NORPLANT® CONTRACEPTIVE IMPLANTS - A COMPARISON OF CAPSULES VERSUS RODS IN SINGAPORE

K Singh, O A C Viegas, S S Ratnam

ABSTRACT

The NORPLANT® system is one of the most modern long acting steroidal fertility regulatory delivery systems to be introduced. It consists of six silicone capsules. The NORPLANT®-2 rod system on the other hand consists of only 2 rods. The comparative study undertaken suggests that the NORPLANT®-2 rod system is highly effective, safe and acceptable as the NORPLANT® six capsule system in Singapore. It would thus appear that the NORPLANT®-2 rod system as compared to the NORPLANT® six capsule system has a great potential for acceptability in terms of ease of insertion and removal.

Keywords : Long acting, reversible, levonorgestrel, subdermal implants

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INTRODUCTION

The NORPLANT® system consists of six silicone capsules, each containing 36 mg of levonorgestrel and having a diameter of 2-4 mm and a length of 3.4 cm. It is one of the most modern long acting steroidal fertility regulatory delivery systems to be introduced and is currently undergoing preintroductory clinical trials in Singapore and other countries. Encouraged by the excellent results with the NORPLANT® six capsule system, the Population Council went on to develop the NORPLANT®-2 rod system. This new system consists of two 2.4 mm and 4.4 cm rods in which levonorgestrel is homogenously dispersed with a silastic matrix - medical grade elastomer 382. This is then covered by a thin sheet of silastic (1).

The two rod system has been shown to deliver amounts of levonorgestrel equivalent to those of the six capsules in the NORPLANT® system. The rationale for developing the NORPLANT® - 2 rod system was that a reduction in the number of implants would offer the advantage of ease of insertion and removal and thus be more acceptable to potential users.

A study was thus undertaken to compare the NORPLANT®-2 rod system versus the NORPLANT® six capsules system among Singaporean women. The results of this study are presented in this paper.

Department of Obstetrics & Gynaecology
National University Hospital
Lower Kent Ridge Road
Singapore 0511

K Singh, MBBS,M Med, MRCOG, MA(Exon), AM, MD
Senior Lecturer

O A C Viegas, MBChB, DA, MRCOG, MD, AM, FRCOG
Associate Professor

S S Ratnam, MBBS, MD, FRCS, FRCS(Edin), FRCSG, FRACS, FACS, FRCOG, FRACOG(Hon), FACOG (Hon)
Professor and Head

Correspondence to : Dr K Singh

MATERIALS AND METHODS

A total of 100 women were recruited to each group. In recruiting acceptors, we followed the principal selection criteria used by the Population Council's International Committee for Contraception Research. Acceptors in the study met the following criteria: they had to be between 18 and 40 years of age, sexually active, of demonstrable fertility (at least one birth), be neither pregnant nor breastfeeding at the time of insertion and have none of the standard contraindications to the use of steroids. Women with a history of liver disease, jaundice, sickle cell anaemia, herpes gestationis or having any evidence of thrombo-embolic disease, hypertension, pelvic inflammatory disease, undiagnosed vaginal bleeding and cancer were excluded from the study. They should be easily followed-up on a regular basis and also were agreeable to use no other contraceptives during the study period.

Women who met all the criteria for conclusion were fully informed about the purpose of the study and the risks and benefits associated with the use of this contraceptive method. Each woman who volunteered to participate in the study was requested to give informed consent by signing a Volunteer Agreement. Each acceptor was also given a complete physical examination including a gynaecological examination before insertion and on subsequent follow-up visits.

Acceptors were asked to maintain diaries of menstrual events throughout their participation in the study. Each woman participating in the study was asked to keep a diary record of her menstrual bleeding events coding '0' for no bleeding, '1' for spotting or light bleeding but no sanitary protection needed and '2' for heavy bleeding where sanitary protection in needed. Data analysis of the daily bleeding calendar is based upon completed 90 day intervals or reference periods (2-4).

