapter 4
The Effects of Vaginal Lubricants on Sperm Function

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Abbreviations

CASA Computer-assisted sperm analysis
LM Light microscopy

Introduction

Personal lubricants encompass a large number of friction-reducing substances that are used in several settings relevant to male fertility including sexual intercourse, sperm extraction, and vaginal ultrasonography. The prevalence of lubricant use with sexual intercourse remains understudied. Results from a US survey of women reported that 62 % of women had previously used lubrication with intercourse, while 25.3 % noted use within the past month [1]. Among women trying to conceive, 25 % self-reported routine use of vaginal lubricants on baseline questionnaires, while subsequent prospective observation obtained from self-maintained diaries identified actual use in 43 % of women [2].

Classes of Lubricants

Lubricants may be broadly classified as water soluble, oil soluble, or silicone based. See Table 4.1 for a listing of lubricants with data evaluating their effects on sperm

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parameters. Although variations exist within classes, water-soluble compounds are generally condom-safe and frequently include additive substances to retain moisture, balance osmolarity and/or pH, provide thickening or viscosity, alter sensation (e.g., warming, cooling), and give fragrance. Water-soluble agents are prone to rapid drying and may require reapplication or addition of moisture/saliva, which may result in deposition of additional substances or further concentrate the product applied. Oil-based lubricants frequently incorporate fewer additional substances and are often not compatible with condom use. Silicone-based lubricants are less commonly utilized and are less prone to skin absorption or dehydration. They are often incompatible with condoms and may adversely affect other silicone-containing compounds upon contact. No data is currently available reporting the impact of silicone-based lubricants on semen parameters or fertility.

Mechanism for Fertility Impairment

Lubricants have demonstrated varied effects on sperm including reduced viability, altered morphology, DNA damage, and impaired motility/progression [3–8]. Several mechanisms for lubricant-induced impairments have been proposed including increased viscosity, creation of a barrier effect, direct cytotoxicity, or indirect cellular damage via altered pH and osmolarity [3–5, 8].

Despite these hypothesized mechanisms, there are currently limited data reporting the etiologic role of osmolarity and/or pH on impairing sperm motility/progression. Rossato and colleagues evaluated and compared seminal osmolarity among normospermic and oligospermic males and noted that seminal plasma is slightly hyperosmolar (336 mOsm/L) compared to serum plasma (291 mOsm/L) [9]. Men with normospermia were found to have significantly lower seminal osmolarity values (318 mOsm/L vs. 345 mOsm/L) compared to asthenospermic patients. The authors additionally noted dose-dependent impairments in motility with increasing levels of osmolarity, with 50 % reductions noted in solutions >400 mOsm/L.

To assess the impact of varied osmolarity lubricants on semen parameters, Kutteh and colleagues performed an in vitro comparison of four water-based lubricants (KY Jelly®, Astroglide®, Replens®, Touch®), canola oil, and olive oil on normospermic samples [5]. Results demonstrated significant reductions in sperm motility with higher osmolarity agents (Astroglide®, KY Jelly®, Replens®, Touch®) compared to relatively iso-osmolar agents. These findings are consistent with other studies which demonstrated a minimal impact on motility with Pre-Seed® (iso-osmolar), compared to various hyper-osmolar agents [3, 4].

However, other studies have reported contradictory results, suggesting a less significant role for osmolarity on sperm motility. In the previously cited study by Kutteh and colleagues, despite relatively equivalent osmolality and pH levels for canola and olive oils (canola 378 mOsm, 7.6 pH; olive 390 mOsm, 7.4 pH), greater impairments were noted with the olive oil (42 % vs. 70 % motility) [5]. Similarly, in

Table 4.1 Lubricants with published data evaluating impact on semen parameters or fertility

Water-based lubricants
Aquasonic Gel® (Parker Laboratories, Inc., Fairfield, NJ)
Astroglide® (Biofilm Management, Inc., Vista, CA)
Femglide® (Wallace O'Farrell, Inc., Puyallup, WA)
Glycerin
H-R Lubricating Jelly® (HR Pharmaceuticals, Inc., York, PA)
Keri Lotion® (Novartis Pharmaceuticals, Basel, Switzerland)
K-Y Jelly® (Johnson & Johnson, New Brunswick, NJ)
Lubifax® (E. Fougera & Co, Melville, NY)
Ortho-Gynol® (Personal Products Co, Skillman, NJ)
Pre-Seed® (INGfertility, Valleyford, WA)
Replens® (Vifor SA, Villars-sur-Glane, Switzerland)
Saliva
Surgilube® (E. Fougera & Co, Melville, NY)
Oil-based lubricants
Alpha-Keri® (Mentholatum Co Ltd, Melbourne, Australia)
Baby oil (Mineral oil; Johnson & Johnson, New Brunswick, NJ)
Canola oil
Olive oil
Peanut oil
Petroleum jelly
Safflower oil
Vegetable oil
Other/unknown
Egg white
pHisonex®
Searle Skin Lotion®

comparing baby oil (hyperosmolar), KY Jelly® (hyperosmolar), olive oil (iso-osmolar), and saliva (hypo-osmolar), baby oil had the least impact on sperm motility, while saliva had the greatest effect, opposite of what would be expected based on osmolarity alone [7]. These findings question the significance of osmolarity and suggest that alternative factors are likely responsible for a portion of sperm impairment observed with lubricants.

