Randomised Controlled Trial

ANNALS OF MEDICINE & SURGERY

OPEN

Assessing the impact of lubricant on liquid-based Pap smear test outcomes: a randomized clinical trial

Mansooreh Yaraghi, MD[a], Sarvenaz Gharavi, MD[b], Ayda Najafian, MD[a], Vajihe Hazari, MD[c,*]

Background: Since today cervical cancers are growing, there is an increasing need to use screening and examination methods. Meanwhile, liquid-based Pap smear test is a common screening method for women, which is widely applied today. Studies have found that use of lubricant gel in this test can affect the pathology and cytology results. Accordingly, the authors intended to evaluate the effect of use of lubricant gel on the Pap smear test results.

Methods: This study was of single-blind clinical trial, the study population consisted of candidate patients for screening in terms of cervical pathology, for whom liquid-based Pap smear was done. In this study, 506 patients participated, divided into two groups of 253. One group used lubricant gel during the Pap smear, while the other group underwent this test without lubricant. The data were analyzed by SPSS 21.

Results: The study results indicated that once the two groups were compared in terms of age, interval of menstruation time and intercourse time from the sampling, no significant relationship was found between the two groups ($P > 0.05$). It was also found that use of lubricant did not affect the cytology and pathology results of patients ($P > 0.05$).

Conclusion: The use of lubricant gel in patients can reduce pain in patients during examination and testing, but does not affect the cytological and pathological results of patients.

Keywords: Cervical cancers, liquid-based Pap, lubricant gel, menstruation, Pap smear

Introduction

The Pap smear, a key cervical cancer screening tool, is performed in a physician's office to detect precancerous or cancerous cells in the cervix. Despite potential mild discomfort, its benefits in early detection outweigh temporary discomfort. This test also aids in identifying changes that may lead to cervical cancer. In women aged 30 and above, combining the Pap smear with an human papillomavirus test enhances diagnostic evaluation for cervical cancer prevention[1,2].

In 1996, the FDA approved ThinPrep as the first liquid-based Pap test, marking a significant advancement in cervical cancer screening. Studies have consistently shown improved diagnostic accuracy for cervical dysplasia with liquid-based Pap smears compared to traditional methods[3,4]. These innovations underscore a commitment to enhancing the precision of cervical cancer screening and improving patient outcomes.

HIGHLIGHTS

- Since today cervical cancers are growing, there is an increasing need to use screening and examination methods.
- Meanwhile, liquid-based Pap smear test is a common screening method for women, which is widely applied today.
- -Studies have found that use of lubricant gel in this test can affect the pathology and cytology results.
- The use of lubricant gel in patients can reduce pain in patients during examination and testing,

In contrast to conventional methods, where specimens were directly transferred onto slides, the ThinPrep liquid-based Pap test employs semi-permeable membranes for collecting cell specimens. This innovative approach effectively filters out contaminants and debris, resulting in a single cellular layer devoid of extraneous materials or contamination. This streamlined composition significantly facilitates the interpretation of cellular changes, enhancing the accuracy of histological analysis. Notably, the presence of additional and ambiguous elements such as blood, inflammatory cells, lubricants, and other factors can compromise the histological adequacy of liquid-based Pap smears, representing a notable drawback of filter-based methods[5].Given these considerations, it is recommended to use warm water or, in essential cases, a minimal amount of lubricant on the external surface of the speculum[6]. However, it is crucial to highlight that the manufacturers of ThinPrep explicitly advise against the use of lubricants during the procedure[7]. This caution stems from the understanding that the presence of lubricants can introduce potential artifacts, affecting the quality of the specimen collected.

[a]Department of Obstetrics and Gynecology, School of Medicine, Shariati Hospital, [b]Department of Obstetrics and Gynecology, School of Medicine, Tehran University of Medical Sciences, Tehran and [c]Department of Gynecology, School of Medicine, Birjand University of Medical Sciences, Birjand, Iran

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

*Corresponding author. Address: Assistant Professor of Infertility and Ivf, Birjand University of Medical Sciences, Birjand, Iran. Tel.: +98 563 244 30419; fax: +98 563 244 0488. E-mail: dr.vhazari@gmail.com (V. Hazari).