Women were told that they could terminate use of implants at any time by returning to the clinic to have them removed. Follow-up of all acceptors was scheduled at 1,3,6 and 12 months after admission and therefore twice yearly. However, the women were encouraged to return to the clinic for any problems that occurred at any time, regardless of the next scheduled follow-up visit. Follow-up of all acceptors at each scheduled visit in the first two years was 100 percent.

RESULTS

(i) Socio-demographic characteristics of acceptors

Selected socio-demographic characteristics of the women in the two groups are presented in Table I.

Table I.
Socio-Demographic Characteristics of Norplant® Acceptors

	Norplant® Acceptors	Norplant®-2 Acceptors
Mean Age (years)	29.5	29.9
Education (years)	7.8	7.7
Parity	2.1	2.1
Women wanting no more children (%)	69.0	80.0
Average height (m)	155.5	154.6
Average weight (kg)	54.8	55.5
Systolic Blood Pressure (mm Hg)	113.8	111.6
Diastolic Blood Pressure (mm Hg)	70.8	70.6

The NORPLANT® six capsule and the NORPLANT®-2 rod acceptors were comparable with regards to age, parity, education. height, weight and blood pressure reading. Any differences noted were not statistically signifant.

(ii) Contraceptive effectiveness

No accidental pregnancy occurred during the two years of NORPLANT®and NORPLANT®-2 implant use (Table II).

(iii) Termination/Removal rates

A total of twenty-one removals were reported in the first two years of NORPLANT® use as compared to twenty-two removals in the group using the NORPLANT®-2 rods.

For the NORPLANT® group, ten implants were removed in women planning for a pregnancy, another ten were removed for menstrual disturbances and there was only one removal for non-menstrual medical problems (Table II). In the NORPLANT®-2 group, eleven removals were in women planning a pregnancy, eight removals were for menstrual disturbances and there were three removals for other non-menstrual medical problems (Table II). These differences were not statistically significant.

Table II.

Two-Year Cumulative Termination And Continuation Rates Per 100 Norplant® Acceptors

Reason/Rate	Norplant® Acceptors	Norplant®-2 Acceptors
Accidental Pregnancy	0.0	0.0
Menstrual Problems	10.0	8.0
Planning Pregnancy	10.0	11.0
Other Medical	1.0	3.0
Total Termination	21.0	22.0
Continuation	79.0	78.0
Number of women/months	2209.0	2175.0

Of the ten removals due to menstrual disturbances in the NORPLANT® group, seven were in women who complained of prolonged bleeding or spotting lasting more than 10 days, two were in women with increased frequency of menstruation and only one removal was for prolonged amenorrhoea (Table III). Similarly in the NORPLANT®-2 group, four removals were for prolonged bleeding or spotting lasting more than 10 days; one removal was for increased frequency of menstruation and three removals were for prolonged amenorrhoea varying from 270-450 days (Table III). The differences between the two groups was minimal and not statistically significant.

Table III.

Menstrual Problems Accounting For Norplant® Implant Removal During The First Two Years

Menstrual Problems	Norplant® Acceptors	Norplant®-2 Acceptors
Prolonged Bleeding/ Spotting	7	4
Frequent Bleeding	2	1
Amenorrhoea	1	3
Total	10	8

The only removal for non-menstrual medical problems in the NORPLANT® group was in a woman who had weight loss of 7 kg over a period of 18 months. In the NORPLANT®-2 group, there were three removals for non-menstrual medical problems; one removal was in a woman who complained of mastalgia throughout the 18 months of NORPLANT®-2 rod use, the second removal was in a woman who complained of persistent nausea and giddiness for 15 months after insertion. The third removal was in a woman who was noted to have a raised blood pressure of 140/100 mm Hg at the one year follow-up. Her blood pressure on recruitment was 130/80 mm Hg. The blood pressure returned to normal within six weeks after removal (Table IV).

Table IV.