The role of lubricant pH on semen impairment is also currently understudied. The optimal pH for sperm transport through the female genital tract is reported at 7.0–8.5, with cervical pH increasing to similar ranges during ovulation [10, 11]. However, this is of unclear clinical significance given that the majority of lubricants are within the 7.0 pH range and that the native vaginal pH is <4.5–5.5.

Lubricants

Impact on Semen Parameters

Several studies have evaluated the impact of various lubricants on semen parameters in vitro. See Table 4.2 for the effect of common lubricants on semen parameters and/or fertility. Given the large number of lubricants currently available, the current review will only focus on agents with published data available, with additional information provided on more commonly utilized agents. Although the majority of lubricants discussed are used with sexual intercourse or for extraction of semen samples via masturbation, additional substances used during surgery, ultrasonography, and/or intrauterine insemination will also be discussed due to their relevance in routine fertility practice.

Water-Based/Soluble Lubricants

Aquasonic Gel®

Aquasonic Gel® is a high-viscosity coupling gel commonly utilized in ultrasonography applications, including transvaginal imaging. In the only in vitro study evaluating its effect on sperm, Vargas and colleagues combined 0.1, 1, 5, and 10 % Aquasonic Gel® with normospermic samples from three to five donors diluted to achieve a total sperm concentration of 10–20 million/mL [3]. Following an incubation period of 1 or 24 h, sperm motility and osmolality were assessed and compared to controls. Results demonstrated an increase in total osmolality to 408 mOsm/kg in the 10 % group only, with the lower concentrations remaining under a predefined threshold of 400 mOsm/kg. In the 1 % group, total motility was unchanged at 1 h, and significantly reduced by 46 % at 24 h compared to controls. The authors concluded that despite its labeling as nonspermicidal, Aquasonic Gel® could result in significant impairments to sperm motility at concentrations as low as 1 %.

Astroglide®

Astroglide® is a water-soluble lubricant which contains water, glycerin, propylene glycol, polyquaternium 15, methylparaben, and propylparaben. Alternative versions of Astroglide® are available, including silicone based and formulations without glycerine or paraben; however, all currently published reports have evaluated the water-soluble, glycerin-containing version only.

Several studies have compared Astroglide® to various agents including KY Jelly®, Replens®, Touch®, FemGlide®, Pre-Seed®, canola oil, and olive oil

Table 4.2 Summary of data on the effect of vaginal lubricants on semen parameters and fertility

Agent/date (Author)	Population (n=)	Study design	Outcome measure	Duration of exposure	Result	Notes
Aquasonic Gel®						
2011 (Vargas)	Norm	In vitro; comparison of 0.1 %, 1 %, 5 %, 10 % Aquasonic Gel®, Felis®, Pre-Seed®, Replens® to controls	SA via CASA	1, 24 h	1 h—mot unchanged 24 h—↓ mot 46 %	Used predominantly with U/S
Astroglide®						
2012 (Steiner)	15 Tx 221 Cont Women aged 30–44 No history of infertility	Prospective, observational; in vivo comparison of lubricant vs. non-lubricant users	Fec at 6 cycles of attempts	Natural intercourse	72.7 % Fec (lubricant users) 68 % Fec (non-lubricant users) $p = 0.87$	Lubricant users include multiple types of lubrication
2008 (Agarwal)	13 Norm	In vitro; comparison of 10 % Astroglide®, FemGlide®, Pre-Seed®, Replens®, KY Jelly®	SA via LM; DNA frag	30 min	↓ mot 99 %	Greatest impact on mot of four agents tested
1996 (Kutteh)	Norm	In vitro; compared 30 % Astroglide®, canola oil, KY Jelly®, olive oil, Replens®, and KY Touch® to pos and neg cont	SA via CASA; viability	1, 15, 30, 60 min	No mot, non-viable at 60 min	Astroglide® and Replens® with greatest impact on mot and viability

(continued)

Table 4.2 (continued)

Agent/date (Author)	Population (n=)	Study design	Outcome measure	Duration of exposure	Result	Notes
1992 (Frishman)	10 Norm	In vitro; comparison of Astroglide® and KY Jelly® at 100, 50, 25, and 12.5 %	SA via LM	1, 15, 30 min	Dose dependent decrease in progressive motility	No sig difference between Astroglide® and KY Jelly® except with KY Jelly® at 12.5 %
Baby oil						
1998 (Anderson)	16 Norm semen samples[a]	In vitro; compared baby oil, olive oil, KY Jelly®, saliva to control at 12.5 and 6.25 %	SA characteristics; LM	5, 15, 30 min	No sig effect on mot, vel, head mov at 12.5 or 6.25 % conc	Least impact of four agents tested
Canola oil						
1996 (Kutteh)	Norm	In vitro; compared 30 % Astroglide®, canola oil, KY Jelly®, olive oil, Replens®, and KY Touch® to pos and neg cont	SA via CASA; viability	1, 15, 30, 60 min	No sig effect on mot, viability	Least impact of agents tested
FemGlide®						
2008 (Agarwal)	13 Norm	In vitro; comparison of 10 % Astroglide®, FemGlide®, Pre-Seed®, Replens®, KY Jelly®	SA via LM; DNA frag	30 min	↓ mot 23 %, ↑ DNA frag 14 %	

