



Comparative study on the adequacy of cervical smears using wooden Ayre's spatula, VS Papcone® sampling device

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ABSTRACT

This is a comparative study on the adequacy of cervical smears obtained using the Papcone® sampling device or wooden Ayre's spatula conducted from two tertiary health facilities — Nnamdi Azikiwe University Teaching Hospital Nnewi and Chukwuemeka Odumegwu Ojukwu University Teaching Hospital Awka, in Anambra State, Nigeria. Slides from smears obtained using both devices were read by a cytopathologist blinded for the study. The primary outcome was the proportion of smears with an adequate endocervical component. Significantly higher adequate cervical smears were obtained in 177/192 (92.2%) women using the Papcone® sampling device, compared to 152/192 (79.2%) using wooden Ayre's spatula ($p < 0.001$). Kappa analysis showed moderate inter-rater agreement between the two devices. We recommend the use of the Papcone device when it is available, as the adequacy of cervical smears obtained with the Papcone® was better than that obtained using wooden Ayre's spatula.

1. Introduction

The Papanicolaou (Pap) smear test remains an important tool in the prevention of invasive cervical cancer, (Adinma, 2018) but inadequate specimens, which are usually due to a lack of an endocervical component, can limit its utility. (Martin et al., 2012) A smear is adjudged adequate when the cell samples from endocervix, transformation zone and ectocervix are represented. (Martin et al., 2012) If the endocervical cells are absent, the cytopathologist is obliged to request a repeat specimen. This in turn brings dissatisfaction to women and their providers and inflate the cost of health services. (Martin et al., 2017; Marchand et al., 2005) Inadequate smears could arise from poor sampling technique or the use of ineffective sampling devices. (Martin et al., 2017; Soleimani et al., 2012; Marchand et al., 2005; George et al., 2004) The Cochrane systematic review of collecting devices for obtaining cervical cytology samples, made it clear that the use of an effective

device to obtain cervical smear enhances the adequacy of smears (Martin et al., 2017).

Over the years, the strengths and weaknesses of many sampling devices employed in the collection of Pap smears, have been reviewed. (Martin et al., 2017) This explains why modification of pre-existing cervical sampling devices and the invention of newer ones have been geared towards improving the smear adequacy. (George et al., 2004) The traditional wooden Ayre's spatula has long been in existence and samples endocervix and ectocervix at the same time. The cytobrush is structured to obtain predominantly endocervical cells, hence a spatula must be used in conjunction with it to guarantee the collection of ectocervical cells. (O'Mahony et al., 2006; Shorey et al., 2011; Vatana-sapt, 2002)

Recently the PapCone® sampling device has been introduced, as a product of Otto Bock company, Duderstadt, Germany; was approved by the Food and Drug Agency of the United States of America in 2009 and

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structured to obtain cells simultaneously from the ectocervix and the endocervix. (Sander et al., 2007; Lukic et al., 2013; Petruzzello et al., 2011) It is a cone-shaped, polyurethane (foam) sampling device, originally designed by the University Hospital Gottingen Germany and consists of a long, cylindrical, plastic grip and a round platform at one end with a compressible foam cone, which is adapted to fit two-thirds of its proximal part into the external cervical os. (Sander et al., 2007) As a soft, compressible device it is less traumatic and able to sample both the ecto- and endocervix with one sampling. (Sander et al., 2007)

In consideration of the enormous burden of cervical cancer, the underutilization of Pap smear test in developing countries, the inconvenience due to inadequacy of cervical smears especially to the women, the cost implications of repeating cervical cytology test, and the dearth of histopathologists in many centres in developing countries, every opportunity secured to screen a woman is considered to be golden and should be maximized. An effective device should therefore be employed, to guarantee the adequacy of smears and reduce smear rejection.

The wooden Ayre's spatula is readily available, inexpensive and commonly used in low and middle income countries for sampling the cervix. However, it may be associated with the provision of inadequate smears which may necessitate repeat collection. (Soleimani et al., 2012; Rabiou et al., 2019) If the reduction of inadequate smears (associated with ineffective sampling device) must be pursued; then there is an overwhelming need to reappraise the sampling device options commonly used in our environment. In general, cervical sampling devices have been sparsely studied in our centres. The PapCone® sampling device is relatively new in many settings in low and middle income countries and has features more likely to provide a better sampling yield in cervical cytological studies. The hypothesis to this study therefore is that the adequacy of cervical smear obtained using PapCone® is better than that obtained using wooden Ayre's spatula. This study has been conducted to compare the adequacy of pap smears obtained using wooden Ayre's spatula and PapCone® sampling device.

