

CHAPTER FOUR

4.0 Results:

The study was conducted over a period of 12 months from the 1st June 2020 to the 26th of May 2021.

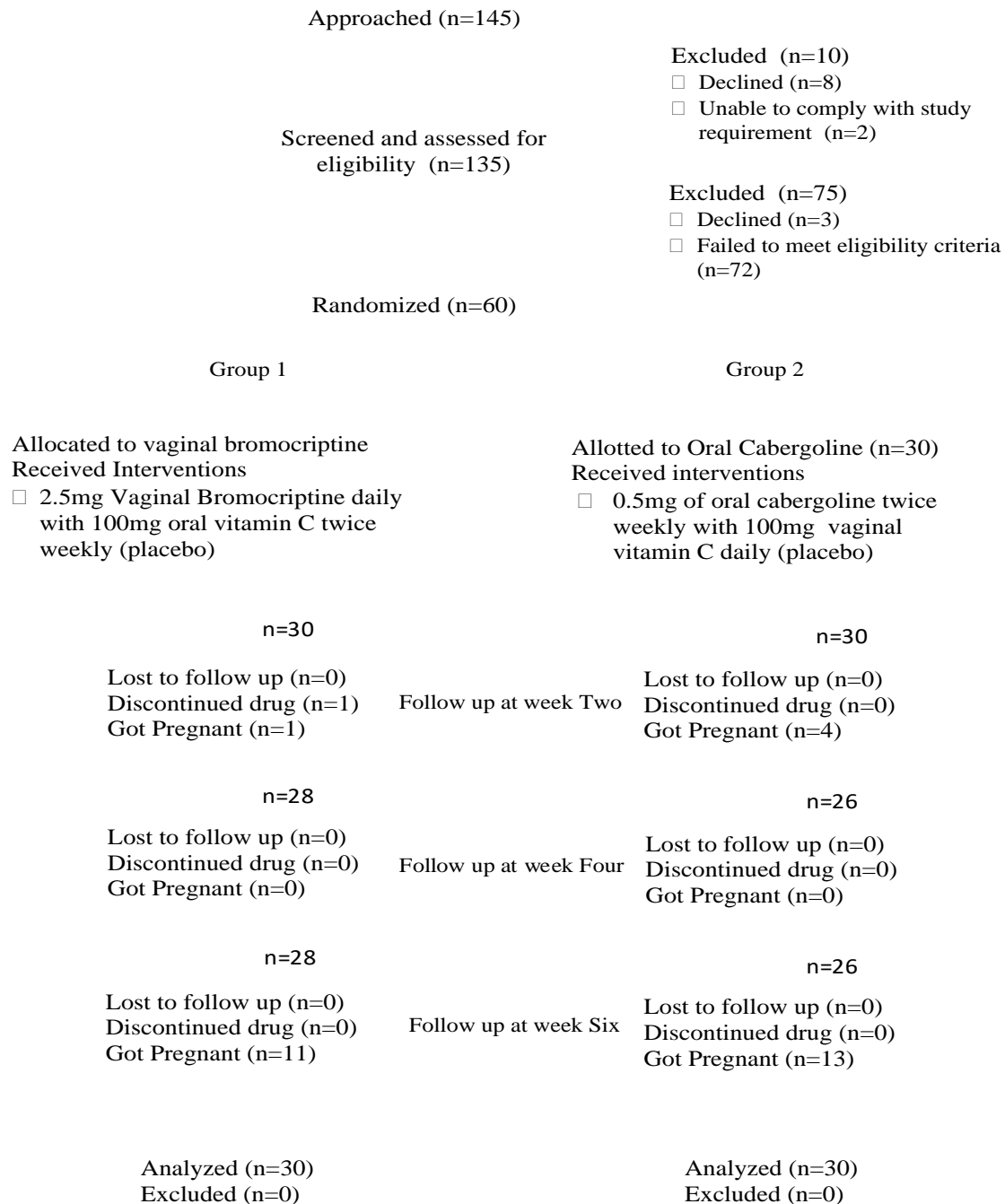


Figure 4.1: Study protocol

Table 4.1: Sociodemographic Characteristics and body mass index

		Group 1	Group 2
		Vaginal Bromocriptine (n=30)	Oral Cabergoline (n=30)
Age (years)	18-25	9 (30.0%)	10 (33.4%)
	26-35	17 (56.7%)	16 (53.3%)
	36-45	3 (10.0%)	3 (10.0%)
	>45	1 (3.3%)	1(3.3%)
Monthly household Income (₦)	< 30,000	19 (63.3%)	16 (53.3%)
	30,001-50,000	4 (13.3%)	2 (6.7%)
	50,001-100,000	2 (6.7%)	2 (6.7%)
	100,001-200,000	2 (6.7%)	4 (13.3%)
	>200,000	3 (10.0%)	6 (20.0%)
Religion	Muslim	17 (56.7%)	14 (46.7%)
	Christian	13 (43.3%)	16 (53.3%)
Tribe	Hausa	14 (46.7%)	12 (40.0%)
	Yoruba	7 (23.3%)	8 (26.6%)
	Igbo	4 (13.3%)	5 (16.7%)
	Other	5 (16.7%)	5 (16.7%)
Level of Education	No Formal	2 (6.7%)	1 (3.3%)
	Islamic	3 (10.0%)	2 (6.7%)
	Primary	8 (26.7%)	3 (10.0%)
	Secondary	7 (23.3%)	9 (30.0%)
	Tertiary	10 ((33.3%)	15 (50.0%)

Parity	Nullipara	9 (30.0%)	10 (33.3%)
	Multipara	19 (63.3%)	18 (60.0%)
	Grandmultipara	2 (6.7%)	2 (6.7%)
Body Mass Index (kg/m²)	Underweight	0 (0.0%)	3 (10.0%)
	Normal	9 (30.0%)	12 (40.0%)
	Overweight	11 (36.7%)	4 (13.3%)
	Grade 1 obesity	7 (23.3%)	5 (16.7%)
	Grade 2 obesity	1 (3.3%)	6 (20.0%)
	Morbid obesity	2 (6.7%)	0 (0.0%)

4.1. Sociodemographic characteristics and body mass index (BMI) of patients:

