

## Short-Term Use of Injectable Contraception: An Effective Strategy for Safe Motherhood

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### Introduction

Use of contraception is a substantial and effective preventive strategy to reduce maternal mortality, especially in developing countries. Numbers of unintended pregnancies and unmet contraceptive need are still high in many developing countries, and hence abortion-related deaths are also very high. Every two hours a woman dies from an unsafe abortion in India! Hence, the problem of unsafe abortions is especially acute. There were 620,472 reported abortions in 2012; experts say the true number of abortions performed in the country could be as high as 7 million, with two-thirds of them taking place outside authorized health facilities [1]. The global perception is also stark; the number of women with an unmet need for family planning has been projected to grow to 962 million by 2015.

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## Safe Motherhood Programme

Good antenatal care, intrapartum care, post-partum care and appropriate use of contraception are four ways to achieve safe motherhood.

Contraceptive use averts almost 230 million births every year, and family planning is the primary strategy for prevention of unwanted pregnancies [2].

A study showed that 342, 203 women died of maternal causes in 2008, but that contraceptive use averted 272, 040 (uncertainty interval 127 937–407 134) maternal deaths (44% reduction), so without contraceptive use, the number of maternal deaths would have been 1 × 8 times higher than the 2008 total. Satisfying unmet need for contraception could prevent another 104 000 maternal deaths per year (29% reduction) [3].

So now the question is how to satisfy this unmet need for contraception? Are all choices safe and effective? Which methods are being commonly used? Because of increasing numbers of divorces and other social issues, global trends are changing in favour of long-acting reversible contraceptive methods rather than permanent methods [4]. However, in developing countries permanent methods are still widely practised, so an ideal strategy for planning of a family would be adopting a short-acting method before first pregnancy, followed by either a short- or a long-acting method for spacing and a very long acting reversible or a permanent method as per need of the patient.

## Why Injectable Contraception is a Better Option as a Tool Towards Safe Motherhood?

Choice of contraceptive methods will depend upon various factors like reversibility, efficacy, safety, acceptance, accessibility and availability of devices, availability of skilled providers and user dependence, frequency of sexual activity and personal preferences of a method. Today we have a wide choice of hormonal contraception which can be administered by various routes like oral, injectable, transdermal, transvaginal or intrauterine. Even though the ideal contraceptive is yet not available, injectable hormonal contraception will be rated high among various choices. They have the best balance of all the parameters of any contraceptive method. They are less user dependent than combined oral contraceptives, progesterone-only pills (POP)s. We have understood the human behaviour over the last 50 years and learnt that nonuser-dependent long-acting methods would result in greater acceptance and efficacy. Even though the perfect use of combined oral contraception (COCs) and progesterone-only contraception (POCs) carries <.1/HWY

failure rate, typical use carries a very high failure rate leading to unintended pregnancies.

Our experience and literature reports show that the discontinuation rate of injectables is very high [5].

So use of these methods beyond 2 years may not be practised and may lead to unintended pregnancy. So if we advise these methods as interim methods till the time the couple makes a decision of accepting a nonuser-dependent terminal method with lowest failure rate, we will achieve near-total abortion-free population. This will reduce the abortion-related and of course other maternal deaths which would occur by nonusage of contraception in general.

Depot medroxyprogesterone acetate (DMPA) and norethisterone-enanthate (NET-EN) are the two progesterone-only injectable contraceptives (POICs) available. DMPA is licensed as a first-line contraceptive for long-term and short-term use. NET-EN is licensed for short-term use (up to two injections) by women whose partners undergo vasectomy, until the vasectomy is effective, and by women immunized against rubella, to prevent pregnancy until immunity develops [6].

However, apart from these indications for short-term use, there are many clinical situations where conventional reversible or very long acting reversible (LARC) or permanent methods cannot be advised and are contraindicated or cannot be used by the couple. In some situations, the couple is in indecisive phase as to which method to choose for long-term contraception.

In all these situations, the couple may land up in an unintended pregnancy and then MTP will also be risky and continuation of pregnancy will also be risky. Progesterone-only contraception method has very few contraindications hence can be used in many high-risk situations, when other methods are contraindicated, and can be followed up and actually provided by less skilled health workers. If these are adopted by policy makers, it will help reduce or almost eliminate unintended pregnancies.

The situations are listed in Table 1.

**Table 1** Clinical situations when DMPA use will prevent unintended pregnancy

Misplaced CuT
Failure of COC
Anaemia
Heart disease
Liver disease[recent, past]
Not willing for conventional methods
Pelvic inflammatory diseases
Post-missed abortion
Patient indecisive
Post-vasectomy
DMPA use by choice

### How Does POIC Compare with Other Contraceptive Methods?

We have defined short-acting methods as those which need to be used less than once a month, long-acting methods as those which need to be used every one to three months, very long acting methods as those that need to be administered every 2–10 years and irreversible methods to be administered only once. As per timing and frequency of usage, these methods have been categorized as follows and compared in Table 2.

