ORIGINAL ARTICLE

Comparative Study of the Cervical Cytopathological Changes Among Intrauterine Device and Injectable Contraceptive Users at Aminu Kano Teaching Hospital, Kano

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ABSTRACT

Background: The intrauterine contraceptive device (IUCD) is a commonly used method of birth control that requires minimal skill and does not interfere with fertility once removed. It has been reported to produce inflammation and cervical cytopathology which can result in premalignant changes. **Objective:** To determine the cytopathological changes among copper-containing IUCD and injectable contraceptive users at Aminu Kano Teaching Hospital. **Method:** This was a comparative cross-sectional study, of two groups of 140 consenting women using the copper T IUCD and another 140 using the injectable contraceptive who came for follow-up after four weeks of insertion at the family planning clinic over a period of 10 weeks. A structured questionnaire was administered and information on socio-demographic data and contraceptive behaviour were obtained. A Pap smear was taken from the two groups and reported according to the Bethesda system. **Results:** A negative smear with inflammation was found among 60(43.5%) women using the IUCD, compared to 31(22.8%) using the injectable contraceptive. Also, negative smear without inflammation was found in 76(55.1%) of the women on IUCD compared with 105(77.2%) on injectable contraceptives (p-value 0.012). Only 2(1.5%) of the women on the IUCD had low-grade squamous intraepithelial lesion, but none in the other group. Parity and duration of use for each of the methods had no statistically significant association with cytological findings in each of the groups (p-value 0.533 and 0.495 for parity and duration respectively). However, marital status had a statistically significant association with inflammatory changes (p-value< 0.001).
Conclusion: There were more inflammatory cytological changes among women using IUCD compared with those using the injectables.

Keywords: cervical cytopathology, intrauterine device, injectable contraceptives, comparative study

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Introduction

The intrauterine contraceptive device is a commonly used method of birth spacing.[1] It is a device inserted into the uterine cavity and exerts its action by inducing a sterile inflammatory environment within the cavity which is believed to be the bedrock of its mechanism of action and is very safe and effective.[1]
This study considered the copper-containing intrauterine device. This is a small 'T' shaped flexible plastic frame with copper sleeves or wire around it. It has two strings attached to the vertical arm, to serve as indicators of correct positioning throughout use. It requires a specially trained health care provider to insert it into the uterus through the vagina and cervix. It has been recommended for use for up to 10 years making it suitable for long-term use and return to fertility is immediate after removal.[2]

The intrauterine device has been reported to produce inflammation and changes in cervical cytopathology[3,] therefore increasing the risk of cervical premalignant changes among its users, however studies are inconclusive, and some even suggest a protective effect of copper IUCD on the development of invasive cervical cancer.[4]

This inflammation results from the thread of the device tail producing constant irritation and causing cervical erosion, which will, in turn, cause vaginal discharge and other symptoms in the users.[4] The injectable contraceptives commonly used are depomedroxyprogesterone acetate (DMPA) and norethisterone enanthate (NET-EN).

Both are administered intramuscularly within the first 5 days of the cycle. DMPA has a dose of 150mg every 3 months, while NET-EN is 200mg at 2 monthly intervals.

They act by suppressing the mid-cycle Luteinizing Hormone (LH) surge, thereby preventing ovulation, thickening of cervical mucus and making sperm penetration difficult, and by thinning the endometrium and preventing implantation of the blastocyst.

The association between the IUCD and cytopathological changes of the cervix has been an area of interest for researchers. Many studies done have conflicting results about the influence of IUCDs on cervical cytology from Pap smear. Most studies show increased inflammatory exudates, inflammatory epithelial changes, or extensive metaplastic cells among IUCD users.

They concluded that the IUCD does not increase the incidence of squamous intraepithelial lesions and should it be encountered, it is merely a coincidence and not due to the presence of the IUCD. Local vaginal treatment then a repeat pap smear should be done as treatment for such lesions.[3,5,6,7,8-12]

Another study found reactive/reparative changes with the use of more than 3 years, ASCUS from 1-3 years and LSIL less than 3 years of use.

In cytological studies done among IUCD users, the rate of inflammatory cytology is higher compared to controls but decreases with an increasing interval of time between insertion and cytologic examination.[13] These inflammatory alterations are the reasons for the higher rate of suspicious smears seen in IUCD users. No higher rate of precancerous lesions was seen in the IUCD group than in the control group.[13] The type of cells seen are single or clustered glandular cells with a hyperchromatic nucleus, and an increase in nuclear-cytoplasmic ratio.