Table 4.1 shows the sociodemographic characteristics and BMI of the patients who participated in the study. The patient's ages ranged between 18-46 years with 55% of the patients in the 26-35year group. The mean age was 27.5years \pm 6.7years.

The median monthly house hold income was N25000 \pm 59848 with a range of N2000-250,000.

The majority (58%) of the patient's monthly income fell below the national minimum wage of N30,000.

Forty two percent of the respondents had or were pursuing tertiary education of which majority had a Higher National diploma (HND) while only 5% had no formal education.

Thirteen out of the 37 multipara had no children alive while all the four grand multiparas had all their children alive. The average number of children alive was 2. Thirteen of the nullipara suffered from primary infertility while six had not carried any pregnancy beyond 28 weeks of

gestation. Seven in the bromocriptine group and six in the cabergoline group suffered from primary infertility.

Only 35% of the patients had a normal BMI while 60% of the patients had a BMI of $\geq 25\text{kg/m}^2$ with a mean BMI was $27.6\text{ kg/m}^2 \pm 5.9$.

Table 4.2: Comparison of the mean of baseline characteristics in both study groups

	Group 1	Group 2	P Value
	Vaginal bromocriptine (n=30)	Oral Cabergoline (n=30)	
Age in years	28.2	28.3	0.939
BMI in kg/m²	27.7	27.6	0.916
Parity	1.9	1.8	0.816
Baseline serum prolactin levels in ng/ml	49.8	49.2	0.911

4.2. Comparison of the mean of baseline characteristics in both study groups

Table 4.2 represents the comparison of baseline characteristics between the two study groups.