### Overview of Types of Injectables and Dosages

#### Combined Injectables

- Combination of 25 mg of medroxyprogesterone acetate and 5 mg of estradiol cypionate (MPA/E<sub>2</sub>C) is to be given monthly. These appeal to women who are concerned about daily pill administration and those who prefer regular cycles to amenorrhoea. Currently, oestrogen-related contraindications are almost similar as those for combined OC.
- Norethisterone-enanthate 50 mg plus estradiol valerate 5 mg.

These may be useful for women in whom oestrogen use is not contraindicated, But these will lose the advantage of eliminating the drawbacks of oestrogen and will carry disadvantage of need for monthly injections. It may be then safer to use POICs.

### POIC

- Depo medroxyprogesterone (DMPA) is an aqueous suspension for intramuscular injection: at a dose of 150 mg (in 1 ml) every 12 weeks.
- Norethisterone-enanthate (NET-EN) is a thick oily fluid for intramuscular injection: at a dose of 200 mg (in 1 ml) every 8 weeks.

With each of these, there is a sharp rise in progestogen blood concentration over one to 2 days, followed by a gradual decline over the following weeks.

- Micronized formulation of DMPA is to be given subcutaneously at a dose 104 mg every 12 weeks. The subcutaneous formulation also suppresses ovulation for more than 13 weeks in all subjects and is not affected by body mass [7].

### Efficacy

In a multinational RCT, comparison of DMPA to NET-EN showed failure rates as 0.1% versus 0.4% at 1 year and 0.4% in both groups at 2 years [8].

A cohort study in Kenya (n = 1076) reported a pregnancy rate of 1.5% in TCU 380A users, 2.1% in users of a COC, and 0.3% in DMPA users at 1 year [9].

Our study of 108 patients given DMPA did not report a single unintended pregnancy when DMPA was used as an interim method and followed up to a maximum of 2 years [10].

It is proven beyond doubt that it is a highly effective method, so its preferential use will practically eliminate

**Table 2** Comparison of Various Methods

	Short acting (reversible)			Long acting (reversible)	Very long acting (reversible)	Irreversible
Frequency and timing of usage	On demand	Daily	Once or twice weekly	Once in three months	Once in 2–10 years	Once only
Administration by	Self	Self	Self	Provider or self	Skilled provider	Skilled provider
Ease	Good	Good	Good	Moderate	Moderate	Moderate
Privacy	Good	Good	Good	Good	Moderate	Poor
Necessary provider skill	Not necessary	Not necessary	Not necessary	Paramedics already trained Minimal	Highly skilled provider required	Skilled specialist with requisite training
Perfect use and typical use	Irregular typical use common	Irregular typical use common	Irregular typical use common	If forgotten, delay up to 2 weeks permitted	–	–
Discontinuation rate <sup>9</sup>	High	80%/1 year	–	39%/1 year	20%/1 year	–
Side effects	–	Thromboembolic phenomenon	–	Weight gain, Irregular bleeding	Irregular bleeding	Risks inherent to surgery
User dependency	High	High	High	Low	Nil	Nil
Return of fertility	Immediate	Immediate	Late	Late up to 1 year	Immediate	Never
Pregnancy rates or failure rate <sup>9</sup>	–	2.1% after 1 year	–	0.3% after 1 year	1.5% after 1 year	–

unwanted pregnancy as its typical and perfect use both are equally effective as against COCs and other short-acting methods.

### Discontinuation Rates

The overall discontinuation rate for all reasons among DMPA users is around 50% at 1 year. The discontinuation rate due to bleeding problems is between 30 and 40% among DMPA users [5].

### Reasons for Discontinuation

- Bleeding problems occur in 20 to 40% of DMPA users. Counselling women about bleeding disturbances reduces discontinuation rates. Ethinylestradiol and mefenamic acid may be effective in the management of bleeding problems associated with DMPA use.
- Counselling about bleeding disturbances associated with DMPA use is beneficial in improving continuation rates.

Since discontinuation rates are higher, there short-term use only should be recommended as interim methods.

### Weight Change

DMPA may be associated with an increase of up to 2–3 kg in weight over 1 year. However, altered mood and libido, acne, headache and migraine are not associated with DMPA.

### Health Concerns

#### *Breast Cancer*

The small increased risk with recent use reduced with time after stopping, and no increase was observed among former users of DMPA (i.e. those who last used DMPA more than 5 years ago). There is possibly a weak association between current use of DMPA and breast cancer. Any increased risk is likely to be small and reduces with time after stopping.

No new occurrence of breast cancer happens in merely 3 months, but already existing tumour may get prominent and be noticed by the women. So it may be a boon in disguise!

#### *Cardiovascular Disease*

Unlike the COC, DMPA is not associated with any increase in the risk of stroke, venous thromboembolic events (VTE) or myocardial infarction (MI). An international hospital-based case–control study ( $n = 3697$  cases, 1% being POIC

users;  $n = 9997$  controls) assessed CVD risks among users of progestogen-only or combined hormonal contraceptives compared with nonusers of steroid hormone contraceptives.