Felis®						
2011 (Vargas)	Norm	In vitro; comparison of 0.1 %, 1 %, 5 %, 10 % Aquasonic Gel®, Felis®, Pre-Seed®, Replens® to controls	SA via CASA	1, 24 h	1 h—mot unchanged 24 h—↓ mot 48 %	
KY Jelly®/Touch®						
2012 (Steiner)	33 Tx 221 Cont	Prospective, observational; in vivo comparison of lubricant vs. non-lubricant users	Fec at 6 cycles of attempts	Natural intercourse	72.7 % Fec (lubricant users) 68 % Fec (non-lubricant users) $p = 0.87$	Lubricant users include multiple types of lubrication
2008 (Agarwal)	13 Norm	In vitro; comparison of 10 % Astroglide®, FemGlide®, Pre-Seed®, Replens®, KY Jelly®	SA via LM; DNA frag	30 min	↑ DNA frag 10 %	
1998 (Anderson)	16 Norm semen samples[a]	In vitro; compared baby oil, olive oil, KY Jelly®, saliva to control at 12.5 and 6.25 %	SA via LM	5, 15, 30 min	12.5 % Conc: ↓ mot 74 % at 30 min; ↓ vel 52 % at 30 min; ↓ head mov 37 % at 5 min 6.25 % Conc: no sig effect on mot, ↓ vel 27 % at 30 min, ↓ head mov 33 % at 5 min	More impact than baby oil; less impact than saliva

(continued)

Table 4.2 (continued)

Agent/date (Author)	Population (n=)	Study design	Outcome measure	Duration of exposure	Result	Notes
1996 (Kutteh)	Norm	In vitro; compared 30 % Astroglide®, canola oil, KY Jelly®, olive oil, Replens®, and Touch® to pos and neg cont	SA via CASA; viability	1, 15, 30, 60 min	KY Jelly® with no mot at 60 min KY Touch® with 10 % mot at 60 min KY Jelly® and Touch® with min impact on viability	
1992 (Frishman)	10 Norm	In vitro; comparison of Astroglide® and KY Jelly® at 100, 50, 25, and 12.5 %	SA via LM	1, 15, 30 min	Dose dependent decrease in progressive motility No sig impact on motility with KY Jelly® at 12.5 % No sig difference between 1, 15, and 30 min time points	No sig difference between Astroglide® and KY Jelly® except with KY Jelly® at 12.5 %
1975 (Goldenberg)	20	In vitro; compared Alpha-Keri®, glycerin, H-R Jelly®, Keri Lotion®, KY Jelly®, Lubifax®, olive oil, Ortho-Gynol®, peanut oil, petroleum jelly, pHisohex®, safflower oil, Searle Skin Lotion®, Surgilube®, vegetable oil	Motility using scale 0 to 4+ (0 = no mot; 4+ = cont mot)	15, 120 min	15 min: 0 mot 120 min: 0 mot	

1972 (Tagatz)	20 semen samples from 24 to 36 year old infertile couples	In vitro; compared 50 mg of KY Jelly® or Surgilube® to control	SA via LM	15, 30 min	No mot at 15 min with KY Jelly® or Surgilube® No viability at 15 min with KY Jelly® or Surgilube®	Compared norm to abnormal SA with similar impact on motility and viability
Olive oil						
1998 (Anderson)	16 Norm semen samples[a]	In vitro; compared baby oil, olive oil, KY Jelly®, saliva to control at 12.5 and 6.25 %	SA via LM	5, 15, 30 min	12.5 % Conc: ↓ mot 91 % at 30 min; ↓ vel 38 % at 30 min; ↓ head mov minimally 6.25 % Conc: mot, vel, head mov unchanged at 30 min	More impact than baby oil; less impact than saliva
1996 (Kutteh)	Norm	In vitro; compared 30 % Astroglide®, canola oil, KY Jelly®, olive oil, Replens®, and Touch® to pos and neg cont	SA via CASA; viability	1, 15, 30, 60 min	40 % mot at 60 min No impact on viability	Greater impact than canola oil. Lesser than KY Jelly® and Replens®
1975 (Goldenberg)	20	In vitro; compared Alpha-Keri®, glycerin, H-R Jelly®, Keri Lotion®, KY Jelly®, Lubifax®, olive oil, Ortho-Gynol®, peanut oil, petroleum jelly, pHisohex®, safflower oil, Searle Skin Lotion®, Surgilube®, vegetable oil	Motility using scale 0 to 4+ (0 = no mot; 4+ = cont mot)	15, 120 min	15 min: 2+ mot 120 min: 3+ mot	

