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Acceptability and side effects of Cyclofem© once-a-month injectable contraceptive in Kerman, Iran

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Abstract

Background: When family planning programmes offer a wide variety of contraceptives, contraceptive prevalence would be higher overall.

Objective: To determine the acceptability of Cyclofem© and to evaluate its side effects and continuation rate in Iran.

Materials and Methods: An introductory study of Cyclofem© was conducted in seven districts of Kerman Province, the largest province of Iran, in three phases. At first, 14394 women attending randomly selected urban and rural health centers representing different socioeconomic classes were invited to choose Cyclofem© after a standard schedule of counselling. At the second phase 418 of those who accepted Cyclofem© and 354 of those who refused to use the method were randomly selected to participate in an interview. At the third phase the first group was followed up for one year at regular one-month intervals.

Results: Nearly 12.6% (n=1809) of 14394 women counselled to choose Cyclofem© accepted the contraceptive method. They had a mean (±SD) age of 28.5 (±6.5) years. Fear of side effects was the most common cause of refusal to use Cyclofem©. The one-year continuation rate was 21.2%. The three main side effects leading to early discontinuation of Cyclofem© were nausea (18%), prolonged menses (15.8%), and amenorrhea (14.7%), respectively.

Conclusion: The one-year continuation rate of Cyclofem© use in Iran has been lower than other countries. Further research is necessary to improve continuation rates.

Key words: *Injectable contraceptives, Side effects, Family planning, Cyclofem©, Iran.*

Introduction

Over the last two decades, Iran has achieved significant success in terms of family planning (1). Some authorities have recognised Iran as a model for other developing countries in this era (2, 3). However, despite this success in family planning, Iran`s family planning has failed to address unwanted pregnancies (4) so that population growth in Iran is still unexpected in the future years. This goes back to lack of population control in 1980s and then marriage amongst those large populations born in the 80s (1). On the other hand, recent reports indicate that there is a high rate of unplanned pregnancy (4) and induced abortion in the country (5, 6). According to investigations, one third of pregnancies in the capital city (Tehran) have been unplanned (4). This has led to significant rate of illegal abortions and therefore putting mothers' health at risk (6). One way of extending family planning coverage, would be providing the option of choosing among different methods of contraception (7). Using Cyclofem© as an injectable once-monthly hormonal contraceptive has been increasing around the world

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over the last two decades (8). Cyclofem© injection consists of 25 mg Medroxy Progestrone Acetate and 5 mg Estradiol Cypionate (8). Despite the use of Cyclofem© in many countries and reports from WHO regarding its efficacy and safety (9), this method has just been introduced in Iran`s family planning program. The failure rate of the method has been reported to be less than 0.5% at one year of use (8). One study conducted to compare the bleeding patterns of Cyclofem© and DMPA (depot medroxyprogesterone acetate) users found no difference between the two methods (10), and the main menstrual side effect of both methods was spotting (10). The only published study on the reasons for discontinuation of DMPA was a retrospective study including a total of 900 women referring to health centers in Tehran (11). The three most frequent reasons for the discontinuation of the method were amenorrhea (50.6%), headache (33.5%) and depression (28%). On the other hand, amenorrhea was the most important reason (50.6%) for deciding to discontinue the DMPA (11). To the best of our knowledge, no study has addressed the acceptability of injection methods in Iran. Considering that acceptability of any contraception method depends on its nature, customer service quality and the consumer's characteristics, it is suggested to conduct an introductory study before the widespread use of any contraceptive method (12). Such a study, not only would improve our understanding of customers' views, but also would help authorities in planning the needed changes (13).

Materials and methods

This cross-sectional study was approved by the Ethics Committee of the Kerman University of Medical Sciences. It was conducted in Kerman province, the largest province of Iran. Of 14394 consecutive eligible women who received family planning counselling in both urban and rural areas of 7 districts of the province (two urban and two rural health centers from each district) during a one month period, 1809 subjects (12.6%) chose to use Cyclofem© injection. Three hundred fifty-four of those who refused, and 418 of those who accepted the method entered the study through systematic random sampling. We calculated that at least 350 subjects would be required to have 90% power to detect an odds ratio of 1.5 patients. The sample size was calculated with PASS software version 6.0. Participants in both groups provided demographic information including their age, number of children, place of residence, education level, occupation and the current method of contraception. If a subject refused Cyclofem© injection, the main reason would be clarified from her. Cyclofem© injection was applied as deep intramuscular every 30±3 days and probable side effects were investigated. Cyclofem© injection was applied only if the subject met required criteria according to WHO. Exclusion criteria included (14): pregnancy, lactation, abnormal uterine bleeding, history or presence of liver, renal, cardiovascular disease, cerebrovascular disorders and thromboembolism; history or presence of any malignancy; hypertension and chronic conditions requiring treatment (e.g., diabetes). Noticeably, all methods of contraception including Cyclofem© are supplied through public health system, free of charge. The acceptors were followed up for one year at regular one-month intervals and the possible side effects were recorded.