An independent sample t test was performed to compare the means. There was no statistically significant difference in age, BMI, parity and the baseline serum prolactin levels in both groups as all p values were greater than 0.05.

Table 4.3: Comparison of hyperprolactinemia related symptoms at presentation in both study groups

Symptom at presentation		Group 1 Vaginal Bromocriptine (n= 30)	Group 2 Oral Cabergoline (n= 30)	X^2	P value
Amenorrhoea	Yes	13 (43.3%)	8 (26.6%)	1.845	0.174
	No	17 (56.7%)	22 (73.4%)		
Oligomenorrhoea	Yes	5 (16.7%)	9 (30.0%)	1.507	0.220
	No	25 (83.3%)	21 (70.0%)		
Galactorrhoea	Yes	11 (36.7%)	12 (40.0%)	0.071	0.791
	No	19 (63.3%)	18 (60.0%)		
Decrease Libido	Yes	14 (46.7%)	12 (40.0%)	0.271	0.602
	No	16 (53.3%)	18 (60.0%)		
Other	Yes	2 (6.7%)	0 (0.0%)	2.000	0.368
	No	28 (93.3%)	30 (100%)		

4.3. Comparison of hyperprolactinemia related symptoms at presentation in both study groups.

Table 4.3 shows the presenting complaint amongst the patients. Forty three percent complained of decreased libido, 38% of galactorrhoea, 35% of absent menses (both primary and secondary amenorrhoea) and 23% of oligomenorrhoea.

One (1.7%) patient in the bromocriptine group complained of persistent headache with a normal Contrast enhanced brain MRI and another patient (1.7%) in the same group complained of dyspareunia which was associated with hypo-estrogenic vulva changes.

An independent sample t test was performed to assess the level of significance. There was no statistically significant difference in terms of presenting complaints among participants in both study groups.

Table 4.4: Comparison of mean prolactin levels during follow up in both study groups

	Mean Pre-treatment prolactin (ng/ml)	Mean Serum prolactin at week 2 (ng/ml)	Mean Serum prolactin week 4 (ng/ml)	Mean Serum prolactin week 6 (ng/ml)	P Value
Group 1	49.8 ± 21.5	35.7 ± 11.3 ^a	28.4 ± 6.1 ^b	20.7 ± 6.3 ^c	0.001
Vaginal Bromocriptine					
n	30	28	28	28	
Group 2					
Oral Cabergoline	49.2 ± 20.1	32.9 ± 9.1 ^d	26.2 ± 5.3 ^e	18.6 ± 4.3 ^f	0.001
n	30	26	26	26	
P Value	0.911	0.295	0.165	0.161	

a = comparison of mean prolactin levels between pre-treatment prolactin and prolactin levels at week two in bromocriptine group. (p=0.0001)

b = comparison of mean prolactin at week two with mean prolactin at week four in bromocriptine group. (p=0.001)

c = comparison of mean prolactin at week four with mean prolactin at week six in bromocriptine group. (p=0.001)

d = comparison of mean prolactin before treatment with mean prolactin at week two in cabergoline group. (p=0.001)

e = comparison of mean prolactin at week two with mean prolactin at week four in cabergoline group. (p=0.001)

f = comparison of mean prolactin at week four with mean prolactin at week six in cabergoline group. (p=0.001)

4.4 Comparison of mean prolactin levels during follow up in both study groups

Table 4.4 above shows the mean serum prolactin levels at week two, four and six in both study groups.

A reduction in serum prolactin levels is noticed in both study groups, however, this difference is not statistically significant when compared between the study groups.

One patient in the bromocriptine group developed severe nausea and vomiting at the end of the second week of treatment and had to discontinue treatment. Also, one patient in the bromocriptine group and four patients in the cabergoline group respectively had a positive serum pregnancy test at the end of week 2 (accounting for the change in “n” at follow up). Their drug treatment was also discontinued and they were booked at the ANC for ongoing management.