Annals of Medicine & Surgery (2024) 86:2702–2707

Received 30 December 2023; Accepted 29 January 2024

Published online 28 February 2024

http://dx.doi.org/10.1097/MS9.0000000000001803

While the use of lubricant gel has been shown to alleviate patient discomfort during Pap smear tests[8], it is essential to recognize that such examinations can pose challenges and discomfort for patients. The insertion of the speculum into the vagina may induce pain and discomfort due to its protuberance and diameter. To address this, the use of a lubricant gel during Pap smear tests is recommended to facilitate pain-free and gentle speculum insertion. Nevertheless, previous studies have indicated that the use of lubricant gel can influence the test results by affecting the cells within the vagina, leading to potential inaccuracies in the obtained results. Thus, a judicious approach to the use of lubricants in Pap smear testing is warranted, balancing patient comfort with the imperative of obtaining accurate and reliable diagnostic information[9,10].

Based on the above points, the studies conducted in this regard have achieved contradictory results[10]. The present study will test the hypotheses of whether use of lubricant would change the adequacy of cervical sampling in ThinPrep liquid-based Pap test or not. In case of adequacy of tissue collected through liquid-based Pap test as well as increase of reliability of the relevant cytology results through use of lubricant, this method will be of note in performing all candidate cases for Pap smear.

Materials and methods

In this randomized clinical trial, the study population consisted of candidate patients regarding screening cervical pathology at Shariati Hospital from Tehran, Iran (2019–2020), for whom Pap smear was done with a liquid-based Pap method. Based on the results of Lin *et al.*[11], around 506 patients could participate. The patients who did not have personal consent or satisfaction with use of Pap smear, the patients with any structural or functional disorder in the vaginal, cervical, or endometrial region for whom Pap smear was not feasible in any form, were excluded from the study. The patient's disease had been diagnosed and confirmed based on laboratory results as well as clinical symptoms. The candidate patients for Pap smear test via liquid-based Pap method were randomly assigned into two groups through a random numbers table.

In the first group, during the liquid-based Pap test, lubricant was used for the speculum(for vaginal exams), while in the second group, no use of lubricant was considered. Both groups were fully unaware of the protocol of use or nonuse of lubricant. After the test and taking specimens, they were sent to the cytology. The parameters compared between the two groups included (1) cytology results regarding benignity or malignancy of the specimen, and (2) the extent of adequacy of the sample tissue in the form of "existence of at least 5000 samples of observable and preservable squamous cells".

According to the results of the study by Lin and colleagues, the frequency of non-natural findings in cytology in samples with and without the use of lubricant was 0.331 and 0.45, respectively. Assuming a confidence level of 95% and a study power of 90%, the required sample size for each group would be 253 individuals, resulting in a total of 506 individuals.

$$n_1 = n_2 = \frac{(p_1(1-p_1) + p_2(1-p_2))\left(Z_{1-\frac{\alpha}{2}} + Z_{1-\beta}\right)^2}{(p_1 - p_2)^2}$$

$P1 = 0.331$, $P2 = 0.45$
$Z_{1-\alpha/2} = 1.96$, $Z_{1-\beta} = 1.29$
$N1 = N2 = 253$

Data analysis

Ultimately, the obtained results are expressed as mean and standard deviation for quantitative variables (mean ± SD), and as percentage for stratified qualitative variables. For comparing the quantitative variables, t test, and for comparing qualitative variables, χ^2 test would be used. The significance level was considered lower than 0.05. SPSS 23 was used for statistical analysis of the data.

This study was approved by the Research Ethics Board of (Tehran University of Medical Sciences).

This clinical trial was carried out in Iran at the centre of clinical trial registered with a special registration code: (Tehran University of Medical Sciences).

The work has been reported in line with the CONSORT criteria[12].

Results

In this study, 506 patients participated and were assigned into two groups in terms of use of lubricant. In one group of 253 subjects, lubricant gel was used for performing Pap smear test in the patients. In the other group in which 253 patients participated, Pap smear test was done without using lubricant gel. The mean age of patients was 40.8 ± 11.5 years. The maximum age was 75 years and the youngest was 19 years. The mean age in the group in which gel had been used was 40.7 ± 11.6, while in the other group, it was 40.8 ± 11.4, showing no significant difference ($P > 0.05$) (Fig. 1). In addition, the date of the last sexual intercourse in the two groups indicated that the mean last day of intercourse was 7.1 ± 14.2 in the group that had used the gel, while 8.7 ± 27.11 in the gel nonuse group. Nevertheless, it was observed that there was no significant difference between the two groups ($P > 0.05$) (Fig. 2). Furthermore, the last day of menstruation was also investigated in the patients. The results showed that the mean last day of menstruation was 7.06 ± 3.9 in the group that had used the gel, while being 7.9 ± 4.4 in the nonuse-of-gel group, showing no significant difference ($P > 0.05$) (Fig. 3). The results were satisfactory in all specimens taken from both groups and the pathology of both groups was normal (Table 1).