Nucleoli may be present and prominent vacuoles may cause a signet ring appearance to the cells. To avoid a diagnosis of AGUS, cellular changes must be correlated with patient history.[14]

Method

The study was conducted among consenting women who came for follow-up visits after at least four weeks of IUCD insertion at the family planning clinic of Aminu Kano Teaching Hospital. The controls were those women who came for their due doses of injectable contraceptives, at least four weeks after the last dose. The study was a comparative cross-sectional study. A structured interviewer-administered questionnaire was used for the study, which was divided into sections. One each for socio-demographic characteristics, the method of contraceptive used and level of satisfaction with the method, perceived complications encountered as a result of its use and pelvic examination findings.

The sampling was done by consecutive sampling technique on all consenting women who satisfied the inclusion criteria

To conduct the conventional Pap smear technique, the patient was counselled on the indication and importance of the test and then reassured that it is not painful or harmful but, she may experience some discomfort. Precautions taken included avoidance of sexual intercourse, douching, use of any vaginal creams, or contraceptive sponges at least 48 hours before the test. Also, avoid lubricants and taking the sample when the woman is bleeding.

The woman was placed in a dorsal position. A bivalve speculum was introduced into the vagina to expose and visualize the cervix under a good light source, any obscuring discharge was removed. The spatula was introduced gently into the cervix and rotated 360 degrees to sample the squamocolumnar junction.

The material was then evenly smeared on a prelabelled glass slide and fixed immediately in 95% alcohol in a coupling jar. The specimen was sent to histopathology for cytologic analysis. Though it has a high false negative and false positive result, it is cheap, easy to perform and is still widely used as a cervical screening method. For this research, the Bethesda system was used for reporting the smears.

The Bethesda system in comparison to the WHO and BSCCP systems is more comprehensive, gives a well-

defined diagnostic terminology and takes into consideration those lesions of undetermined significance (ASCUS) and those in which a high-grade lesion cannot be excluded (ASC-H). The LGSIL corresponds to HPV infection and CIN I, while HGSIL corresponds to CIN II and III.[15]

Laboratory Analysis.

The fixed smeared slides were taken through decreasing concentrations of alcohol from 95%, to 90%, to 70% then water for 15 minutes each. Next, they were stained in Harris haematoxylin for 5 minutes and then rinsed in tap water for one minute. The slides were placed in Scott's tap water for 30 seconds, rinsed in water, and transferred to 95% alcohol again for 15 seconds. They were then stained in O.G 6 for 1 minute, rinsed in 95% alcohol for 15 seconds, then stained in EA 50 for 1 minute and rinsed again in 95% alcohol and then 100% alcohol 2-3 changes 15 seconds each. The slides were then cleared in xylene and mounted in D.P.X mountant, then examined under the microscope and the results read.

Data Analysis

Data was verified, coded and entered into Microsoft Excel spreadsheet. Then analysed using MINITAB computer software version 14.0 for windows. The results were expressed in descriptive statistics; for the quantitative variables, they were summarised using mean, standard deviation and range while qualitative variables were estimated using percentages and Pearson's Chi-square. Statistical significance level was taken at P< 0.05 (5%). The Binary logistic regression model was used to control for potential confounders.

Results

A total of 280 women, 140 each on IUCD and injectable contraception, were recruited for the study, and each had a pap smear done after counselling and obtaining informed consent. Four of the Pap smears obtained from women using injectable contraceptives and 2 from women using IUCD were unsatisfactory and were therefore not analysed. A total of 274 smears were analysed. The ages of the clients ranged from 19-56 years, with a mean of 30.9 ± 6.8 years. As shown in Table I, overall, the majority of the women (46.7%) on the IUCD were in the 30-39 age group, followed by the 19-29 age group accounting for 34.1%; 18.8% for the 40-49 age group and only 2(1.5%) in the 50-59 age group. In contrast, most of the women (61.1%) on injectables were in the 19-29 age group, followed by the 30-39 age group (31.6%), 6.6% for the 40-49 age group and 0.7% for those in the 50-59 age group. There was a significant association between age and choice of contraceptive method in this study (P-value of <0.001) with younger women preferring injectables over IUCDs.

The mean parity of all the clients was 3 ± 1, with 117 (42.7%) being of low parity (para 1-4). The majority of the women on IUCD were of high parity i.e., Para ≥5 accounting for 92 (66.7%), while most of the women on injectables 71(52.2%) were of low parity (Para 1-4). This difference was also statistically significant, (p-value = 0.002).

The majority of the women on IUCD 75(54.4%) had tertiary education followed by those with secondary education 33(23.9%) than those with primary education 17(12.3%). The least were those with no formal education and these accounted for 13(9.4%) of IUCD clients. On the other hand, majority of the women on injectable contraceptives had secondary education 75(55.2%), followed by those with tertiary education 49(36.0%), then those with primary education accounting for 8(5.9%) and the least was also among those with no formal education 4(2.9%). There was a statistically significant association between educational status, and choice of contraceptive method, p-value <0.001.