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Table 4.2 (continued)

Agent/date (Author)	Population (n=)	Study design	Outcome measure	Duration of exposure	Result	Notes
Petroleum jelly						
1975 (Goldenberg)	20	In vitro; compared Alpha-Keri®, glycerin, H-R Jelly®, Keri Lotion®, KY Jelly®, Lubifax®, olive oil, Ortho-Gynol®, peanut oil, petroleum jelly, pHisohex®, safflower oil, Searle Skin Lotion®, Surgilube®, vegetable oil	Motility using scale 0 to 4+ (0 = no mot; 4+ = cont mot)	15, 120 min	15 min: 2 to 3+ mot 120 min: 3 to 4+ mot	Petroleum jelly and glycerin with least impact among agents tested
Pre-Seed®						
2013 (Agarwal)	22 Norm	Paired, randomized, crossover; obtained samples with or without use of Pre-Seed® lubricant	SA; viability, DNA frag	Used during masturbation	No sig effect on mot, viability, DNA frag	Unclear extent of SA contamination with Pre-Seed®
2012 (Steiner)	7 Tx 221 Cont	Prospective, observational; in vivo comparison of lubricant vs. non-lubricant users	Fec at 6 cycles of attempts	Natural intercourse	72.7 % Fec (lubricant users) 68 % Fec (non-lubricant users) $p = 0.87$	Lubricant users include multiple types of lubrication
2011 (Vargas)	Norm	In vitro; comparison of 0.1 %, 1 %, 5 %, 10 % Aquasonic Gel®, Felis®, Pre-Seed®, Replens® to controls	SA via CASA	1, 24 h	1, 24 h—mot unchanged	Least impact of agents tested

2008 (Agarwal)	13 Norm	In vitro; comparison of 10 % Astroglide®, FemGlide®, Pre-Seed®, Replens®, KY Jelly®	SA via LM; DNA frag	30 min	No sig effect on mot, DNA frag	Least impact of agents tested
Replens®						
2011 (Vargas)	Norm	In vitro; comparison of 0.1 %, 1 %, 5 %, 10 % Aquasonic Gel®, Felis®, Pre-Seed®, Replens® to controls	SA via CASA	1, 24 h	1 h—↓ mot 97 % 24 h—↓ mot 88 %	Greatest impact among agents tested
2008 (Agarwal)	13 Norm	In vitro; comparison of 10 % Astroglide®, FemGlide®, Pre-Seed®, Replens®, KY Jelly®	SA via LM; DNA frag	30 min	↓ mot 60 %	
1996 (Kutteh)	Norm	In vitro; compared 30 % Astroglide®, canola oil, KY Jelly®, olive oil, Replens®, and Touch® to pos and neg cont	SA via CASA; viability	1, 15, 30, 60 min	No mot, non-viable at 60 min	Astroglide® and Replens® with greatest impact on mot and viability
Saliva						
1998 (Anderson)	16 Norm semen samples[a]	In vitro; compared baby oil, olive oil, KY Jelly®, saliva to control at 12.5 and 6.25 %	SA via LM	5, 15, 30 min	12.5 % Conc: ↓ mot 95 % at 15 min; ↓ vel 100 % at 30 min; ↓ head mov 100 % at 15 min 6.25 % Conc: Sig ↓ mot, vel, head mov	Greater impact than baby oil, KY Jelly®, olive oil

(continued)

Table 4.2 (continued)

Agent/date (Author)	Population (n=)	Study design	Outcome measure	Duration of exposure	Result	Notes
1982 (Tulandi)	38 Norm	In vitro; 1, 2, 4, 10, 20 % saliva concentration	SA via LM	15, 30, 60, 120 min	Dose and time dependent ↓ mot and progression 20 % saliva at 30 min with 51 % mot vs. 69 % (control)	
Surgilube®						
1994 (Miller)	Norm semen samples, 7 females <40 year	RCT; 5-mL of Surgilube® per vagina at time of ovulation; tested at 5, 10, 20, 30 %	Post-coital test via LM at ovulation	0, 15, 30, 60, 120 min	Time and concentration dependent ↓ mot	
1972 (Tagatz)	20 Semen samples from 24 to 36 year old infertile couples	In vitro; compared 50 mg of KY Jelly® or Surgilube® to control	SA via LM	15, 30 min	No mot at 15 min with KY Jelly® or Surgilube® No viability at 15 min with KY Jelly® or Surgilube®	Compared norm to abnormal SA with similar impact on motility and viability