In the current WHO-MEC recommendations, DMPA and NET-EN are assigned to category '3' for women with multiple risk factors for arterial CVD, current VTE, ischaemic heart disease or history of stroke. The risks of using POICs may outweigh the benefits.

DMPA is assigned to category '4' for women with a blood pressure of over 160/110 mmHg.

DMPA is medically safe for women to use if oestrogen is contraindicated.

The risk of thrombosis with combined hormonal contraception is well known, but they are more common with combined oral contraceptives, and there is no evidence of increased risk of thromboembolism with POIC.

#### *Bone Mineral Density*

There is conflicting evidence that DMPA reduces bone mineral density which may be reversible on discontinuation. Women who wish to continue DMPA use beyond 2 years should have their individual clinical situations reviewed; the balance between the benefits and potential risks are discussed, and be supported in their choice of whether or not to continue [2]. Because of the possible effects on bone mineral density, care should be taken in recommending DMPA to adolescents, but it may be given if other methods are not suitable or acceptable [2]. Because of the possible effect on bone mineral density, care should be taken in recommending DMPA to women older than 40 years, but in general the benefits outweigh the risks, and it may be given if other methods are not suitable or acceptable [2].

In view of the concern of reduced BMD beyond 2 years use, short-term use seems to be more judicious.

If pregnancy occurs during DMPA use, there is no evidence of congenital malformation to the foetus.

### Return to Fertility

POICs are known to cause a delay in the return of fertility. The delay for DMPA is greater than for NET-EN. Women should be informed that there could be a delay of up to 1 year in the return of fertility after stopping the use of injectable contraceptives [11].

Women who stop using injectable contraceptives should start using a different contraceptive method immediately even if amenorrhoea persists.

There is no known clinical thrombogenic effect of progestogen-only contraceptives; therefore, POICs can be safely used immediately following miscarriage [12].

DMPA and NET-EN are assigned to category '1' for women immediately after abortion in the current WHO-MEC recommendations [13].

### When to Administer the First Dose of Injectable

- Up to and including the fifth day of the menstrual cycle without the need for additional contraceptive protection.
- At any other time in the menstrual cycle, but additional barrier contraception should be used for the first 7 days after the injection.
- Immediately after first- or second-trimester abortion, or at any time thereafter.
- At any time after post-partum or earlier in nonbreast-feeding women.

### Use of DMPA in Specific Groups

1. Adolescents: it can be used with caution.
2. Women over 40 years of age: POICs are assigned to category '2' for women over 45 years of age in the current WHO-MEC recommendations [13].
3. Women with body mass index over 30 kg/m<sup>2</sup>. We did not identify any studies which assessed the relationship between body weight and efficacy of POICs. However, in our experience we have observed that obese women tolerate the method better and have better amenorrhoea rates than thin women [10]. A systematic review to update the WHO-MEC reported no significant differences in the incidence of increased or excessive bleeding between obese (BMI over 30 kg/m<sup>2</sup>), overweight (BMI 25–29.9 kg/m<sup>2</sup>) and nonobese (BMI under 25 kg/m<sup>2</sup>) DMPA users of at least 9 months [14].
4. Injectable contraceptives are not contraindicated in women with diabetes.
5. DMPA use may be associated with a reduction in the frequency of seizures in women with epilepsy.
6. There is no evidence that DMPA use increases the risk of STI or HIV acquisition. DMPA is a safe and effective method of contraception for women with STIS, including HIV/AIDS (safer sex using condoms should be encouraged in this group).

### Drug Interactions

Healthcare professionals should be aware that women taking liver enzyme-inducing medication may use DMPA and that the dose interval does not need to be reduced.

### Follow-up

In a 1-year RCT ( $n = 250$ ), sending reminders of their next injection to women did not reduce the number of missed appointments compared with those not sent a reminder (39 vs. 33%; RR 1.16, 95% CI 0.83–1.62). Continuation rates were not significantly different between groups (43 vs. 45%; RR 0.94, 95% CI 0.71–1.25) [6].

### Conclusion

Safe contraception is one of the four strong pillars of safe motherhood. The unmet need for contraception can be met by promoting use of highly effective POICs by healthcare providers, policy makers with the help of paramedical staff. Their use is better than other less effective methods with which chances of unwanted pregnancies are higher leading to possibility of unsafe abortion risking lives. Paramedical staff, ANMs, can pay house-to-house visits to find the eligible couples and use POICs as interim methods till the final permanent, or very long acting method is accepted by the couple. Post-partum IUCD programme is good, but women missing that opportunity can opt for POIC. This may be promoted more than the procedure-based IUCDs which require a special training and are associated with inherent risks, especially when it is carried out by less skilled health workers in field rather than hospitals setting.

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