Discussion

The acceptable proposed protocol for screening cervical cancer according to the American Cancer Society in 2012 is performing Pap smear test once every 3 years in 21–65-year-old women. According to our national protocol, again all women above 20 years of age who have gotten married at least once should undergo Pap smear test[12]. Nevertheless, it is estimated that only 5% of women in developing countries participate in screening programs of Pap smear test, while this value is about 90% in the US[13]. Pap smear test is a simple cytology test for screening and diagnosing cervical cancer as well as its precancerous lesions. This method identifies 13 000 aggressive cancers and around 1 million precancerous lesions annually. By introducing Pap smear as a measure for screening cervical cancer, its prevalence has diminished by around 79% since 1950[14]. Also, implementation of screening programs in several countries for five years indicated that the Pap smear test can lower the mortality of cervical cancer by up to 60%[15]. Before creation and development of Pap smear, mortality resulting from cervical cancer in the US was reported

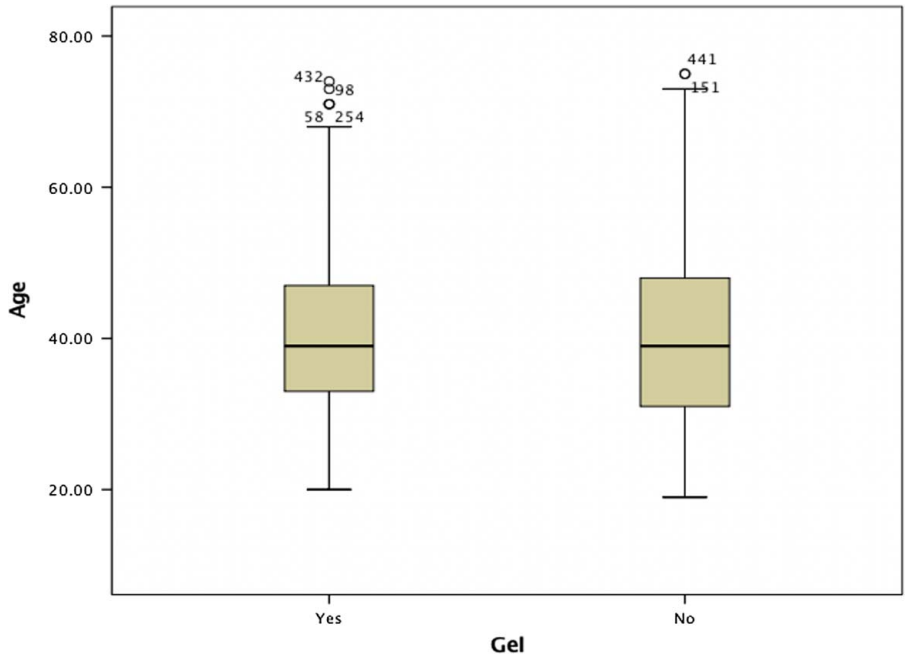

Figure 1. The average age within the cohort where gel application occurred.

25 per 1000, which was like the mortality rate resulting from this disease in some developing countries[16].

Studies conducted in Iran and other countries suggest that various cultural, emotional, and practical factors affect performing screening tests and their repetition at standard time intervals[17]. Thus, despite the availability of screening programs and the desirable effectiveness of tests, the extent of women's referral to healthcare centres for undergoing Pap smear test is not favourable[18,19]. Studies performed in different parts of the world (Nigeria, Saudi Arabia, and Kenya) have shown that despite women's awareness of Pap smear, only a limited number undergo this test[20,21]. Studies suggest