Others					
1984 (Tulandi)	15 Norm	In vitro; compared 16.7 % egg-white and 1, 2, 5, 10 % glycerin to control	SA via LM	15, 30, 60 min	Egg-white: at 60 min non-sig change in mot (62 % vs. 66 % control) and progression (51 % vs. 56 % control) Glycerin: at 30 min sig ↓ in mot and progression at 2 % and above (43 % mot vs. 72 % cont at 10 % conc)
1975 (Goldenberg)	20	In vitro; compared Alpha-Keri®, glycerin, H-R Jelly®, Keri Lotion®, KY Jelly®, Lubifax®, olive oil, Ortho-Gynol®, peanut oil, petroleum jelly, pHisohex®, safflower oil, Searle Skin Lotion®, Surgilube®, vegetable oil	Motility using scale 0 to 4+ (0 = no mot; 4+ = cont mot)	15, 120 min	H-R®: 1+, 0 Lubifax®: 0, 0 Surgilube®: 0, 0 Ortho-Gynol®: 0, 0 Alpha-Keri®: 0, 0 Keri Lotion®: 0 to 1+, 0 pHisonex®: 0, 0 Searle Skin Lotion®: 0 to 1+, 0 Vegetable oil: 3+, 2+ Safflower oil: 3+, 3+ Peanut oil: 3+, 3+ Glycerin: 3+, 3 to 4+

CASA computer-assisted semen analysis, *Conc* concentration, *Cont* controls, *Fec* fecundability, *Frag* fragmentation, *LM* light microscopy, *Mot* motility, *Mov* movement, *Neg* negative, *Norm* normospermic, *Pos* positive, *RCT* randomized controlled trial, *Retro* retrospective design, *SA* semen analysis, *Tx* treatment, *Vel* velocity

[a]Prepared by two-step discontinuous Percoll gradient centrifugation

[4–6]. All studies used an in vitro design with normospermic samples and lubricant concentrations ranging from 10 to 100 %. Samples were assessed following varied incubation periods (1, 15, 30, 60 min) using light microscopy (LM), computer-assisted sperm analyzer (CASA), and DNA fragmentation. Results demonstrated that among agents tested, Astroglide® had the greatest impact on fertility with dose-dependent decreases in motility achieving complete immotility at 30–60 min [4, 5]. Concentrations above 12.5 % resulted in similar impairments with KY Jelly®, Astroglide®, and Replens® [5, 6].

The mechanism for the significant impairment observed with Astroglide® has not been elucidated, with some suggesting that it may be due, in part, to the presence of glycerin [4]. Although an early report failed to identify decreases in motility with glycerin, several studies have subsequently noted significant reductions, with one author suggesting that the earlier findings were likely due to inadequate mixing of specimen [4, 5, 12, 13]. No studies to date have evaluated Astroglide® without glycerin to further isolate the individual impact of glycerin on observed findings.

In the only in vivo assessment of lubricants among couples attempting to conceive, Astroglide® accounted for 20 % of lubricants reported [2]. Although subset analyses were not performed on individual lubricants, overall results demonstrated no significant differences in fecundity among lubricant vs. non-lubricant users. Results from this study and its implications are discussed in greater detail in the "Overall Impact on Fertility" section.

FemGlide®

FemGlide® is a water-soluble lubricant containing water, polyethylene oxide, sodium carbomer, and methylparaben and is also manufactured under the trade name Slippery Stuff Gel®. One study using 13 normospermic samples compared the effect of 10 % FemGlide® on sperm motility and DNA fragmentation using 13 normospermic samples [4]. Following an incubation period of 30 min, motility was decreased by 23 %, and DNA fragmentation increased by 14 % compared to controls. In relation to other agents tested, FemGlide® had a lesser impact than Astroglide® and Replens® and greater impact than Pre-Seed® on overall motility (statistical assessments not performed between groups). DNA damage was similar between FemGlide® (14 %), KY Jelly® (10 %), and Pre-Seed® (7 %), although statistically significant increases in DNA damage were only noted with FemGlide® and KY Jelly® compared to controls.

Felis®

Felis® is a water-soluble lubricant with limited data available regarding its ingredients and properties. One in vitro, dose–response assessment of Felis® combined various concentrations (0.1, 1, 5, and 10 %) with normospermic samples

[3]. Concentrations of 5 % and 10 % resulted in significant increases in sample osmolality to 511 mOsm/kg and 734 mOsm/kg, respectively. At 10 %, no changes in motility were noted at 1 h, although a 48 % reduction occurred over the 24-h period of incubation. In comparing with other agents assessed, results were better than Replens® (88 % reduced), worse than Pre-Seed® (7 % reduced) and similar to Aquasonic Gel® (46 % reduced).

KY Jelly®/Touch®

KY brand lubricants are water-based products of various formulations, with published data evaluating the impact of KY Jelly® and Touch® on semen parameters. Ingredients vary based on formulation and product: KY Jelly® contains water, glycerin, hydroxyethylcellulose, chlorhexidine gluconate, gluconolactone, methylparaben, and sodium hydroxide; KY Touch® contains propylene glycol, PEG-8, hydroxypropylcellulose, and tocopherol. Alternative formulations are available without glycerin (KY Ultra®), although there are currently no data evaluating their impact on sperm or fertility parameters.

