

Efficacy and safety of herbal spermicidal contraceptive, Consap

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Consap is a locally acting, non-hormonal, herbal spermicidal contraceptive isolated from *Sapindus mukorosii*. It has been observed to be free from systemic side-effects such as nausea, vomiting and irregularities in the menstrual cycle. It is a woman-controlled reversible method which needs to be used before intercourse. It has additional antitrichomonas activity and is more vaginal-friendly. In the present study, 521 women volunteers in the reproductive age group have been screened at six centres. Of these, 470 were included in the trial covering 2076 months of Consap cream use with 2358 total cycles covered during the study. Out of a total, 324 cases who used this cream for at least 6 months and more were considered to have completed the trial. In this study only nine patient failures and four method failure pregnancies resulted with a Pearl index of 2.3, which is acceptable for the general population. This study thus shows that Consap cream when used as prescribed is an effective contraceptive. It is a good alternative for women who do not want to use oral contraceptive pills or intrauterine devices.

Keywords: Herbal contraceptive, Pearl index, saponins, *Sapindus mukorosii*.

THE current world population of 7 billion is projected to reach 9.3 billion by the middle of this century¹. This rapid population growth would exhaust the Earth's resources and diminish human well-being. In this situation control of population growth has become a necessity and use of contraceptives is perhaps the most effective way of controlling the population growth. There is no single 'best' method of contraception; so individuals have to decide which is the most suitable for them. Currently, oral contraceptive pills are dominating the markets, but locally acting contraceptives are coming back due to increase in sexually transmitted diseases. Local contraceptives with additional anti-infective properties would be of great value. Very promising spermicidal activity was observed in the saponin fraction isolated from the fruit pericarp of *Sapindus mukorosii*^{2,3}. The high yield of the saponins and easy availability of the plant material prompted us to undertake a detailed evaluation of the spermicidal activity of *S. mukorosii*. The total saponins were incorporated into water-dispersible cream for vagi-

nal application. Toxicity studies of continuous vaginal application of the spermicidal cream at 5%, 10% and 25% for three months in rabbits and Rhesus monkeys did not affect haematology, organ functions and histopathology. The total saponins from this plant were found to be equipotent to the currently used synthetic spermicide nonoxynol-9 (ref. 4). About 3 g of cream was required to be applied in the vagina before coitus, which killed all the spermatozoa instantaneously. Structure–activity relationship studies with saponins revealed that the spermicidal activity was associated with the β -amyrin C-28 carboxylic acid-type of saponins linked to a particular sequence of sugar moieties⁴. This spermicidal also acts against the sexually transmitted disease caused by the protozoan *Trichomonas vaginalis*⁵, which would greatly add to the value of the product/method. Studies show that *Sapindus* saponins compared to nonoxynol-9 are far less toxic to *Lactobacillus* species and therefore, saponins containing spermicidal preparations are likely to be more vaginal-friendly than the equivalent nonoxynol-9 preparations⁶. *Sapindus* saponins were formulated into a spermicidal cream preparation named Consap. The phase-I trial showed that this cream is tolerable up to 10% concentration. Phase-II trial in 181 volunteers showed encouraging results⁷ with Pearl index of only 1.4 (O. P. Asthana and Swarn Nityanand, unpublished).

The objective of the phase-IIIa clinical trial was to determine the contraceptive efficacy and safety of 2.5% Consap cream when used intravaginally 2–5 min prior to coitus.

The trial was conducted at six medical colleges, i.e. six sites in India with approval of Drugs Controller General, India and an Institutional Review Board at each site. All volunteers signed written informed consent. The study was conducted in women of reproductive age group with normal clinical and gynaecological history. Healthy, sexually active women, who were at low risk for sexually transmitted infections, who wished to rely on a spermicide as their only contraceptive method for 7 months, and who were willing to accept a moderate risk of pregnancy were eligible for the study. Women with a history of allergy, urinary and vaginal infection or any other major illness were excluded. Volunteers taking steroidal or non-steroidal contraceptives for at least 3 months prior to enrolment were also excluded from the study.

After providing informed consent, each volunteer had an interview and a general and pelvic examination. She was screened for haematological and biochemical tests and Pap smear. She was given a supply of the assigned spermicidal Consap cream and instructed to use 3 g of the same 2–5 min prior to each sexual intercourse with the help of standard applicator. Volunteers were under constant observation at frequent intervals and all complaints were carefully recorded. Each volunteer was also asked to return if she had medical problems, or if she wished to stop relying on the assigned spermicide as her primary

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Table 1. Demographic characteristics of participants at various centres

Site	Number of volunteers		Mean age	Parity
	Screened	Enrolled		
S.N. Medical College, Agra	126	106	25.57 ± 4.42	1.82 ± 0.68
M.L.N. Medical College, Allahabad	46	45	28.6 ± 6.40	2.55 ± 0.96
B.R.D. Medical College, Gorakhpur	24	24	27.25 ± 3.37	2.66 ± 1.23
Government Medical College, Jammu	64	64	29.34 ± 5.59	1.92 ± 0.84
G.S.V.M. Medical College, Kanpur	136	136	26.33 ± 4.59	2.28 ± 1.02
L.L.R. Medical College, Meerut	125	95	27.29 ± 4.39	2.44 ± 0.98

Table 2. Data showing exposure of test drug Consap

Total no. of cases screened	No. of cases included in the trial	Total months of use	Total cycles covered	Pregnancy	
				Patient failure	Method failure
521	470	2076	2358	9	4

Table 3. Number of women who discontinued the study for various reasons

Reasons	Total no. of patients
Patient failure	9
Method failure	4
Opted for Cu-T	21
Opted for ligation	7
Husband died/objection	8
Lost to follow up	63
Did not want to use cream	23
Burning after use of cream	11
Total	146

contraceptive. The participant was asked about specified symptoms of vulvar or vaginal irritation or of urinary tract infection within the previous week, about other adverse events, about complaints which her partner may have had about the spermicide.