Table 4.5: Comparison of percentage and unit reduction in serum prolactin levels during follow up in both study groups

	Reduction in serum prolactin at week 2 in ng/ml (%)	Reduction in serum prolactin at week 4 in ng/ml (%)	Reduction in serum prolactin at week 6 in ng/ml (%)
Group 1 Vaginal Bromocriptine	14.1 (28.3%)	7.3 (20.4%)	7.7 (27.1%)
Group 2 Oral Cabergoline	16.3 (33.1%)	6.7 (20.3%)	7.6 (29.0%)
P Value	0.509	0.659	0.720

4.5 Comparison of percentage and unit reduction in serum prolactin levels during follow up in both study groups

Table 4.5 above shows the average reduction in serum prolactin levels at each follow up visit. Both groups demonstrated over 50% reduction in serum prolactin levels at the end of the study with the maximum reduction at week 2. An independent sample t test was performed to determine the level of significance. All p values were >0.05 indicating no statistical significance in the differences observed in both groups.

Table 4.6: Proportion of patients with normal prolactin levels at 6 weeks.

	Group 1	Group 2	X^2	P value
	Vaginal bromocriptine	Oral Cabergoline		
Achieved normal serum prolactin level ($\leq 25\text{ng/ml}$)	22 (73.3%)	23 (76.7%)		
			0.76559 ($df=1$)	0.50
Failed to achieve normal serum prolactin level	8 (26.7%)	7 (23.3%)		

4.6. Proportion of patients with normal prolactin levels at 6 weeks.

Table 4.6 above is a representation of patients who had normal serum prolactin levels at the end of the study. Forty-five (75%) patients had normal ($\leq 25\text{ng/ml}$) serum prolactin levels at the end of the study with comparable values in both study groups (73.3% vs 76.7%).

Table 4.7: Side effects experienced in both study group at follow up

		Side effects at week 2	Side effects at week 4	Side effects at week 6
		n	n	n
Group 1 Vaginal Bromocriptine	Yes	16 (53.3%)	1 (3.6%)	1 (3.6%)
	No	14 (46.7%)	27 (96.4%)	27 (96.4%)
Group 2				
Oral Cabergoline	Yes	12 (40.0%)	1 (3.8%)	0 (0.0%)
	No	18 (60.0%)	25 (96.2%)	26 (100.0%)
X²		0.301 (df=1)	0.957 (df=1)	1.260 (df=1)
P value		0.80	0.50	0.358

4.7. Side effects experienced in both study groups

Table 4.6 represents the distribution of side effects in both study groups at week two, week four and week six. The overall side effect rate in this study was 46.7% mostly experienced during the first 14 days and persisting in 3.7% and 1.9% over the follow up period. 53.3% of patients in the bromocriptine group and 40.0% of patients in the cabergoline group experienced at least one side effect. There was no statistically significant difference between the two study groups in terms of side effects experienced. All experienced these side effects during the first 14 days of the study with persistence of side effects in only one patient in the bromocriptine group at the end of the study. No patient experienced de novo side effects in the middle of the study.

Only 2 patients experienced side effects at week 4. One in bromocriptine group and one in the cabergoline group with nausea and vaginal dryness respectively while the only patient who experienced side effect (nausea) in the sixth week was on bromocriptine

It should be noted that one patient in the bromocriptine group had to discontinue treatment at the end of week 2 due to severe nausea and vomiting. All the others had mild side effects which resolved by week 4 in most. Discontinuation rate for bromocriptine was 3.33% and 0% for cabergoline. This difference was not statistically significant.

