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# Evaluation of Contraceptive Properties of Neem Oil - A Prospective Study

***Abstract*** **: Indigenous methods of contraception have been used in India from immemorial time through age-old Ayurvedic system of medicine. The present study has attempted to explore the contraceptive effect of Neem seed oil as local application for reproductive female as family planning method apart from the conventional measures. In this study, total 246 women in the fertile age group were selected, among them only 4 women dropped out and remaining were followed up for a period of 12 - 36 cycles. No such serious adverse reaction and event were noticed during the study period. Nine cases had conceived due to drug failure and four cases had conceived due to drug omission. The general observation indicates that Neem seed oil may be used as an external barrier as cost-effective herbal contraceptive for its spermicidal property and safe for regular use. Moreover, it was also observed that trial subjects had very less incidences of leucorrhoea, urinary tract infections and other common sexual transmitted diseases during the treatment period.**

***Keywords:*** Contraception, Neem oil, Ayurveda

The population explosion is a major problem worldwide. The family planning is essential for the welfare of the individual family and population control for the socio-economic development of the nation. The various methods of family planning as well as birth control method with high success rate and low risk are being practised in present days.

Many studies had been conducted on the oral contraceptive effects of herbal drugs. However, an external barrier herbal contraceptive was not explored earlier. Therefore, National Research Institute of Ayurvedic Drug Development, Kolkata has taken initiative to establish the Ayurvedic barrier contraceptives from indigenous medicinal plants origin. The study of Neem seed oil (*Azadirachta indica* A. Juss.) was carried out through special RCH clinic of Out Patients Department and 246 healthy fertile females were selected as a local applicant in vaginal passage before coitus. The consent was taken from each subject and study was in accordance with Biomedical Ethics guidelines of ICMR, Government of India through IEC- Human Research of the Institute.

The first reference to contraception was found in China about 1300 years ago. Contraceptive prescriptions are included in a book entitled "Thousands of Gold prescriptions" by Sun Ssu Mo in the 7$^{th}$ century A.D. In ancient Japan, "*Misugami*", a thin transparent paper disc made of bamboo tissue was placed in front of cervix to prevent conception.[1]

In ancient India, "*Kama Sastra*" by *Vatsayana* (4$^{th}$ Century A.D.) was the first authoritative book which dealt with the science of sex of men and women. The first documented method of birth control in India goes back to about 2000 years. The great physician "*Charaka*" mentioned many contraceptive prescriptions in his writings one hundred years before the birth of Christ.

Among later works of this nature mention may be made of "*Ratirahasya*", "*Koka Sastra*" and "*Panchasayaka*". [2]

There are 29 formulae. While some bring about sterility on women, others prevent conception by preventing fertilization and yet others stop the menstrual cycle.[3]

The Neem (*Azadirachta indica* A. Juss) is such a medicinal plant and symbolizes all that is wonders in nature: every part of the tree is being used as traditional medicine for household remedy against various human ailments from antiquity. In fact, it was considered the "Village pharmacy" in many parts of India and has played a key role in Ayurveda medicine and agriculture science time immemorial.

In Ayurvedic medicine, a decoction made from the bark, leaf, root, fruit, and flower is being used in the treatment of blood morbidity, biliary afflictions, itching, skin diseases and peptic ulcers. The bitter astringent bark is applied as a decoction for haemorrhoids. The leaves are steeped for malaria. Neem green leaves juice, infusion, or paste is applied externally to wounds and carbuncles. The twigs are used to clean the teeth, firming up the gums and preventing gum diseases.[4] Neem seed oil is commonly used for hairdressing and is strongly antifungal[5], antiviral and active against spermatozoa[6]. Neem seed oil has been used to treat leprosy and serves as a vehicle for other active ingredients.

The seed oil of *Azadirachta indica* A. Juss (Neem) is used in traditional medicine for its anti-diabetic, spermicidal, anti-fertility, anti-bacterial, and wound-healing properties[7]. A study result shown through histological study and flow cytometry indicate that the mechanism of its anti-fertility effect involves mainly the inhibition of sperm motility and the arrest of spermatogenic process.[8]

Another study was carried out to evaluate the effective concentration of aqueous extract of old and tender neem leaves to immobilize and kill 100% human spermatozoa within 20s. Sander-Cramer test was used to study the spermicidal activity of neem leaf extract. Under the test conditions, minimum effective spermicidal concentrations for tender and old leaf extracts were 2.91 +/- 0.669 mg/ million sperm and 2.75 +/- 0.754 mg/million sperm, respectively. The effect of extracts on morphology and viability of sperm was also studied and no change was observed in morphology of head, mid-piece and tail and no viable sperm seen. The leaf extracts were found to be water-soluble and carbohydrate in nature. The effect of different concentrations of extracts (old and tender) on percentage motility of the sperm was also studied.[9]

The oral administration of the neem seed extracts in rodents and primates could completely abrogate pregnancy at an early post-implantation stage. Complete restoration of fertility was observed in the animals treated in the subsequent cycles. For the purpose of using neem as a long term contraceptive. An activity-guided fractionation, followed by identification and characterization of the biologically active fraction from neem seeds was carried out. The treatment with the active fraction caused a specific activation of T lymphocyte cells of CD8+ subtype as well as phagocytic cells, followed by elevation in cytokines gamma-interferon and TNF. The results of the study show that a pure active fraction of neem seeds could be obtained for the purpose of early post implantation contraception when given orally, and its mechanism of action seems to be by activating cell mediated immune reactions.[10]