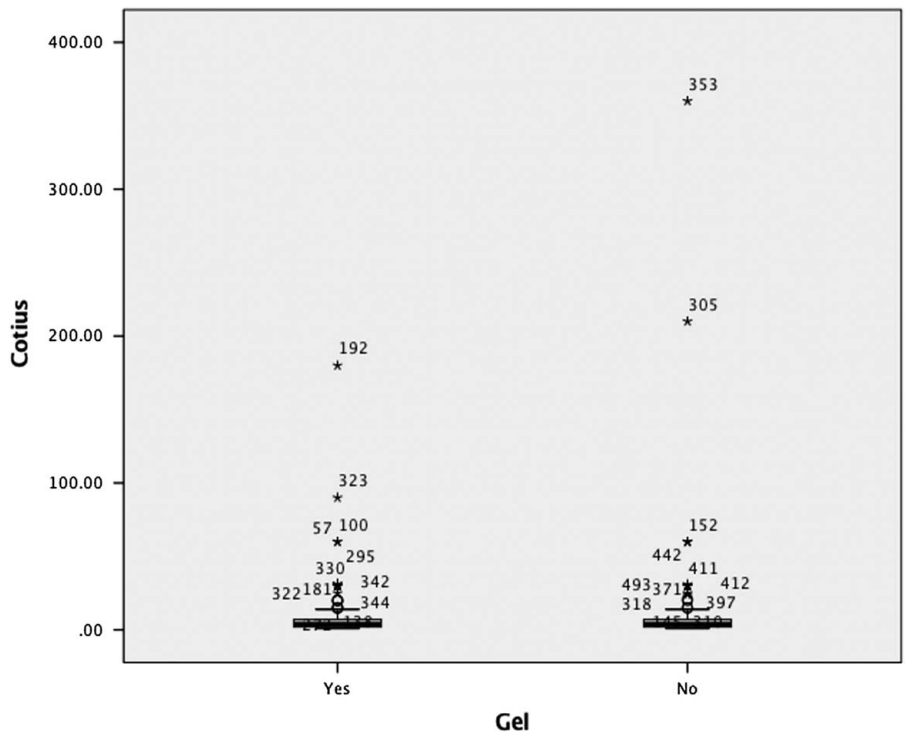

Figure 2. The average final day of sexual activity in the groups that utilized the gel and those that did not.

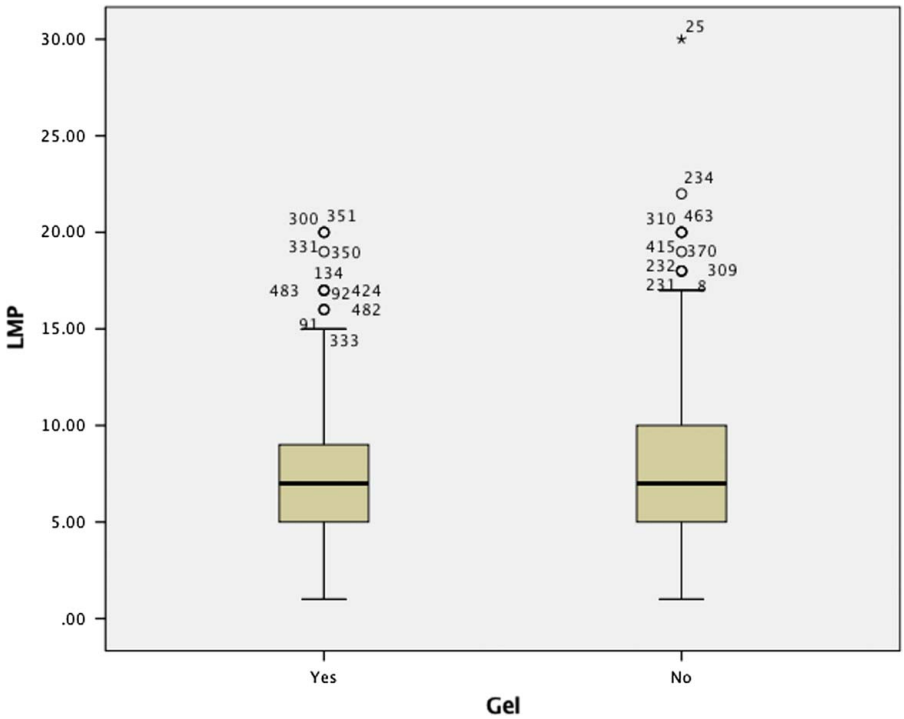

Figure 3. The average of the last day of menstruation in the groups that utilized the gel and those that did not.

that the reasons behind women's lack of referral for this test can include lack of awareness of the necessity of the test, lack of physician recommendation, stress, shame, pain during the test, the test cost, lack of access to its centers, inconvenience during the test, unethical behaviours of healthcare providers, lack of privacy, and the fear of the positivity of the test as well as the aggressiveness of the follow-up methods in case of the test positivity[22,23].