Several studies have assessed the effect of KY Jelly® and Touch® on sperm motility, morphology, viability, and DNA fragmentation [4–7, 13, 14]. Early studies by Tagatz and Goldenberg performed in vitro assessments of various compounds, including KY Jelly® and demonstrated no motility or viability of sperm on LM at 15 min [13, 14]. Frishman and colleagues subsequently evaluated varying concentrations of KY Jelly® and Astroglide® (12.5, 25, 50, 100 %) and reported a dose-dependent, time-independent reduction in motility [6]. At the 12.5 % concentration, a non-statistically significant decrease in motility was noted with KY Jelly® at 1 min, with no subsequent progressive decreases noted among agents over the remaining time points assessed (1, 15, 30 min). A further study by Anderson and colleagues compared KY Jelly® at 12.5 and 6.25 and reported no significant changes in motility with 6.25 %, while 12.5 % reduced motility by 74 % at 30 min [7]. Osmolarity at the 6.25 % concentration was noted to be 600 mOsm/L with the addition of sperm, reinforcing the idea that hyper-osmolarity alone does not result in reduced motility.

One study comparing 30 % KY Jelly® to KY Touch® demonstrated greater reductions in motility with KY Jelly® (100 % vs. 90 % at 60 min) [5]. Although these findings provide support for the possible detrimental effect of glycerin (present in KY Jelly® and absent in KY Touch®), given the varied ingredients between agents, direct comparisons are limited. KY Jelly® (10 % concentration) was also shown to increase DNA fragmentation by 10 % compared to controls, highlighting another potential mechanism for impaired sperm function [4].

In the previously discussed in vivo comparison of fecundity between lubricant users and nonusers, KY Jelly® accounted for 44 % of lubricants reported and represented the largest group [2]. Given the similar rates of conception identified between groups, this would suggest that despite contrasting in vitro data, use of KY Jelly® during attempted conception may not reduce successful fecundity.

Pre-Seed®

Pre-Seed® is a water-soluble, hydroxycellulose-based lubricant and currently represents the agent with the fewest detrimental effects on sperm parameters among tested, water-based substances. Ingredients include hydroxyethylcellulose, water, Pluronic (poloxamer), sodium chloride, arabinogalactan, sodium phosphate, potassium phosphate, carbomer, methylparaben, and sodium hydroxide.

Two recent studies compared Pre-Seed® to other compounds including Aquasonic Gel®, Astroglide®, Felis®, FemGlide®, Replens® and KY Jelly® at varied concentrations (0.1, 1, 5, 10 %) [3, 4]. Both studies demonstrated no significant reductions in sperm motility (incubation with 10 % Pre-Seed® for 30 min and 24 h) with a mild, non-statistically significant increase (7 %) in DNA fragmentation identified. Among the agents tested, Pre-Seed® was consistently noted to have the least impact on sperm parameters, with osmolality levels remaining below a pre-defined threshold of 400 mOsm/kg at all concentrations [3, 4].

Pre-Seed® was additionally evaluated for use during masturbation to produce sperm samples in a paired, randomized, crossover design study [8]. Samples were assessed for motility, viability, and DNA fragmentation, with results demonstrating no significant impairments compared to controls. Although the extent of semen contamination with any lubricant used during masturbation is unclear, these results provide support for the permissible use of Pre-Seed® during sample production.

In the in vivo trial comparing fecundity between lubricant users and nonusers, 9 % of the lubricant cohort endorsed using Pre-Seed®, representing the third most common lubricant reported [2]. As previously mentioned, no significant difference was noted in fecundity between groups, suggesting the acceptable use of lubricants among couples attempting to conceive.

Replens®

Replens® is a water-based lubricant which utilizes a polycarbophil polymer as an adhesive base to provide epithelial adherence. Ingredients include carbomer 934P, glycerin, hydrogenated palm oil glyceride, mineral oil, polycarbophil, water, methylparaben, sodium hydroxide, and sorbic acid. Compared to many of the previously discussed agents, Replens® has a significantly lower pH (2.8), although in vitro assessments with sperm at 5 % and 10 % concentrations resulted in increased pH levels of 6.6 and 5.5, respectively [3].

Three studies reported in vitro comparisons of Replens® to Aquasonic Gel®, Astroglide®, canola oil, Felis®, FemGlide®, KY Jelly®, KY Touch®, olive oil, and Pre-Seed® at concentrations of 0.1, 1, 5, 10, and 30 % [3–5]. Evaluation at varied time points (1, 15, 30, 60 min and 24 h) demonstrated consistent reductions in motility (60–100 %) and viability, with impairments identified at concentrations as low as 1 %. Among the agents tested, Replens® and Astroglide® were consistently

noted to have the greatest impact on sperm function, with one author suggesting that this may be due, in part, to the shared ingredient glycerin [4]. However, the extent of the impairment attributable to glycerin alone is unknown.