Statistical analysis

To assess the association between selected characteristics and acceptance of Cyclofem© use multivariate logistic regression was used. The Kaplan-Meier method was used for analysis of continuation rate of Cyclofem©.

Results

Mean (±SD) age of Cyclofem© acceptors was lower than non-acceptors (28.5±6.5 and 30.5±6.8, respectively, $p<0.001$) and rural residents were more likely to accept the method (adjusted OR= 1.9, CI 95%: 1.4-2.6). Selected baseline characteristics of both groups and their association with acceptance of Cyclofem© use are shown in Table I. The odds of acceptance were highest among those who were DMPA users. Table II summarizes the reasons for non-acceptance of Cyclofem© by women who received counselling. The main reason for non-acceptance was fear of side effects (54%). One-year continuation rate for the method was 21.2%. The mean survival time for the method was 173.1±8.2 days. Overall 203 individuals (48.6%) continued the method through the first 3-months period and 123 subjects (29.4%) continued it for 6 months. Nearly 54% (144 out of 278 women) of reasons for discontinuation of Cyclofem© were related to changes in menstrual pattern (Table III). The three main side effects leading to early discontinuation of Cyclofem© were nausea (18%), prolonged menses (15.8%), and amenorrhea (14.7%), respectively. Roughly more than 80 percent of side effects occurred in the first three months of Cyclofem© use (Table IV).

Table I. Logistic regression analysis to assess the association between selected characteristics and acceptance of Cyclofem© use*.

Characteristic		Cyclofem© acceptance		Adjusted odds ratios	95% confidence intervals	p- value
		Yes (n=418)	No (n=354)			
Mean age (±SD)		28.5±6.5	30.5±6.8	0.94	0.92-0.97	0.001
No. of children (±SD)		2.4±1.5	2.1±1.4	NA**	NA	NA
Place of residence	Urban	152(36.4%)	189(53.4%)	Ref	--	0.001
	Rural	266(63.6%)	165(46.6%)	1.89	1.37-2.61	
Education	Illiterate/Primary school	54(12.9%)	36(10.2%)	Ref	--	--
	Incomplete secondary	228(54.6%)	176(49.6%)	0.84	0.49-1.41	0.51
	Complete secondary	121(28.9%)	111(31.4%)	0.76	0.42-1.37	0.37
	College	15(3.6%)	31(8.8%)	0.36	0.13-0.98	0.04
Occupation	Housewife	403(96.4%)	335(94.6%)	Ref	--	--
	Others	15(3.6%)	19(5.4%)	0.60	0.23-1.62	0.32
Method of contraception	Pills	206(49.2%)	112(31.6%)	Ref	--	--
	Condom	69(16.6%)	97(27.4%)	3.50	2.34-5.22	0.001
	DMPA	73(17.4%)	20(5.6%)	7.30	3.95-13.50	0.001
	IUD	10(2.4%)	8(2.3%)	2.98	1.06-8.35	0.038
	None	60(14.4%)	114(33.1%)	1.53	0.97-2.53	0.06

* Only variables with p<0.25 in bivariate analysis were entered in the final model . ** NA=not applicable

Table II. Main reasons for non-acceptance of Cyclofem© in 354 women who received family planning counselling.

Reason	No.	%
Fear of side effects	191	54.0
Satisfied with the current contraceptive method	56	15.8
Fear of injection	28	7.9
Difficult to come for visits	28	7.9
Wish for pregnancy	18	5.1
Absolute or relative contraindication*	18	5.1
Others	15	4.2

*Those who accepted to receive Cyclofem© but were excluded due to concomitant diseases or conditions

Table III. Reasons for discontinuing Cyclofem© in acceptors (n=418).

Reason	No.	%
Prolonged bleeding	44	15.8
Amenorrhea	41	14.7
Irregular bleeding	26	9.4
Frequent bleeding	21	7.6
Infrequent bleeding	12	4.3
Nausea	50	18.0
Headache	17	6.1
Weight gain	6	2.2
Weight loss	2	0.7
Dizziness	5	1.8
Husband objection	4	1.4
Desire for pregnancy	4	1.4
Others	46	16.6

Table IV. Frequency of reported side effects of Cyclofem© according to the time of onset during the one year follow up study of acceptors (n=418).

Reason	0-3 months		3-6 months		6-12 months		Total	
	No.	%	No.	%	No.	%	No.	%
Prolonged bleeding	80	83.3	10	10.4	6	6.3	96	23.0
Infrequent bleeding	65	78.3	15	18.1	3	3.6	83	19.9
Irregular bleeding	73	88.0	7	8.4	3	3.6	83	19.9
Weight gain	52	76.4	8	11.8	8	11.8	68	16.3
Frequent bleeding	59	88.1	3	4.5	5	7.4	67	16.0
Amenorrhea	46	80.7	5	8.8	6	10.5	57	13.6
Headache	47	87.0	7	9.3	2	3.7	54	12.9
Nausea	44	83.0	7	13.2	2	3.8	53	12.7
Weight loss	40	88.9	3	6.7	2	4.4	45	10.8
Dizziness	27	77.1	8	22.9	0	0	35	8.4

Discussion

Although it has been more than 2 decades since Cyclofem© was introduced to the market, authorities are still focusing on research around increasing acceptability of this product in developing countries (15). In this study, 21.2% of subjects continued to use Cyclofem©. The most common reason for stopping this method was menstrual changes.