Other Medical Reasons For Norplant® Implant Removal During The First Two Years

Eugenic	Norplant® Acceptors	Norplant®-2 Acceptors
Weight Loss	1	-
Mastalgia	-	-
Nausea/Giddiness	-	-
Increased Blood Presssure	-	-
Total	1	3

(iv) Continuation rates

The two-year cumulative life-table rates are presented in Table II. The net termination rate at the end of two years was 21 per 100 women for the NORPLANT® group and 22 per 100 women for the NORPLANT®-2 group. The continuation rate at the end of two year was 79% and 78% for the NORPLANT® and NORPLANT®-2 groups respectively (5,6).

(v) Weight, blood pressure and menstrual changes

Changes in body weight, blood pressure, menstrual cycle length and menstrual flow duration during the two years, for both groups, are shown in Table V. The changes in mean weight, blood pressure and menstrual cycle length are quite similar in booth groups. The main difference was in the menstrual flow duration which decreased by 0.7 days in the NORPLANT® group as compared to an increase of 0.4 days in the NORPLANT®-2 group. However these changes were not statistically significant.

(vi) Adverse experiences

A listing of all adverse experiences reported by the women in both groups during any follow-up visit is shown in Table VI. The adverse experiences reported in both groups were similar and decreased progressively over the two years (5-8). There were only two scheduled clinical visits in the second year as compared to four in the first year. However patients were encouraged to come for unscheduled clinical visits (at any time) should they have any complaints. As such it would appear that the putative decline in the frequency of adverse experiences from year 1 to year 2 is not related to the less frequent clinical visits in the second year. Moreover since each acceptor could have reported more than one adverse experience at any one visit or at different visits, the total number of events in Table VI exceeds the total number of women with adverse experiences.

Table V.

Changes In Clinical Measures At Two Years Of Norplant® Implant Use As Compared To Preinsertion Reading

Clinical Measures	Norplant® Acceptors	Norplant®-2 Acceptors
Mean Weight (kg)	+ 1.7	+ 1.7
Systolic Blood Pressure (mm Hg)	+ 2.4	+ 1.4
Diastolic Blood Pressure (mm Hg)	+ 0.9	+ 2.0
Menstrual Cycle Length (days)	+ 0.3	+ 0.3
Menstrual Flow Duration (days)	- 0.7	+ 0.4

Table VI.

Adverse Experiences Reported At Follow-up Visits By Implant Acceptors In Singapore

Adverse Experience/ Number Reported	Norplant® Acceptors		Norplant®-2 Acceptors	
	Yr 1	Yr 2	Yr 1	Yr 2
Body As A Whole				
Abdominal pain	7		8	1
Chest pain	6		2	
Chills	3		3	
Sleepiness	5		-	
Weakness/fatigue	8	1	6	
Loss of libido			2	
Breast				
Breast pain	1		1	2
Insertion Site				
Haematoma	1		16	
Local reaction	19			
Implants visible		2		
Digestive System				
Anorexia	6		2	
Increase in appetite	3		2	
Nausea	4		2	

Table VI. *(Cont'd)*

Adverse Experiences Reported At Follow-up Visits By Implant Acceptors In Singapore

Adverse Experience/ Number Reported	Norplant® Acceptors		Norplant®-2 Acceptors	
	Yr 1	Yr 2	Yr 1	Yr 2
Metabolic and Nutritional				
Weight increase	6	6	12	4
Weight loss		2		
Musculo Skeletal System				
Arm pain	6		1	1
Back pain	4	1	3	1
Numbness or weakness in arm/hand	5		3	
Weakness in legs	1			
Nervous System				
Dizziness/giddiness	14		8	5
Headache/head pain	4		8	3
Insomnia/Sleeplessness	4		3	
Nervousness	1		-	
Blurred vision			1	
Respiratory System				
Breathlessness	5		2	
Skin and Appendages				
Acne	1		4	
Alopcia	3		1	1
Pruritus	1	1	2	1
Skin rashes	3	1	3	2
Ulcers in mouth	1			
Urogenital System				
Cervical lesion	1			
Enlarged uterus	1			
Ovarian cyst	3			
Vaginal discharge/itch	7	3	13	1
Total number of adverse experiences reported	134	22	108	21
Total number of women reporting adverse experiences	57	16	56	19