Saliva

Two studies have assessed the impact of saliva on sperm parameters [7, 15]. Tulandi and colleagues compared various salivary concentrations (1, 2, 10, and 20 %) at 15, 30, 60, and 120 min and noted time- and concentration-dependent impairments in motility (51 % motility vs. 69 % control with 20 % concentration at 30 min) [15]. A subsequent study by Anderson and colleagues reported even greater reductions in sperm motility (95 % at 15 min), curvilinear velocity (100 % at 30 min), and lateral head movements (100 % at 15 min) at lower concentrations (12.5 % vs. 20 %) than the Tulandi study [7]. Compared to baby oil, KY Jelly®, and olive oil, saliva resulted in the greatest impairment in sperm parameters, despite favorable osmolality levels (274 mOsm/kg with sperm added). The etiology for the variable results between studies is unclear and may reflect differences in salivary compositions among individuals.

Surgilube®

Surgilube® is a common, water-based lubricant used in multiple applications in clinical medicine and surgery including with urinary catheter placements. Although a full list of ingredients is not readily available, it consists predominantly of water-soluble gums (viscous substances isolated from plant exudates) and chlorhexidine gluconate.

Two studies evaluated the effect of Surgilube® on sperm motility and viability [14, 16]. Tagatz and colleagues performed an in vitro assessment of Surgilube® and KY Jelly® compared to controls in 20 samples obtained from young infertile couples [14]. Sperm motility and viability assessed at 15 and 30 min demonstrated no motility or viability of sperm with either Surgilube® or KY Jelly® at the 15-min time point. Subset analysis of normal vs. abnormal semen samples showed similar impairments between groups. This study is significant in that it is the only one to assess samples from infertile couples and suggests that lubricant-induced impairments are independent of baseline fertility status.

Miller and colleagues subsequently performed an in vivo, randomized controlled evaluation of the impact of various concentrations of Surgilube® (5 mL of 5, 10, 20, 30 %) administered per vagina on sperm obtained from post-coital cervical mucus [16]. Results demonstrated time- and concentration-dependent decreases in sperm motility, with approximately 50, 60, 70, and 90 % reductions in motility at the 5, 10, 20, and 30 % concentrations, respectively. Similar reductions were noted within each concentration at each subsequent time point assessed (15, 30, 60, 120 min). As with the Aquasonic Gel®, these findings are relevant to clinical

practice, given that Surgilube® is commonly used during clinical vaginal examinations and instrumentation.

Oil-Based/Soluble Lubricants

Baby Oil

Baby oil includes several varieties of lubricants which utilize mineral oil as a common ingredient. The only brand of baby oil with data evaluating its effect on sperm is produced by Johnson & Johnson (New Brunswick, NJ) and incorporates aloe vera, vitamin E, acetate, and additives for fragrance. In an in vitro comparison of baby oil, olive oil, KY Jelly®, and saliva at 6.25 and 12.5 % concentrations, baby oil had no significant effect on sperm motility, velocity, or head movement and was found to have the least impact among agents tested [7].

Plant Oils

Canola, olive, peanut, safflower, and vegetable oils are combination fatty acids obtained from various seeds and plants. In the earliest evaluation of the effect of various oils on sperm motility, Goldenberg and colleagues reported subjectively assessed sperm motilities (scale: 0 = no motility to 4+ = similar to controls) of olive, peanut, safflower, and vegetable oils [13]. At 15 and 120 min time points, reported motilities were similar among all oils tested: olive (15 min = 2+, 120 min = 3+); peanut (3+, 3+); safflower (3+, 3+); vegetable (3+, 2+). These results were superior to all water-based products assessed and slightly inferior to glycerin and petroleum jelly, although it is unclear if sufficient mixing was achieved with the non water-soluble agents.

Two additional in vitro trials were performed to evaluate the effect of olive and canola oils on sperm motility [5, 7]. Using a 30 % concentration of olive and canola oils, Kutteh and colleagues reported no significant impairments in sperm viability, with motility either unchanged (canola oil) or decreased by 40 % (olive oil) [5]. The authors concluded that canola oil had the least impact of the agents tested (Astroglide®, canola oil, KY Jelly®, olive oil, Replens®, Touch®). Anderson and colleagues similarly compared olive oil to baby oil, KY Jelly®, and saliva at 12.5 and 6.25 % concentrations [7]. Although motility, velocity, and head movements were all significantly reduced with olive oil at the 12.5 % concentration, no significant impairments were identified at 6.25 %. The authors noted that compared to the other agents, olive oil had a greater impact than baby oil and lesser impact than saliva at all concentrations.

Petroleum Jelly

Petroleum jelly is a semisolid mixture of hydrocarbons, with the most recognized brand being Vaseline® (Unilever N.V., Rotterdam, Netherlands). Very limited data is available on its effect on sperm parameters, with the only published study reported by Goldenberg and colleagues [13]. In their evaluation of multiple commercially available lubricants, the authors reported preserved motility of sperm at the 15 min (2 to 3+; scale 0 to 4+) and 120 min (3 to 4+) time points. Compared to all other agents, petroleum jelly and glycerin were noted to have the least impact on sperm motility. However, as glycerin has subsequently been shown to consistently impair sperm, some authors have questioned whether the Goldenberg study performed adequate mixing of samples, thus potentially underestimating the effect of glycerin (and by inference petroleum jelly) on sperm motility [4].