Accordingly, in this study, we evaluated the effect of lubricant gel on the results obtained from Pap smear test. In 2009, Michal and colleagues conducted a study to evaluate the effect of use of lubricant gel in patients undergoing Pap smear test. They found that use of lubricant gel in patients can lead to pain mitigation resulting from the speculum during the Pap smear test. In addition, it was found that use of gel had no impact on the results obtained from a pathology of patients[24]. In another study by Kittipat and colleagues on the effect of use of lubricant gel on the results obtained from cytology in patients undergoing Pap smear test, the data, and the results indicated that although the lubricant gel causes pain mitigation during the testing patients, it would affect the results of uterus cytology in the Pap smear test, causing false result interpretations[25]. In another study by Chen and colleagues, it was observed that use of lubricant gel in patients causes decreased discomfort and pain during examination. In addition, use of this method is far more convenient and causes improvement of pathological results in patients.

Considering that the use of lubricant gel has significantly reduced discomfort and pain in patients in all previous studies, but in some studies, it has been identified as a factor increasing the rate of unsatisfactory samples. The timing of the last sexual intercourse and the last menstrual period has been recognized in some studies as influential factors on this issue. In our study, we investigated the difference in these three parameters between the two groups. All samples in both groups were collected using cytobrush and the liquid-based method, with cytobrush rotations performed ten times. In our study, all samples in both groups were found to be satisfactory, and no significant differences were observed in the other two parameters between the two groups.

Conclusion

In this study, it was found that use of lubricant gel had no impact on the cytology and pathology results of patients undergoing Pap smear test. Thus, it can be stated that usage of lubricant gel

Table 1

Group characteristics

Characteristics	Total	Lubricant gel group	Non-lubricant gel group	*P*
Age	40.8 ± 11.5 (years)	40.7 ± 11.6 (years)	40.8 ± 11.4 (years)	> 0.05
Last sexual intercourse		7.1 ± 14.2 (days)	8.7 ± 27.11 (days)	> 0.05
Last day of menstruation		7.06 ± 3.9 (days)	7.9 ± 4.4 (days)	> 0.05
Pathological results		Normal	Normal	> 0.05

despite reducing the pain of patients has no effects on the cytology and pathology results. Thus, it is suggested to investigate this issue in further studies in patients who have cervical pathologies.

For further investigations, it is suggested to conduct this study on a larger sample size. Also, these parameters should be examined in patients with underlying conditions as well.

Ethical approval

No animals were used in this research. All human research procedures followed were in accordance with the ethical standards of the committee responsible for human experimentation Tehran University of Medical Sciences (IR.TUMS.MEDICINE.REC.1399.1308), and with the Helsinki Declaration of 1975, as revised in 2013. This study was approved by the Research Ethics Board of Islamic Azad University.

Consent

Informed consent was obtained from the patient and patient's parents/legal guardian for publication and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Sources of funding

None.

Author contribution

M.Y.: conceptualized and designed the study, drafted the initial manuscript, and reviewed and revised the manuscript. A.N. and V.H.: designed the data collection instruments, collected data, carried out the initial analyses, and reviewed and revised the manuscript. S.G.: coordinated and supervised data collection, and critically reviewed the manuscript for important intellectual content.

Conflicts of interest disclosure

The authors deny any conflicts of interest in any terms or by any means during the study.

Research registration unique identifying number (UIN)

This clinical trial was carried out in Iran at the centre of clinical trial registered with a special registration code: IRCT20160615028486N2.

Guarantor

Mansooreh Yaraghi.

Availability of data and materials

All relevant data and materials are provided within manuscript.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Human and animal rights

No animals were used in this research. All human research procedures followed were in accordance with the ethical standards of the committee responsible for human experimentation (institutional and national), and with the Helsinki Declaration of 1975, as revised in 2013.