2. Subjects, materials and methods

2.1. Study site and design

This is a single-blind comparative study conducted among 192 sexually active women, attending Gynaecology Clinics of Nnamdi Azikiwe University Teaching Hospital (NAUTH) Nnewi and Chukwuemeka Odumegwu Ojukwu University Teaching Hospital (COOUTH) Awka, both in Anambra state of southeastern Nigeria; from 1st June to 30th November 2015. Ethical approval for the study was obtained from the ethical committees of the study institutions. Following appropriate counseling, an informed consent was obtained from each of the 192 subjects who had accepted to participate in the study.

3. Research methods

A proforma questionnaire to elicit information in respect of the biosocial characteristics together with other relevant gynecological history, was completed for each subject. Sample collection was made with the subject placed in a dorsal lithotomy and a Cusco's speculum placed expose the cervix. Two different cervical smears were obtained from each subject at four week intervals by the same gynaecologist in each institution, using the wooden Ayre's spatula and the Papcone® sampling device respectively. Each subject therefore served as her own control. The four week interval allowed between the collections of samples with the two devices ensured that no device got preferential sufficiency of the cervical cells by virtue of being the first to be used. The labelling on the slides was number-coded for appropriate blinding for each of the collection devices. The specimen obtained, whether with wooden Ayre's spatula or Papcone® sampling device, was smeared across the labelled glass slide, fixed in 95% ethyl alcohol and stained in the histopathology laboratory by the Papanicolaou's method. The slides

were then read under the light microscope and interpreted by the cytopathologists. All the slides were read by two cytopathologists, who were blinded to the particular cervical sampling device used for each subject. The primary outcome was the cell adequacy for each of the smears obtained using the Ayre's spatula and the Papcone® sampling device respectively. For the purposes of this study; adequacy was judged by the presence of at least 10 well-preserved (columnar) endocervical cells, either singly or in clusters, to validate the sampling of the transformation zone, according to the 2001 Bethesda system of reporting cervical and vaginal cytology specimens. (National Cancer Institute, 2002)

3.1. Data analysis

Data from the proforma questionnaires were fed into the Microsoft Excel for sorting and cleaning with subsequent transfer to Statistical Package for Social Sciences (SPSS) Software window version 21.0 (IBM Corporation) for analysis. Socio-demographic and baseline gynaecological variables were analysed. Mean and standard deviation were computed for the age of the subjects as well as the proportions for their marital status and parity.

Proportions were calculated for the adequacy of PapCone® and adequacy of Ayre's spatula respectively. The McNemar's test was done to show the differences in proportions between the adequacy of cell yield when PapCone® was used and when Ayre's spatula was used. The McNemar test was used because two samples, at two different times, were extracted from the same subject. A p-value of < 0.05 was deemed significant at 95% confidence intervals. In addition, relative risk for the inadequacy of PapCone® and inadequacy of Ayre's spatula was computed at 95% confidence intervals, using the MedCalc-statistical software available at <https://www.medcalc.org>. Cohens kappa analysis was also done for inter-rater agreement. The measurement of observer agreement for categorical data were calculated as follows: 0.01 – 0.20 slight agreement; 0.21 – 0.40 fair agreement; 0.41 – 0.60 moderate agreement; 0.61 – 0.80 substantial agreement and 0.81 – 1.00 almost perfect or perfect agreement, using the software available at <https://idostatistics.com/cohen-kappa-free-calculator/#risultati>.

4. Results

A total of two hundred and twenty-seven subjects were assessed for eligibility. Of these; nine subjects were excluded (four declined to participate; while five did not meet inclusion criteria). Two hundred and eighteen subjects were therefore enrolled into the study. One hundred and ninety-two subjects completed the study while twenty-six subjects dropped out of the study. Analysis was therefore made based on these 192 subjects who completed sampling with the second device.