Relationship Between Method of Contraception, Speculum Examination Findings and Pap Smear Results

Of the 274 women, speculum examination findings showed healthy cervix in 146 (53.3%), discharge in 100 (36.5%) and erosion in 28 (10.2%); Pap smear examination on the other hand showed that negative smears constituted 181(66.1%), negative with inflammation 91(33.2%) and low grade squamous intraepithelial lesion 2(0.7%).

Of the 146 women that had healthy cervices, 59(40.9%) of them were on IUCD, out of which 52 (88.1%) had negative smears while 7 (11.9%) had coexisting significant inflammation in addition to the negative smears. This is comparable to 79 (90.8%) of women on injectables who also had a negative smear and 8(9.2%) that had a negative smear with remarkable inflammation. There was no statistically significant association found between the health of the cervix and the method of contraceptive used (p-value = 0.60).

Among the 62 women on IUCD that had discharge on speculum examination of the cervix, 20(32.3%) had a negative smear, while 42(67.7%) had negative smear with inflammation, compared to 38 among the injectable users in whom 21(55.3%) had a negative smear and 17(44.7%) had negative smear with inflammation reported. There was a statistically significant association between cervical discharge and the method of contraceptive used (p-value= 0.02).

Twenty-eight women had erosion, of which 17(60.7%) were IUCD users. Of these 17, 4(23.5%) had negative smears while 11(64.7%) had reportable accompanying inflammation. The remaining 2(11.8%) had low grade squamous intraepithelial lesions (LSIL). The remaining 11 (of 28 women with erosion) were injectable contraceptive users, and among them, 5(45.5%) had negative smears, while 6(54.5%) had negative smears with reportable inflammation. The association of cervical erosion with dysplasia was not statistically significant (p-value= 0.3). These were subjected to tests of association and the results are shown in the table below; the relationship between cytopathological changes and method of contraception is shown in table 4.

To test for statistical significance, and to control for confounding factors in this finding, such as duration of use of the method of contraception and parity, a binary logistic regression model was used. As shown, in table III; A binary logistic regression model was used to establish whether there was a relationship between the cytological findings/ Pap smear result with the marital setting, parity, duration of use and method of contraception, independent of other confounding factors such as parity and duration of use. After adjusting for these factors, IUCD was found to be twice more likely to be associated with a negative smear with inflammation (odds ratio OR 2.12, 95% CI 1.18-3.82, p- value 0.012) than other factors. Polygamy was also found to be associated with a negative smear with inflammation result (odds ratio OR 6.12, 95% CI 3.35- 11.18, p-value <0.001). Women in the polygamous setting were found to be more than 6 times more likely to have a negative smear with inflammation compared to those in the monogamous setting. However, duration of use was not found to be statistically significant in its association with a negative smear with inflammatory result (OR 1.29, 95% CI 0.62-2.69, P-Value 0.495) for a long duration (≥2 years).

Also, parity did not have a statistically significant association with a negative inflammation result (OR 0.82, 95% CI 0.45- 1.51, P-Value 0.533).

Table 1: Sociodemographic Characteristics of the Clients

Age Distribution

age	IUCD (%)	Injectable (%)	Total (%)	P-value
19-29	47(34.1)	83(61.1)	130(47.4)	
30-39	63(45.7)	43(31.6)	106(38.7)	
40-49	26(18.8)	9(6.6)	35(12.8)	
50-59	2(1.4)	1(0.7)	3(1.1)	
total	138(100)	136(100)	274 (100)	<0.001

Parity

Parity	IUCD (%)	Injectable (%)	Total (%)	P-value
Para 1-4	46(33.3)	71(52.2)	117(42.7)	
Para ≥5	92(66.7)	65(47.8)	157(57.3)	
total	138(100)	136(100)	274(100)	0.002

Educational status

Educational status	IUCD (%)	Injectable (%)	Total (%)	p-value
No formal education	13(9.4)	4(2.9)	17(6.2)	
Primary	17(12.3)	8(5.9)	25(9.1)	
Secondary	33(23.9)	75(55.2)	108(39.4)	
Tertiary	75(54.4)	49(36.0)	124(45.3)	
Total	138 (100)	136(100)	274 (100)	<0.001

Table 2: Relationship Between Speculum Examination, Cytological Findings and Method of Contraception.