The mechanically extracted oil and solvent extracts of neem seeds have revealed that the anti-fertility activity was present in constituents of low to intermediate polarity. In this study, for the first time, proposes an active fraction from neem seeds, responsible for long term and reversible blocking of fertility after a single intrauterine administration with high efficacy. [11]

The study was to find out the role and mechanism of action of neem oil as a post-coital fertility blocker in mouse. Post-coital intrauterine treatment of neem oil during pre-implantation period causes fertility block in mouse by lowering the EGFR localization in the luminal and glandular epithelium, by causing massive leukocytes infiltration into the uteri, by degenerating the early embryos, and by causing the post-implantation embryonic resorptions in the uteri. The possible mechanism of action of neem oil is discussed.[12]

**TABLE 1: The Failure of Contraceptive efficacy due to drug failure or drug omission.**

| Month exposure | No. of pregnancy due to drug failure | No. of pregnancy due to drug omission | Total no. of women |
|---|---|---|---|
| 3 | 1 | 0 | 1 |
| 4 | 2 | 2 | 4 |
| 5 | 2 | 0 | 2 |
| 6 | 0 | 1 | 1 |
| 7 | 1 | 1 | 2 |
| 9 | 1 | 0 | 1 |
| 15 | 1 | 0 | 1 |
| 18 | 1 | 0 | 1 |

Neem seed oil has been reported to have no role on ovarian function and to possess strong spermicidal action against rhesus monkey and human protozoa in vitro and killed spermatozoa within 30 seconds of mixing with semen. The water-soluble fraction of the oil containing sodium nimbidinate in concentration of 50 mg./ 100 ml. and 2.5 mg./ 100 ml. has been found to kill rat sperms[13] and the lethal concentration of human sperms in the above experiment was 1000 mg. and 250 mg. per 100 ml. respectively.

***Objectives :*** The objectives of the study were as follows-

1. To establish the safe, potent Ayurvedic external barrier contraceptives.
2. To explore spermicidal effect of neem seed oil without any side effect.

***Materials and Methods :*** The study of Neem seed oil (*Azadirachta indica* A. Juss) was carried out at O.P.D, National Research Institute of Ayurveda for Drug Development, Kolkata on 246 healthy fertile females as a local application of 2 ml in vaginal passage 5 minutes before the coitus through a plastic applicator.

The selection was based on availability of healthy fertile female subjects at O.P.D aged between 18 to 40 years and they want to space between birth of two child and some use OCP or IUCD and also they don't want to get permanent sterilization.

The study was carried out in accordance of the ethic principals of Bioethics of ICMR under institutional ethical committee of Human Research of Institute.

1. Level of study – The study had been carried out OPD level
2. Design of study :

   Study type – open observation study

   Purpose – prevention

   Control – not control

   No of group – one

   Level of study – OPD level
3. Drug:

   Neem Oil

   Dose – 2 ml

   Dose form – oil

   Rout of administration – vaginal passage

   Time of administration – 5 minutes before the coitus

   Duration of therapy – minimum 12 cycles and maximum 36 cycles

***Inclusion Criteria :*** The following criteria were fixed for the selection of cases for study.

1. Marital status - Married.
2. Age between 18 to 40 years (fertile age group).
3. Normal sex - life with single male partner.
4. Regular menstrual cycle.
5. Number of children - at least one child.
6. At least one menstrual cycle following delivery / discontinuation of IUCD/ OCP.
7. Consent of couple for trial of antifertility local agent and exposed to risk of pregnancy.
8. Not using any other family planning method.
9. Findings are based on physical examination.

***Exclusion Criteria :***

1. Suspect pregnancy.
2. Diabetes mellitus, hypothyroidism and other metabolic disorders.
3. Hypertension and hypotension.
4. Cardio-vascular problems.
5. Severe hepatic disorder.
6. Suffering from any STDs.
7. Known or suspected CA of Breast.

***Clinical Examination :*** Total cases were thoroughly physically examined and routine pathological and bio-chemical investigations of blood, urine RE / ME was done to include into the study. Menstrual history and obstretic history both are recorded in special proforma.

***Parameter of Assessment :*** Result is considered positive, satisfactory by appearance of menstrual flow and non-pregnant uterus, negative, and unsatisfactory by amenorrhea and pregnant uterus.

***Result and Discussion :*** The contraceptive efficacy of drug failure and drug omission pregnancy is given in Table -1. Out of total registered 246 cases, only 9 (3.65%) cases were pregnant due to drug failure and also 4 (1.62%) cases were pregnant due to drug omission. Out of 246 cases, only 4 (1.62%) women were dropped out due to side effect. It is also observed that 10.29% were drop-outs due to adoption of other modern contraceptives method or unpleasant odor of the Neem seed oil not tolerated by the both partner. Only 45 (10.29%) cases remained for completion of 36 cycles of menstruation. However, 12 cycles of regular drug compliance was the minimum accorded for analysis.

Distribution of subject according to contraceptives used earlier, length of menstrual cycle; menstrual period and parity were recorded in the Case Record Form. It shows that 65.85% of the cases were not using any contraceptive, 27.23% of them used OCP followed by 6.91% used IUCD. 67.88% of them were having the length of menstruation cycle not more than 26 – 30 days. Also 95.12% of them were having menstrual flow for 3 to 5 days. 41.46% of them were having two children, followed by 25.6% having one child and 20.32% having three children.

***Conclusion :*** The result of this observational study revealed that the contraceptive effect of neem seed oil is significant when applied intra-vaginally. Neem seed oil is merely safe and easily available in the market; because this oil dose not show any adverse reaction and Neem tree is found in more or less all over India. So, this study recommended the use of Neem seed oil as an external barrier contraceptive with its spermicidal effects. ❐

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