Other Lubricants

Egg white

Hen egg white has been reported as a potential lubricant for sexual intercourse with limited impact on fertility [17]. Although the origins for egg white as a lubricant are unclear, one of the earliest reports highlighted its use as a viable analog for cervical mucus in sperm penetration assays [18]. Subsequent introduction of hyaluronate resulted in the replacement of egg white due to improved passage of sperm, better linearity, and less lateral head displacement [19, 20].

In the only in vitro study evaluating the impact of egg white on sperm motility, Tulandi and colleagues noted no significant reductions in motility (62 % vs. 66 % controls) or progression (51 % vs. 56 % control) following 60 min of incubation [12].

Overall Impact on Fertility

Currently, there is very limited data on the in vivo impact of available lubricants on fertility. The only trial to assess fecundability as an end-point prospectively observed 296 females, aged 30–44 who were attempting to conceive for less than 3 months [2]. All participants completed a baseline questionnaire followed by a diary to record intercourse frequency and use of lubricants, among other factors. Prior to study initiation, 25 % of women reported use of vaginal lubricants while attempting to conceive, with 43 % subsequently utilizing lubrication during the 6-month study interval. Among users, the frequency of use varied, with 44, 31, and 24 % noting occasional, frequent, and every time use, respectively. Reported

lubricants were Astroglide® (20 %), KY Jelly® (44 %), and Pre-Seed® (9 %), with the remainder not listed. After adjusting for age, partner race, and intercourse frequency during the fertile window, no differences were noted in fecundability in regards to women reporting use of lubricants overall (OR 1.23; CI 0.76–2.00) or during the fertile period (OR 1.05; CI 0.59–1.85).

As the only in vivo study evaluating the impact of lubricants on actual fecundability, this study highlights limitations inherent with in vitro assessments of the impact of lubricants on semen characteristics. Although several studies demonstrated the significant impacts of Astroglide® and KY Jelly® on reducing sperm motility and viability, these agents accounted for 64 % of lubricants reported during the 6-month in vivo study interval, suggesting that in actual use, their impact on fertility is negligible [2, 4–7, 13, 14].

Several possible factors may account for the discrepancy between in vitro and in vivo results. In vitro assessments consistently note concentration and time dependent effects of the various agents on sperm characteristics, with initial impairments evident as early as 5–15 min and significantly reduced motility at 60 min following exposure [5–7, 15]. As the majority of the lubricant is likely attenuated by vaginal secretions and remains in the entroitus/distal vagina, the actual concentration of lubricant reaching the cervical mucus and sperm is likely limited [2]. Similarly, given the rapid progression of sperm to the Fallopian tube (identified within 5 min of ejaculation), the duration of exposure to lubricant may be minimal [21]. In vitro assessments also poorly represent the in vivo vaginal milieu, in which factors such as pH and osmolarity would be rapidly reduced or negated. This likely overestimates the true impact of factors such as osmolarity and/or pH.

Study Limitations

Data on the effect of lubricants on fertility and sperm parameters is limited by the paucity of studies and significant heterogeneity of literature available. The far majority of studies are in vitro assessments using small numbers of normospermic samples, with unclear relevance of findings to couples with baseline impaired fertility. Comparisons between studies are also limited by varied study methodologies, including concentrations assessed, samples obtained, incubation periods, and methods of sperm evaluation. Similarly, as there is no consensus as to which sperm factors are most relevant to fertility, all in vitro evaluations are of unclear clinical utility. Given these limitations, further in vivo studies are required to determine the significance of in vitro observations.

Summary and Conclusions

Lubricants are commonly used by couples attempting to conceive and are important in clinical and operative settings. Available data on the effect of lubricants on sperm parameters and fertility are limited, with the majority of studies performing assessments on in vitro sperm samples. Results of in vitro studies consistently demonstrate effects on sperm motility and viability in a time- and concentration-dependent manner. Although data are unable to be compared between studies, individual results suggest that baby oil (mineral oil), canola oil, egg white, and Pre-Seed® do not result in significant reductions in sperm motility or other measured parameters. In contrast, Astroglide®, KY Jelly®/Touch®, Replens®, saliva, and Surgilube® all significantly impair sperm motility and/or other factors. In general, plant oils have minimal effects, with olive oil demonstrating slightly worse outcomes compared to canola oil. Limited data on Aquasonic Gel®, FemGlide®, and Felis® identify impaired motility at selected time points, while insufficient data is available to draw conclusions on the impact of petroleum jelly.

In vivo data is limited, with one study reporting no significant difference in the rate of fecundity between lubricant users and nonusers among couples attempting to conceive. The results are particularly relevant given that the majority of lubricants reported within the study have been shown in in vitro trials to significantly impair sperm. These data highlight the disparity between in vitro and in vivo assessments and underscore the need for additional in vivo studies to identify the true clinical impact of lubricant use in true-to-life settings.

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