References

[1] McFarland DM. Cervical cancer and Pap smear screening in Botswana: knowledge and perceptions. Int Nurs Rev 2003;50:167–75.
[2] Hyacinth HI, Adekeye OA, Ibeh JN, *et al*. Cervical cancer and pap smear awareness and utilization of pap smear test among Federal civil servants in North Central Nigeria. PLoS One 2012;7:e46583.
[3] Sachan PL, Singh M, Patel ML, *et al*. A study on cervical cancer screening using pap smear test and clinical correlation. Asia Pac J Oncol Nurs 2018;5:337.
[4] Jalilian F, Emdadi S. Factors related to regular undergoing Pap-smear test: application of theory of planned behavior. JRHS 2011;11:103–8.
[5] Obwegeser JH, Brack S. Does liquid-based technology really improve detection of cervical neoplasia? A prospective, randomized trial comparing the ThinPrep Pap Test with the conventional Pap Test, including follow-up of HSIL cases. Acta Cytol 2001;45:709–14.
[6] Alameda F, Fusté P, Albert S, *et al*. Citología en medio líquido (Thin Prep Pap Test). Un año de experiencia. Prog Obstet Ginecol 2007;50:197–202.
[7] Nam J-H, Kim H-S, Lee J-S, *et al*. A comparison of modified MonoPrep2™ of liquid-based cytology with ThinPrep® Pap test. Gynecol Oncol 2004;94:693–8.
[8] Fan Y-B, Wang Q-S, Ye L, *et al*. Clinical application of the SurePath liquid-based Pap test in cytological screening of bronchial brushing for the diagnosis of lung cancer. Cytotechnology 2010;62:53–9.
[9] Tuncer Z, Başaran M, Sezgin Y, *et al*. Clinical results of a split sample liquid-based cytology (ThinPrep) study of 4,322 patients in a Turkish institution. Eur J Gynaecol Oncol 2005;26:646–8.
[10] Goodman A. HPV testing as a screen for cervical cancer. BMJ 2015;350:h2372.
[11] Lin SN, Taylor J, Alperstein S, *et al*. Does speculum lubricant affect liquid-based Papanicolaou test adequacy? Cancer Cytopathol 2014;122:221–6.
[12] Moher D, Hopewell S, Schulz KF, *et al*. CONSORT 2010 Explanation and Elaboration: updated guidelines for reporting parallel group randomised trials (Chinese version). J Chinese Integr Med 2010;8:701–41.
[13] Kunckler M, Schumacher F, Kenfack B, *et al*. Cervical cancer screening in a low-resource setting: a pilot study on an HPV-based screen-and-treat approach. Cancer Med 2017;6:1752–61.
[14] Wright TC Jr, Denny L, Kuhn L, *et al*. HPV DNA testing of self-collected vaginal samples compared with cytologic screening to detect cervical cancer. JAMA 2000;283:81–6.
[15] Denny L. Cervical cancer: prevention and treatment. Discov Med 2012;14:125–31.
[16] Almobarak AO, Elbadawi AA, Elmadhoun WM, *et al*. Knowledge, attitudes and practices of sudanese women regarding the Pap smear test and cervical cancer. Asian Pac J Cancer Prev 2016;17:625–30.
[17] Dhaher EA. Knowledge, attitudes and practices of women in the southern region of Saudi Arabia regarding cervical cancer and the Pap smear test. Asian Pac J Cancer Prevent 2019;20:1177.
[18] Ilter E, Celik A, Haliloglu B, *et al*. Women's knowledge of Pap smear test and human papillomavirus: acceptance of HPV vaccination to themselves and their daughters in an Islamic society. Int J Gynecol Cancer 2010;20:1058–62.
[19] Gyllensten U, Gustavsson I, Lindell M, *et al*. Primary high-risk HPV screening for cervical cancer in post-menopausal women. Gynecol Oncol 2012;125:343–5.
[20] Luyten A, Buttmann-Schweiger N, Luyten K, *et al*. Early detection of CIN3 and cervical cancer during long-term follow-up using HPV/Pap

smear co-testing and risk-adapted follow-up in a locally organised screening programme. Int J Cancer 2014;135:1408–16.
[21] Syrjänen S, Shabalova IP, Petrovichev N, *et al*. Human papillomavirus testing and conventional pap smear cytology as optional screening tools of women at different risks for cervical cancer in the countries of the former soviet union. J Low Genit Tract Dis 2002;6:97–110.
[22] Nieminen P, Vuorma S, Viikki M, *et al*. Comparison of HPV test versus conventional and automation-assisted Pap screening as potential screening tools for preventing cervical cancer. BJOG Int J Obstet Gynaecol 2004;111:842–8.
[23] Nuovo J, Melnikow J, Howell L. New tests for cervical cancer screening. Am Fam Physician 2001;64:780.
[24] Pawlik M, Martin FJ. Does a water-based lubricant affect Pap smear and cervical microbiology results? Can Fam Physician 2009;55:376–7.
[25] Charoenkwan K, Nimmanahaeminda K, Khunamornpong S, *et al*. Effects of gel lubricant on cervical cytology. Acta Cytol 2008;52:654–8.