The mean age of the women was 42.90(11.27)(Table 1). Majority, 84 (43.8%) of the women were multiparous, followed by the grand-multipara 48(25.0%). Similarly majority of the women 157(81.8%) were married while only 17(8.9%) were single (Table 2). Using the papcone's device, significantly higher adequate cervical smears 177 (92.2%) was obtained compared to 152(79.2%) obtained using the Ayre's spatula (p < 0.001). The results of cytology obtained, using the two methods of sampling were the same for each subject; there was no difference between the two time points. The percentage agreement for the two devices was 98.97% , thus Cohen's kappa of 0.49. The level of agreement is, therefore, moderate (Table 4) (see Table 3).

Table 1

Distribution by age for frequency, range, and mean (\pm SD) of the women.

Characteristics	Frequency	Minimum	Maximum	Mean	Standard deviation
Age	192	18	64	42.90	11.27

Table 2
Distribution by parity and marital status of the subjects.

Characteristics	Number	Percent
Parity		
Nullipara	28	14.6
Primipara	32	16.7
Multipara	84	43.8
Grandmultipara	48	25.0
Total	192	100
Marital status		
Singles	17	8.9
Married	157	81.8
Widows	18	9.4
Total	192	100

Table 3
Distribution by adequacy of cervical smears for the collection device.

Adequacy of Smears	Collection device used		RR (95 %CI)	P-Value
	Ayre's spatula	Papcone®		
YES	152 (79.2%)	177 (92.2%)	1.165 (1.071–1.266)	<0.001
NO	40 (20.8%)	15 (7.8%)		
TOTAL	192 (100%)	192 (100%)		

RR = Risk Ratio.

Table 4
Inter-rater agreement between the two devices.

Judgement	Frequency
Both agree to include	192
Both agree to exclude	1
Only the first cytopathologist agree	1
Only the second cytopathologist agree	1

% of agreement: 98.97%.

Cohen's kappa: 0.49.

5. Discussion

Cervical cancer remains one of the most common cancers in women in Nigeria, second only to breast cancer. (Jedy-Agba et al., 2012 Oct) Pap smear is an important component of secondary prevention of cervical cancer. A significant challenge associated with cervical cytology is inadequate collection of endocervical and ectocervical cells leading to a non-informative test. Cervical smears are often associated with anxiety, fear, and pain in the patient. (Braz et al., 2017; Lorenzi et al., 2019) Sample collection method is therefore very important and studies have been carried out comparing the efficacy of different methods of sample collection. (Soleimani et al., 2012; Rabiou et al., 2019)

Vaginal smear self-collection for cervical cancer screening is beginning to enjoy a wide acceptability. In a systematic review evaluating 19 studies, Braz et al found that vaginal smear self-collection method for cervical cancer screening was reported to be well-accepted by the participants, than other methods. (Braz et al., 2017) This study has been undertaken amongst a group of women with socio-demographic profile likely to be associated with cervical lesions – mean age of 42 years; multiparous/grandmultiparous; and mostly married women. Cervical smear yield from them is therefore expected to be reasonable. The study assessed the retrieval of cervical cells using two different sampling devices namely wooden Ayre's spatula and Papcone® on each subject. It also compared the cell adequacy obtained with the wooden Ayre's spatula to that of the Papcone®. The results showed that cell adequacy was significantly better with the Papcone® (92.2%) compared to the wooden Ayre's spatula (79.2%) with a p-value of < 0.001.

Previous studies on Papcone® had shown that it enhances gentle

transfer of retrieved cells to the glass slide without damaging them (Sander et al., 2007). It also encourages an even distribution of cells, without overlapping (Sander et al., 2007; Lukic et al., 2013; Petruzzello et al., 2011). Microscopically, the Papcone® has a porous and spongy structure that picks up numerous endocervical cells on its surface (Petruzzello et al., 2011). It is soft and usually not associated with pain when used in a healthy cervix. Furthermore, it adapts well to the anatomy of the cervical canal. These unique features of Papcone® are lacking in the wooden Ayre's spatula, which has been documented to trap cells within the matrix of the wood and also has a broad head (Martin et al., 2017).