Method failure was said to occur when a woman became pregnant while using the method ‘correctly’ and ‘consistently’ (regularly). The diagnosis of pregnancy was made by a registered medical obstetrics and gynecologist using a combination of methods. The decision of a certified postgraduate specialist was considered valid. The contraceptive efficacy was determined from the number of method failure (70 MF) pregnancies during the trial period. Any pregnancy occurring due to not applying the cream 2–5 min prior to early coitus was classified as patient failure (PF) and recorded. A woman using Consap cream for a period of 6 months or more would be considered to have completed the trial.

The demographic characteristics of volunteers enrolled in this study at each centre are given in Table 1. The average age of women enrolled in this trial was 27.02 ± 4.95 years. The average parity of women was 2.2 ± 0.97.

The number of cases screened/included in the study with total months of use, total cycle covered, and use duration with number of patients and method failure pregnancy from different medical colleges are given in Table 2.

The Pearl index was calculated as follows.

$$\text{Pearl index} = \frac{\text{No. of pregnancies} \times 12 \times 100}{\text{No. of months use}}$$

$$= \frac{4 \times 12 \times 100}{2076} = 2.3.$$

Five hundred twenty-one women volunteers in the reproductive age group have been screened at these six centres. Of these, 470 cases that satisfied the inclusion criteria and executed a written informed consent for participation in the study were included in the trial. In this study 2076 months of Consap cream use and 2358 total cycles were covered. Out of a total 324 cases who completed the trial, only nine patient failure and four method failure pregnancies were recorded during these trials. Pearl index of 2.3 was observed in these multicentric studies carried out at six medical colleges.

During these trials, 146 cases (31.1%) discontinued the study at various time intervals. The reasons for their discontinuation are given in Table 3. There was no volunteer who discontinued the trial for want of a child or transferred or delayed periods or divorce.

Consap is a locally acting, non-hormonal contraceptive which was observed to be free from systemic side-effects such as nausea, vomiting and irregularities in the menstrual cycle. It is a woman-controlled reversible method which needs to be used before intercourse and not daily, in contrast to oral contraceptives. Also, oral contraceptives may disturb the menstrual cycle and the user may forget to take the pill. The efficacy may increase when

used along with barrier methods. The several published reports of other spermicides used have yielded disparate results. Pearl indices, for example, have ranged from 0 to 67 pregnancies per 100 woman-years⁷. This variability may reflect differences in the doses and formulations of the spermicides studied, the underlying fecundity of the study populations, lack of compliance with instructions for use of the spermicide or coital patterns. The pregnancy probabilities we observed were in the range previously accepted for users of spermicides and other barrier methods⁸. In our study the Pearl index was 2.3, which is acceptable for the general population of a developing country. The Drugs Controller General gave permission for this drug after complete review of preclinical and clinical data. Currently, nonoxynol-9 and benzalkonium chloride are available as spermicides, but recent studies have shown that under *in vivo* conditions nonoxynol-9 induces a proinflammatory response in vagina⁹. The main side-effect of spermicides is burning sensation in vagina. In our study we found only 2.34% patient complained of burning, which is very low incidence. No serious adverse events related to the spermicides occurred in our study, and the cumulative risks of the local effects evaluated in our analysis were not alarmingly high in any spermicide group. This study shows that Consap cream when used properly in indicated quantity is an effective contraceptive method. Women who do not want use oral contraceptives or intrauterine devices now have a good alternative.

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Massive emissions of carcinogenic benzenoids from paddy residue burning in North India

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Benzenoids are organic pollutants emitted mainly by traffic and industrial sources. Here, using a combination of on-line *in situ* PTR-MS measurements of several benzenoids and methyl cyanide (a biomass-burning tracer), satellite remote sensing data of fire counts and back trajectory of air masses at a site in Mohali, we show that massive amounts of benzenoids are released from post-harvest paddy residue burning. Two periods, one that was not influenced by paddy residue burning (period 1, 18:00–03:30 IST; 5–6 October 2012) and another which was strongly influenced by paddy residue burning (period 2, 18:00–03:30 IST; 3–4 November 2012) were chosen to assess normal and perturbed levels. Peak values of 3830 ppb CO, 100 ppb NO_x, 40 ppb toluene, 16 ppb benzene, 24 ppb for sum of all C-8 benzenoids and 13 ppb for sum of all C-9 benzenoids were observed during period 2 (number of measurements in period 2 = 570) with the average enhancements in benzenoid levels being more than 300%. The ozone formation potential of benzenoids matched that of CO, with both contributing 5 ppb/h each. Such high levels of benzenoids for 1–2 months in a year aggravate smog events and can enhance cancer risks in northwestern India.

Keywords: Atmospheric chemistry, benzene, cancer, methyl cyanide.

BIOMASS burning affects the environment across varied spatial and temporal scales in several regions of the world¹. It contributes significantly to the global atmos-

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