Table 4.8: Specific side effects experienced in both study groups

		Nausea n (%)	Vomiting n (%)	Headache n (%)	Fainting n (%)	Vaginal discharge n (%)
Group 1 Vaginal Bromocriptine N=30	Yes	12 (40.0)	2 (6.7)	1 (3.3)	2 (6.7)	7 (23.3)
	No	18 (60.0)	28 (93.3)	29 (96.7)	28 (93.3)	23 (76.7)
Group 2 Oral Cabergoline N=30	Yes	10 (33.3)	1 (3.3)	0 (0.0)	1(3.3)	2 (6.7)
	No	20 (66.7)	29 (96.7)	30 (100.0)	29 (96.7)	28 (93.3)
X²		0.287 (df=1)	0.357 (df=1)	1.403 (df=1)	0.351 (df=1)	3.433 (df=1)
P value		0.5920	0.550	0.236	0.550	0.064

4.8. Specific side effects experienced in both study groups

The commonest side effect experienced in both groups was nausea followed by vaginal discharge. The vaginal discharge was described as copious, clear, watery and not foul smelling with no associated vaginal itching.

All side effects were notably more common in the bromocriptine group but the difference was not statistically significant. None of the patients experienced nasal stuffiness, dizziness, drowsiness vaginal dryness, abdominal pain or low mood.

Only two patients experienced side effects at week four. One in bromocriptine group and one in the cabergoline group with nausea and vaginal discharge respectively while the only patient who experienced side effect in the sixth week was on bromocriptine. She complained of mild nausea.

Table 4.9: Symptom resolution at the end of the study in each study group.

Symptoms resolved at the end of the study		Group 1 Vaginal Bromocriptine	Group 2 Oral Cabergoline	χ^2	P Value
Had at least one symptom resolved at the end of the study	Yes	22 (73.3%)	27 (90.0%)	3.413 (df=1)	0.065
	No	8 (26.7%)	3 (10.0%)		
Inability to conceive	Yes	12 (40.0%)	17 (56.7%)	0.834 (df=1)	0.636
	No	18 (60.0%)	13 (43.3%)		
Amenorrhoea	Yes	2 (15.4%)	2 (25.0%)	0.197 (df=1)	0.986
	No	11 (84.6%)	6 (75.0%)		
Oligomenorrhoea	Yes	2 (40.0%)	3 (33.3%)	1.044 (df=1)	0.623
	No	3 (60.0%)	6 (66.7%)		
Galactorrhoea	Yes	9 (81.8%)	8 (66.7%)	0.199 (df=1)	0.982
	No	3 (18.2%)	4 (33.3%)		

				0.779	
Decreased libido	Yes	10 (71.4%)	11 (91.7%)	(df=1)	0.682
	No	4 (28.6%)	1 (8.3%)		
				1.017	
Other	Yes	2 (100.0%)	0 (0.0%)	(df=1)	0.188
	No	0 (0.0%)	0 (0.0%)		

4.9. Symptom resolution at the end of the study in each study group

Table 4.8 represents the resolution of symptoms experienced in each study group. About (49) 82% of the patients experienced resolution of at least one symptom. No statistically significant difference exists between the two groups in terms of resolution of symptoms.

Significant resolution of symptoms occurred in both study groups with the cabergoline group having a higher pregnancy rate of 56.7% vs 40.0% in bromocriptine group. Notably also, 4 out of the 17 pregnancies occurred within the first 2 weeks of treatment (23.5%) compared with one (8.3%) in the bromocriptine group respectively.

Bromocriptine seems to be superior in the resolution of galactorrhoea (81.8% vs 66.7%). However, no statistical superiority was demonstrated.

Two patients in the bromocriptine group complained of severe headaches and dyspareunia. Both patients had resolution of their symptoms at the six-week review.