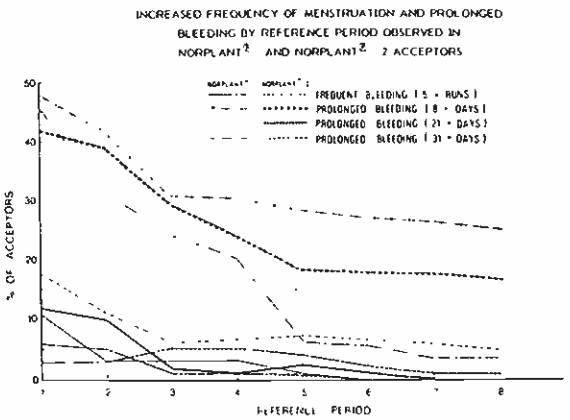
* This tabulation represents all adverse experiences reported at any follow-up visit. It should be noted that any individual woman could report multiple adverse experiences at any given follow-up visit or at different visits during the two years and each occurrence would appear in this table.

(vii) Menstrual pattern changes

In general, frequent bleeding (5+ runs) and prolonged bleeding and/or spotting show a decreasing incidence over time in both groups of acceptors (Fig 1). However from Fig 1, it appears that increased menstrual bleeding is more common in the NORPLANT®-2 group. However this apparent difference is not statistically significant.

The incidence of frequent bleeding (< 2 runs), amenorrhoea and few bleeding days (< 5 days) also decreases over the two years in both NORPLANT® and NORPLANT®- 2 acceptors. Here too it appeared that decreased menstrual bleeding and amennorrhoea is more common in the NORPLANT®-2 group as compared to the NORPLANT® group. However it must be stressed that this apparent difference is again not statistically significant.

Fig 1



(viii) Postmenstrual return of fertility

Postmenstrual conception among the women who had the implants removed due to planned pregnancy

TABLE VII.

Post Implant Removal Pregnancy Rates Per 100 Acceptors In Singapore

Months After Removal	Cumulative Pregnancy Rates	
	Norplant®	Norplant®-2
3	50.0	54.5
6	70.0	54.4
12	90.0	54.5

are as shown in Table VII. For the NORPLANT® group, 50% (5 women) of these women conceived within three months of removal. The rate was 70% by six months and it was 90% at the end of one year. In fact the only woman who had not conceived at one year postremoval was noted to have decided against a planned pregnancy and was now using the condom as a method of contraception. For the NORPLANT®-2 group, 54.5% (6 women) conceived within three months of the removal of the rods. The postremoval conception rates remained the same at six months and after a year of removal. In fact, only one woman out of the five who was not pregnant

at the end of one year postremoval of the rods, was using the condom as a method of contraception. The remaining four were not on any method of contraception. A chi-square test performed showed that there was no significant difference in the postremoval conception rates between the NORPLANT® and NORPLANT®-2 groups.

In both groups, the women who conceived, have had full term normal vaginal deliveries. There has been no untoward incidence of ectopic pregnancy, spontaneous abortion or congenital malformations.

DISCUSSION

The results of this comparative study suggest that the NORPLANT®-2 rod system is an effective, safe and acceptable as the NORPLANT® six capsule system in Singapore. The results are comparable with those of international studies (9-11). As regards reversibility, the 54.5% for NORPLANT®-2 as compared to 90.0% for NORPLANT®. This difference is not statistically significant although it may seem lower than the rate of 76% quoted in other studies (11). However it is still prudent to follow these women and assess their fertility in the future.

Thus considering all factors, it would appear that the NORPLANT®-2 rod system consisting of only two rods as compared to the six capsules in the NORPLANT® system has a great potential for acceptability in terms of ease of insertion and removal.

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