

THE REASONS OF DISCONTINUATION OF TCU380A IUD AND COMPARE IT WITH THE NANO-CU IUD

Negin Mirzaee, A.I. Marakhova

Peoples' Friendship University of Russia, Institute of Biochemical Technologies and Nanotechnologies;
Miklukho-Maklaya St., Build. 10/2, Moscow, 117198, Russian Federation

INFORMATION ABOUT AUTHORS

Negin Mirza – Master student of the Institute of Biochemical Technology and Nanotechnology PFUR, Islamic Republic of Iran. Tel.: +7 (929) 989-44-90. E-mail: neginm993@gmail.com

Marahova Anna Igorevna – Doctor of Pharmaceutical Sciences, Professor of the Institute of Biochemical Technology and Nanotechnology, Peoples' Friendship University of Russia/ Tel.: +7 (926) 600-65-95. E-mail: agentcat85@mail.ru.

Introduction. The study was conducted to the reasons of discontinuation of TCu380A IUD and compare the antifertility effectiveness and side effects of the copper/low-density polyethylene nanocomposite IUD and the copper TCu380a IUD. Intrauterine devices are available in two types: 1 – copper, made of plastic and copper (TCu220c or TCu380a), releasing copper ions that have a spermicidal effect; 2 – hormonal type (Mirena), made of plastic, releasing levonorgestrel, synthetic progesterone. This study is devoted to a comparative study of two variants of copper intrauterine devices: TCu380a-IUD and Nano-Cu IUD.

Materials and methods. Three hundred women who had a TCu380a inserted from June 2012 to June 2013 were selected for interviews in a 45 days period in 2017. The women were registered in the medical health centers of Sanandaj City, Iran. The criteria for entering the study were just the departure of the IUD during this time period. The increase in bleeding is the main reason for premature discontinuation of IUD (TCu380a) use.

Results and conclusions. There were no statistically significant differences in the incidence of menstrual disorders (eg, dysmenorrhea, intermenstrual pelvic pain or intermenstrual bleeding) between two groups of patients with different types of IUD. According to the studies, TCu380a and TCu220c are almost identical in terms of undesirable reactions. In Nano-Cu IUD, the incidence of side effects was lower than in the TCu220c IUD, especially in the manifestation of severe menstrual bleeding. According to the results of and clinical trial, it is suggested that the new design of the Nano-Cu/LDPE IUDs may be a replacement for the conventional copper IUDs and deserves further study for clinical utilization and to solve the disadvantages of conventional IUDs.

Key words: Contraception, Intrauterine Device, Cu/LDPE Nanocomposite, Vaginal Bleeding, Indomethacin

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INTRODUCTION

An intrauterine device (IUD) is a small T-shaped plastic device that is placed inside the uterus to prevent pregnancy [1]. TCu380A has a polyethylene frame wound with 176 mg of copper wire on the stem and collars, and contains 66.5 mg of copper on each of its transverse arms. The total exposed surface area of copper is approximately 380 mm² [2, 3]. The intrauterine device comes in two types, a copper IUD which is made of plastic and copper (TCu220cor TCu380a), and a hormone releasing IUD (Mirena) which is made of plastic and contains levonorgestrel, a synthetic progesterone, that is released slowly into the uterus [1]. Also TCu380a IUD is used in Iran 16%.

The generally recommended duration of use is between 3 and 10 years, depending on the device [4]. The study was designed to determine the factors influencing the IUD discontinuation among women referring to health care centers. The contraceptive mechanism of copper IUDs is mainly to prevent fertilization by stimulating a cytotoxic intrauterine inflammatory reaction that is spermicidal. Furthermore, the IUD changes the intrauterine environment to make it more hostile for implantation [4]. Before insertion, a bimanual examination and a sounding of the uterus are necessary to determine the uterus position and the depth of the uterine cavity. The IUD is inserted into the uterus according to individual protocols, with the threads cut at a

length to allow the patient to check the device's position [5].

In order to decrease the side effects and increase contraceptive efficacy, a new type of copper/low-density polyethylene (LDPE) nanocomposite IUD was invented [6]. Copper/Low-Density-Polyethylene (Cu/LDPE) Nanocomposites have been prepared using a melt-blending technique in a single-screw extruder. The Cu/LDPE nanocomposites is a hybrid of the copper nanoparticles and the polymer matrix, the copper nanoparticles aggregates is existed and distributed uniformly in the matrix in general [7, 11].

Purpose of the Study. The purpose of this study is to explore the reasons of discontinuation of TCu380A IUD and compare TCu380a-IUD and Nano-Cu IUD.

MATERIAL AND METHOD

This is a cross-sectional study. The population under study is all women who are covered by health centers in Sanandaj who have had a history of discontinuing use of IUD. Time to do research: 1 July 2017 – 15 august 2017. The criteria for entering the study were just the departure of the IUD during this time period. Personal-social profile data was obtained through interviews. The date of placing the IUD from the case was obtained. The causes of premature withdrawal of IUD and its association with the duration of use were examined. Three hundred women who had a TCu380a inserted from June 2012 to June 2013 were selected for interviews in a 45 days period in 2017.