The Cochrane systematic reviews highlighted that the wooden Ayre's spatula is less effective in sampling the endocervical cells and detecting abnormal cells, when compared with the extended tip spatulas (Martin et al., 2002). It also showed that the combination of the extended tip spatula and cytobrush was better than the spatula alone in collecting endocervical cells (Martin et al., 2002). However, this combination could be cumbersome in mass screening and busy gynaecology clinics (Vatanasapt et al., 2002). It might also bring about delays in fixing the smears, with the attendant risk of air drying (Soleimani et al., 2012). There is therefore need for a single device which could collect both endocervical and ectocervical cells at the same time (Soleimani et al., 2012; Sander et al., 2007). It would be most rewarding to frequently employ an instrument which combines simplicity and efficiency. The Papcone® has been reported to meet these two criteria having two distinct properties - acting as a soft brush in collecting endocervical cells and at the same time acting as a soft spatula by being pressed to the ectocervix (Sander et al., 2007). It has been shown to grip the transformation zone more effectively (Vatanasapt et al., 2002) and is very good and easy to use.

In their study, Sander et al (Sander et al., 2007) compared the quality of smears obtained with Papcone® to spatula/cytobrush combination, with each of the two categories of sampling devices employed four weeks apart (similar to the interval in our own study). They found no significant difference in adequacy between Papcone® and spatula/cytobrush combination in the retrieval of cervical cells, but the Papcone® was rated more user-friendly by the gynaecologists who took the smears. Papcone® was also more accepted by the patients, as regards discomfort or pain (Sander et al., 2007). They therefore concluded that the single sampling device (Papcone®) was comparable to the cytobrush/spatula combination in its ability to retrieve both endocervical and ectocervical cells (Sander et al., 2007).

In a similar study, Lukic et al (Lukic et al., 2013) compared the adequacy of Papcone® with that of Ayre's spatula/cytobrush combination (Lukic et al., 2013). Although, their repeat smear was taken from each subject 3 months apart instead of the one month interval employed in the present study and that of Sander et al (Sander et al., 2007). They also analysed the ultra-structural features of the devices using the scanning electron microscopy (SEM) before and after sampling the cervix. Papcone® smears revealed less cell overlap and less white blood cells ($p < 0.05$) (Lukic et al., 2013).

The interval between the collection of the first smear and the second smear in Lukic's study was 3 months while the interval in our study as well as Sander's study was four weeks. The reason for allowing an interval of time between the collection of smears in the subjects using the different devices, is to allow for the regeneration of the exfoliated cells in the initial procedure and therefore avoid the bias of tilting the sufficiency of cells towards the respective first sampling devices. This approach of interval collection, however, has the shortcoming of losing to the study some subjects who for one reason or the other are unable to present for the collection of the second sample using the second device. This occurred in 26 women in this study.

In terms of study limitation, the clinicians that collected the samples were not blinded to the devices used because it was not feasible to do so. The study population was also hospital-based and localized to an institution in a part of the country. The participants were also not randomly

assigned to sampling methods. The inter-rater agreement would have been further strengthened by having at least three cytopathologists report the slides. These limitations would therefore affect the external validity and thus generalization to the wider population. A multicenter randomized study, with at least three cytopathologists involved, would therefore be required to address these gaps. Nevertheless, because the participants served as their own control, the strength of the study was further enhanced.

In conclusion, this study has shown the efficacy of Papcone® over the conventional Ayre's spatula in the collection of cervical smear samples – having demonstrated a significantly better adequacy in sample yield compared to the Ayre's spatula. The Papcone® device is simple to use and structured to pick up ecto- and endo- cervical cells more efficiently, making it very attractive to the clinicians. Furthermore, it has been reported to be associated with less discomfort, and little or no pain to the patient and is therefore likely to have a higher acceptability than the wooden Ayre's spatula.

It is recommended, that when available, Papcone® sampling device be used in collecting Pap smears; especially in developing countries where liquid-based cytology is not yet routine. Medical practitioners caring for women in developing countries should be trained and adequately provided with this very useful device – particularly for its simplicity, for mass cervical screening in the prevention of cervical malignancies.

Author contributions

CIE, GUE and DNO contributed to study design, analysis, manuscript writing and revision. JIA, JII, IUE, BON and NOE contributed to study design, data collection, manuscript writing and revision. VIO, MIO, OBE, JOU and CRO contributed to study design, data collection, analysis and manuscript revision.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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