	IUCD	INJECTABLE	%	CHI SQUARE	P-VALUE
HEALTHY (total) 146	**59 (40.9)**	**87 (59.1)**	**100**	**0.27**	**0.6**
• Negative	52(88.1)	79 (90.8)	89.7		
• Negative +inflammation	7(11.9)	8 (9.2)	10.3		
• LSIL	0 (0)	0 (0)	0		
DISCHARGE (total) 100	**62 (62.0)**	**38(38.0)**	**100**	**5.16**	**0.023**
• Negative	20(32.3)	21(55.3)	41		
• Negative +inflammation	42 (67.7)	17(44.7)	59		
• LSIL	0 (0)	0 (0)	0		
EROSION (total) 28	**17 (60.7)**	**11 (39.3)**	**100**	**2.41**	**0.3**
• Negative	4 (23.5)	5 (45.5)	32.1		
• Negative +inflammation	11(64.7)	6 (54.5)	60.7		
• LSIL	2 (11.8)	0 (0)	7.2		

Table 3: Binary Logistic Regression Analysis to Control Confounding Factors.

Predictor	Odds Ratio	Lower CI	Upper CI	p-value
Method				
IUCD	2.12	1.18	3.82	0.012
Injectable	1			
Duration of use				
Long duration	1.29	0.62	2.69	0.495
Short duration	1			
Parity				
High parity	0.82	0.45	1.51	0.533
Low parity	1			
Marital Setting				
Polygamy	6.12	3.35	11.18	<0.001
Monogamy	1			

Discussion

In this study, the ages of the women ranged from 19-56 years, with a mean of 30.9 ± 6.8 years. Contraceptive behaviour of women changed with increasing age, with the younger age group 19-29 years opting for injectable contraceptives in preference to the IUCDs, while the 30–39-year age group opted for IUCDs. This is in agreement with the study conducted by Igwe et al[7] in Abakaliki where the majority of IUCD users were within the 30-39 age group, but higher than the Orlu study by Ojiyi et al[16] where the majority were within 26-30 years.

The reason for this pattern may stem from the fact that older women need a longer-term contraceptive method having completed their family size, in contrast to the younger age groups that have not. Another reason may be that, given the conservative nature of women in northern Nigeria, concerning genital exposure and privacy, the injectable is preferable in the younger women since it does not require much exposure during administration compared to the IUCD.[17,18]

The mean duration of use of the IUCD in this study was, 22.3±28.8 months, this is similar to the duration of use in the Abakaliki study where a majority (79.1%) used the IUCD for ≥2 years but less than the 4 years found in the Orlu study.[7,16] The finding that women of higher parity opted for IUCD in these studies, also reflects the completion of family size and the need for a longer-term contraceptive method.

There was a higher incidence of inflammatory cytology among the IUCD group and this is corroborated by the finding of statistically significant association between discharge and method of contraception (p-value 0.02, DF 1, X^2-5.155). This has been attributed to constant irritation of the cervical epithelium by the thread of the IUCD causing more cervical mucus discharge and inflammation. This result is in agreement with the study conducted by Ajah et al in Enugu[19] on the effects of the IUCD on the cervical smear which concluded that it causes increased inflammation but does not increase the incidence of squamous intraepithelial lesions. The incidence of abnormal cervical smear in this study was 1.5% among the IUCD users, which is lower than that found in the Enugu study of 10.3% even though their study did not report any statistically significant difference from controls. In Malaysia, the incidence

was 4%[20], while in Turkey it was 7.3%.[21] This finding is however in agreement with the study conducted by Abd El All et al in Egypt[93] and others[3,5,6,7,8-12,13,23]
Even though two of the women from our study, on IUCD had Low grade intraepithelial lesions (LSIL), it was not statistically significant. Both women were above 30 years of age, were both para 4 and were married in a polygamous setting. They had been using their IUCDs for 5 and 10 years respectively. This finding is in agreement with studies conducted in India by others (Agarwal, Saroj and Bagchi) [3,23,24], who found LSIL to be more common in women wearing IUCDs from 3- 10 years or more. Naik et al[25] have also concluded that ASCUS and LSIL incidence increases with an increase in the duration of insertion of IUCD being maximum with insertion of more than 3 years. Lassise[26] in the USA suggested a protective effect of the copper IUCD on the cervix against premalignant lesions, but not the inert device. Castellsague et al[4] suggested that the destruction of precancerous lesions by abrasion during insertion brings about the protective effect of the IUCD on cervical dysplasia, while Petry et al[21] disagreed and suggested that tissue trauma associated with IUCD insertion induces a cellular immune response that clears persistent HPV infection and pre-invasive cervical lesions. Baris II et al in Turkey found no association between contraceptive method and changes in epithelial cell abnormalities.[27]
The regression analysis finding that women on IUCDs were two times more likely to have inflammatory smears compared to the women on the injectables is in agreement with the studies by Agarwal and colleagues[2] in India and Ashwani et al.[28].

Conclusion

In conclusion, the women using the IUCD do not have a higher risk of pre invasive cervical lesions than those on the injectable contraceptive. The LSIL found, though, among the women on the IUCD was too infrequent to be statistically significant. They however had statistically significant higher frequency of cervical discharge on speculum examination and inflammatory smears, compared with those taking the injectable contraceptive.

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