EXPERIMENTAL

At the time of IUD insertion, the mean age of the interviewed subjects was 27±4.83 years, ranging from 16 to 46 years. All women (100%) had at least one child at the time of IUD insertion. A total of 59.8 of the women reported that they had no Pap smear test during the 3 years preceding the study (Table 1).

In the present study, the increase in bleeding is the main reason for premature discontinuation of IUD use. Increased or prolonged vaginal bleeding has been described as the most common side effect of IUDs and could be related to the copper content of the IUD. It is believed that these side effects are related closely to their burst release of cupric ions and the endometrial injury caused by the inserted Cu-IUDs. The possible association between use of IUDs in general and pelvic inflammatory disease [PID] has been a concern, and it has led to a decrease in IUD use mainly in the United States. Less than 1 out of 100 women who have been using an IUD for one year will

fall pregnant. Miscarriage and premature birth can occur in the rare occurrence that a woman becomes pregnant whilst an IUD is in place (Table 2).

RESULTS AND DISCUSSION

Nano-Cu IUD

In order to decrease the side effects and increase contraceptive efficacy, a new type of copper/low-density polyethylene (LDPE) nanocomposite IUD was invented [6]. Apparently, two solutions can be adopted to mitigate these side effects of the existing Cu-IUDs, one is the controlled release of cupric ions, and the other is the application of anti-inflammatory drugs. Imaginably, the combined application of these two solutions will have the most desirable efficiency [8]. Therefore, there is a particularly pressing need to develop a novel IUDs material that can control the release of both anti-inflammatory drugs and cupric ions. Many years ago, copper/low density polyethylene (Cu/LDPE) composite, a cupric ions controlled release system, has been designed and developed successfully [8, 12]. The Cu/LDPE nanocomposite sample was formed by compounding the LDPE powders with 15.0 wt. % copper nanoparticles (Nano-Cu) by using a melt-blending process in a single-screw extruder at a screw speed of about 15–20 rpm. Its mean diameter is about 50 nm and purity is over 99.9% [9].

The results of the experiment demonstrated that the Nano-Cu/LDPE material exhibited more satisfactory contraceptive efficacy with less effect on the endometrium prostaglandin E2 (PGE2) and tissue plasminogen activator (TPA) levels than bulk copper. After inserting this new type of material, the results demonstrated that it had high contraceptive effect, low rates of side effects and reliable safety [6].

Table 1

CHARACTERISTICS OF IUD USERS (n=300)

Age (years)	
<25	35,6%
25–30	27,2%
31–35	21,5%
>35	15,7%
Number of Children Alive	
1	45.6%
2	34.2%
>3	20.2%

LIFE TABLE ANALYSIS

Type of termination	Month							Total
	1	6	12	24	36	48	60	
Pain/bleeding	24	19	16	13	8	5	3	122
Expulsion	2	5	8	9	15	19	22	80
Planning pregnancy	0	0	1	3	5	9	13	31
PID	1	2	0	1	2	4	6	16
Recurrent infection	0	2	1	2	3	1	2	11
Cervicitis	1	0	2	1	1	3	2	10
Pregnancy with IUD	0	1	2	1	1	2	1	8
Movement	7	5	2	1	0	3	4	22

According to the results of animal experiments and clinical trial, it is suggested that the new design of the Nano-Cu/LDPE IUDs may be a replacement for the conventional copper IUDs and deserves further study for clinical utilization and to solve the disadvantages of conventional IUDs.

Except for the controlled release of cupric ions, anti-inflammatory drugs can also be applied to avoid these side effects of the existing Cu-IUDs. Indomethacin (IDM) is one of the most potent of the clinically used non-steroid anti-inflammatory drugs [8].

A novel functional material, indomethacin/copper/low density polyethylene (IDM/Cu/LDPE) porous composite, has been developed for medicated copper intrauterine devices (Cu-IUDs). Samples of the IDM/Cu/LDPE porous composite were prepared by a combined technique involved in injection molding, particulate leaching, IDM solution incubating, and solvent vacuum drawing. Although IDM/Cu/LDPE composite with compact structure has been prepared. Its IDM release rate is too low and its IDM release duration is too short to meet the need for clinical use. This novel medicated Cu-IUDs material not only can control their release of IDM, but also can control their release of cupric ions, and that its release properties can be regulated easily by controlling its amount of introduced porosity. It is only a simple hybrid of IDM, copper particles and LDPE, and both the IDM and the copper particles are generally distributed homogeneously in its porous LDPE matrix [8].

Comparison

Since IUD380 and IUD220 are both made from copper and their functions are the same, in this

paper we can make a comparison between copper IUDs (TCu220c and TCu380a) and Nano-IUD. No statistically significant differences were observed in the frequency of experiencing menstrual disturbances (i.e., dysmenorrhea, intermenstrual pelvic pain or intermenstrual bleeding) between the two IUD groups. According to studies, TCu380a and TCu220c are almost identical in terms of disadvantages [10]. In the Nano-Cu IUD, the incidence of side effects was lower than in the TCu220c IUD, especially excessive menstrual bleeding and spotting. There were significant differences between the two groups (Table 3) [6].