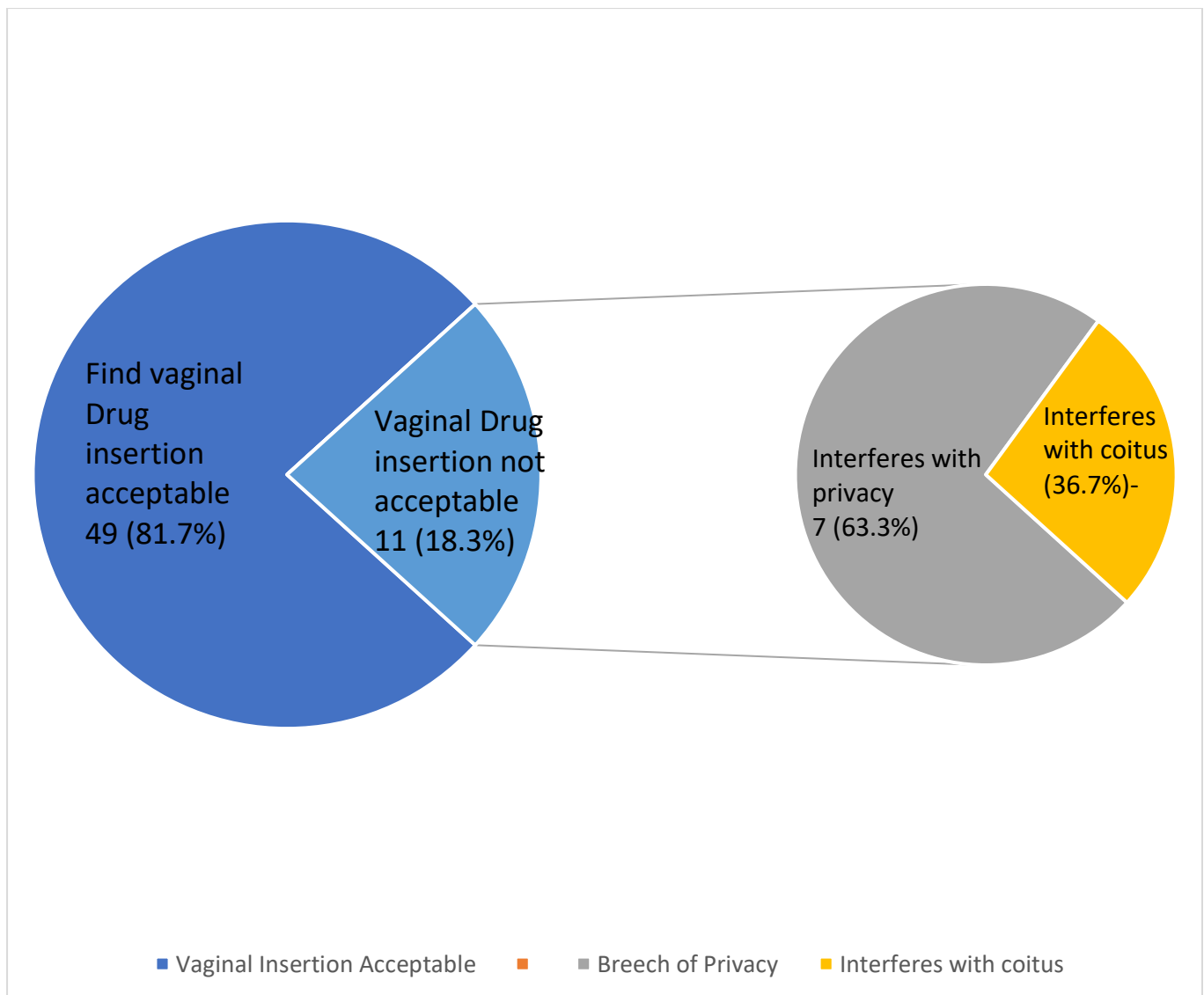


Figure 4.2: Acceptability of vaginal route of drug insertion among participants.

4.10. Acceptability of vaginal route of drug insertion among participants.

Majority of the patients found vaginal drug insertion acceptable with only 18.3% finding vaginal drug insertion as unacceptable sighting reasons such as interference of privacy (63.3%) and interference of coitus (36.7%) as reasons.