Of all clients seeking family planning services, nearly 12.6% chose Cyclofem© injection. The lowest acceptability rate was among individuals using contraceptive pills while the highest rate referred to the ones on DMPA injection (7.3 times higher than pills) and those using condoms (3.5 times higher than pills) (Table I). The percentage of Cyclofem© acceptance in rural residents was two times more than that of urban residents which may be due to more active follow ups in rural health centers comparing to urban ones. As education years progress, women are less likely to accept Cyclofem© (Table I) which shows the higher compliance of less educated women. Acceptors showed a lower mean age than nonacceptors and the higher the education the lower was the acceptance rate, which a similar pattern was also seen in the study conducted on Kenyan women (16).

The highest rate of acceptability was seen in those who were already on DMPA (Table I), which may be due to the similar route of use and the high rate of side effects seen with DMPA (11). In Kenya, most of women who chose Cyclofem© and had previous history of contraception, were previous OCP users (16). Also in Indonesia, acceptability rate for combined injectable contraceptives was more than Progestrone-only injectables (15). However, in Kenya the one-year continuation rate for DMPA was higher than Cyclofem© (16). Anyhow, understanding the "profile of ideal consumer" (12) helps with social marketing of the product.

Fear of side effects has been mentioned as the most important reason for refusing the Cyclofem method (54%) by non-acceptors (Table II). In the initial introduction of a new method, myths would usually trigger unacceptance especially if people realise this method is still under research (12). However, effective education and counselling would solve this problem to a great extent (17).

In this study, 12 month continuation rate of Cyclofem© use (21.2%) was less than of other Muslim countries. In Indonesia and Tunisia, the above mentioned rate was 66.5% and 28.2% respectively (8). In an introductory study conducted in Mexico, the rate of 1 year continuation of Cyclofem© was 25.1% (12). Although the continuation rate in Mexico has been relatively the same as the one we achieved in our study, it is noted that there's been a considerable public acceptance of this method in Mexico (8). In all likelihood the low continuation rate may be due to shortcomings in the provision of the initial counselling (particularly with regard to menstrual changes) and later guidance of users (18-20).

"Menstrual changes" has been noted as the most important reason for discontinuing Cyclofem© (Table III). However, in many countries it has been one of the most frequent complaints but not the main reason for stopping the method. In Indonesia, "personal reasons" has been mentioned as the main reason of early discontinuation of the method (18). According to Graza-Flores, only one-third of discontinuations

were method related (8). It is noteworthy to mention that there was no report of pregnancy amongst Cyclofem© users during the period of the study.

It has been proved that women's reaction to menstrual changes is highly related to socio-cultural factors (19). In Muslim countries, there is higher sensitivity towards menstrual changes due to disturbance of religious practice. Also, sexual activity is of more sensitivity (12). Previous experience on Norplant© in Iran showed that the main reason for discontinuing the contraceptive method implant was "menstrual changes" (20). Although this side effect seems to be a significant barrier in continuous usage of the method, studies in other countries have shown that after 6 months of using the method, most women get back to their normal menstrual pattern (9). Therefore, an efficient counselling could play a significant role so that Cyclofem would not be removed from public health system in Iran as happened to Norplant (20). It is suggested to conduct similar studies in Iran on "women's responses to menstrual changes" so it would be easier to plan for providing contraceptive methods (19). Side effects of Cyclofem© injection were mostly noted in the first 3 months of usage (Table IV). The most frequent side effects such as hypermenorrhea, hypomenorrhea and oligomenorrhea were resolved after 6 months in more than 90% of subjects.

Relevant studies have also shown that side effects of Cyclofem©, particularly "menstrual changes" would decrease by time. In Kenya, prevalence of spotting went down to zero after a 12 month period of usage (16). Also in Mexico, there was a significant decrease in menstrual disturbances after 12 months of usage (21). Hence, this issue should be considered in counselling sessions (8). Furthermore, it is noteworthy that methods that required action by user less frequently than once daily would be of more effect and less cost (22). In a retrospective study conducted on DMPA in Iran it was relieved that menstrual changes was the main reason for discontinuation of the method (11). On the other hand, immunohistochemical studies on Iranian women have been shown that those who used Cyclofem© or DMPA for three to six months had the same endometrial vascular density (10).

The findings of the present study should be generalized with caution, since rural residents consisted about half of our study sample, whilst it was expected that one-third of the sample would be rural.

Overall, although the one-year continuation rate of Cyclofem© use in Iran has been lower than other countries, it should be noted that adding a contraception method to current ones would extend the family planning coverage. Therefore, it is recommended that Cyclofem© be available along with already available contraceptive choices (i.e., pills, condom, DMPA, IUD, tubal ligation, vasectomy) through public health system. However, it should be put in mind that effective counselling for women who decide to use Cyclofem© would be a crucial element. Clearly, further research is necessary to improve continuation rates.

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