CONCLUSIONS

The study suggested that the TCu380a IUD also had high contraceptive efficacy, but had relatively more side effects. Increased or prolonged vaginal bleeding has been described as the most common side effect of copper IUDs.

It may be necessary to use other types of IUD that result in less pain and bleeding. According to the results of animal and clinical trial, it is suggested that the new design of the Nano-Cu IUDs may be a replacement for the conventional copper IUDs. The new design of the copper/low-density polyethylene (LDPE) nanocomposite IUD and IDM/Cu/LDPE showed low pregnancy rate, high contraceptive efficacy and lesser side effects.

Конфликт интересов

Авторы заявляют об отсутствии конфликта интересов.

Conflict of interest

The authors declare no conflict of interest.

**CHARACTERISTICS OF DIFFERENCES BETWEEN GROUPS
OF PATIENTS USING Nano-Cu IUD and TCu220c IUD**

Complaints	Rate of side effects after insertion, %							
	Nano-Cu IUD				TCu220C (TCu380A IUD)			
	1th month	3th month	6th month	12th month	1th month	3th month	6th month	12th month
Excessive Menstrual Bleeding	16,0	8,3	4,3	2,2	34,0	23,4	15,2	10,9
Spotting	6,0	0,0	0,0	0,0	20,0	12,8	6,5	4,3
Pelvic Pain	6,0	0,0	0,0	0,0	10,0	14,9	6,5	2,2
Excessive Leucorrhea	0,0	0,0	0,0	0,0	2,0	2,1	0,0	0,0

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ПРИЧИНЫ ПРЕКРАЩЕНИЯ ИСПОЛЬЗОВАНИЯ ИМПЛАНТА TCu380A IUD И ЕГО СРАВНИТЕЛЬНОЕ ИЗУЧЕНИЕ С ИМПЛАНТОМ NANO-CU IUD

Негин Мирзайи, А.И. Марахова

Российский университет дружбы народов, Институт биохимической технологии и нанотехнологии; Российская Федерация, 117198, Москва, ул. Миклухо-Маклая, д.10/2

СВЕДЕНИЯ ОБ АВТОРАХ

Негин Мирзайи – магистрант Института биохимической технологии и нанотехнологии РУДН, Исламская Республика Иран. Тел.: +7 (929) 989-44-90. E-mail: neginm993@gmail.com

Марахова Анна Игоревна – доктор фармацевтических наук, профессор Института биохимической технологии и нанотехнологии РУДН, Россия. Тел.: +7 (926) 600-65-95. E-mail: agentcat85@mail.ru.

РЕЗЮМЕ

Введение. Исследование посвящено рассмотрению причин прекращения использования импланта TCu380A IUD и сравнению антиретровирусной эффективности и побочных эффектов двух имплантов: из нанокompозитной меди с полиэтиленовым полимером низкой плотности (TCu380a IUD) и меди с наночастицами (Nano-Cu IUD). Имплант (IUD) представляет собой небольшое T-образное пластиковое устройство, которое помещается внутри матки, чтобы предотвратить беременность. Внутриматочные устройства выпускаются 2 типов: 1) медное, изготовленное из пластика и меди (TCu220c or TCu380a); высвобождает ионы меди, обладающие спермицидным действием; 2) устройство гормонального типа (Mirena), изготовленное из пластика; высвобождает левоноргестрел, синтетический прогестерон. Данное исследование посвящено сравнительному изучению 2 вариантов медных внутриматочных устройств: Tcu380a IUD и Nano-Cu IUD.

Материал и методы. 300 женщин были подвергнуты имплантированию TCU380a с июня 2012 по июнь 2013 г. Был организован их опрос в течение 45 дней в 2017 г. Женщины были зарегистрированы в медицинских центрах города Саннанджа, Иран. Критерии отбора для исследования – использование пациентками IUD в течение этого периода времени. Увеличение кровотечения – основная причина преждевременного прекращения использования (TCU380a).

Результаты и заключение. Не наблюдалось статистически значимых различий в частоте возникновения менструальных нарушений (например, дисменорея, межменструальная боль в области таза или межменструальное кровотечение) у пациенток 2 групп, которые применяли разные типы IUD. Согласно исследованиям, TCU380a и TCU220c практически идентичны с точки зрения нежелательных реакций. В Nano-Cu IUD частота побочных эффектов была ниже, чем в BMS Icu220c, где наблюдались сильные менструальные кровотечения. По результатам опроса пациенток и клиническим испытаниям можно сделать вывод: новый дизайн Nano-Cu/LDPE IUDs – адекватная замена для обычных медных IUD и заслуживает дальнейшего изучения в целях клинического использования и устранения побочных эффектов традиционных IUD.

Ключевые слова: контрацепция, внутриматочная дисфункция, Cu / LDPE anocomposite, вагинальное кровотечение, индометацин

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