



The development of new technologies for female sterilization: conclusions and recommendations for research

E.W. Wilson

Puketona Road, Paihia, New Zealand

Abstract

The conclusions and recommendations for research made during the consultation on the development of new technologies for female sterilization are presented. The participants in the consultation agreed that there was no single new method of female sterilization ready for introduction into service programs, but that there were several approaches with the potential to improve existing methods, or to provide new methods for tubal occlusion. A number of areas for future research were recommended including: additional operational research on existing abdominal approaches to tubal occlusion; further research into the physiology and pharmacology of the Fallopian tube; chemical occlusion using a transcervical approach with balloon pumps; techniques for endometrial ablation as sterilization methods; transcervical Fallopian tube cannulation; the use of quinacrine and other chemicals, such as elemental iodine, as tubal sclerosants, provided that these substances meet modern toxicological requirements.

Keywords: Fallopian tube; Tubal sterilization; Laparoscopy; Minilaparotomy; Hysteroscopy; Chemical tubal occlusion; Quinacrine;

1. Introduction

Following the presentation of the background papers the participants were asked to prepare summary comments and recommendations for research for three main topics; abdominal procedures, transcervical procedures, and chemicals for tubal occlusion. The general conclusions that follow are a summary of the discussion of the introductory papers, and particularly the presentation on specifications for female sterilization technologies for use in developing countries.

2. General conclusions

The most appropriate method of female sterilization in a particular family planning program often is determined by local situations and constraints. The ideal female sterilization method would involve a simple, easily learned, single procedure that could be accomplished under local anesthesia. It would include a tubal occlusion technique that caused minimum damage. The procedure would be safe, have high efficacy, be readily accessible, and be individually and culturally

acceptable. The cost for each procedure would be low and there would be minimal costs for the maintenance of equipment. No currently available procedure meets all of these criteria, although minilaparotomy with Pomeroy-type ligation, and laparoscopy with clip or ring application come close.

Training, to ensure adequate surgical skills, and counselling to ensure that women accepting the method understand fully the possibility of both intrauterine and ectopic pregnancy should the method fail, and the highly permanent nature of the procedure, are of major importance in sterilization programs.

Although not a specific topic for discussion during the consultation, the potential reversibility of sterilization methods was touched on by several speakers. It was agreed that where procedures used in a developing country program have a high potential for reversibility there should be centers established where the necessary surgical skills are available. It also was agreed that sterilization methods should be presented to potential acceptors as being permanent methods of fertility regulation.

3. Abdominal procedures

The abdominal procedures that have been developed, namely minilaparotomy (postpartum and interval) with a modified Pomeroy-type ligation, and laparoscopy with clip or ring application, meet the essential requirements of efficacy and safety, with minilaparotomy having the added advantage of simplicity. They are one-time procedures which are immediately effective. Both methods can be provided at relatively low cost, particularly minilaparotomy.

All these abdominal procedures should, where possible, be carried out under local anesthesia with a minimum use of sedatives. Ways of overcoming provider resistance to local anesthesia, through improved training for example, should be given some priority. Training in technical skills should put emphasis on the use of local anesthesia and correct site for placement of clips or rings.

Accurate placement of clips and rings on the tube is critical to ensure high rates of efficacy. The Hulka and Filshie clips provide effective tubal occlusion

when correctly applied. A new clip, the Cambridge clip, currently under development for use both at laparoscopy and minilaparotomy, may be an improvement on currently available clips, may prove less costly, and should be evaluated in appropriate studies.

3.1. Recommendations for research

1. Small studies should be undertaken to evaluate the use of the Chulascope and the Cusco bivalve speculum as aids for identifying the tube at minilaparotomy, particularly during training.

2. Further investigation of the potential for reversibility of the Filshie clip should be carried out. Evaluation should include cost and training requirements. When the Cambridge clip becomes available similar research should be initiated.

3. Studies are needed to determine whether the timing of the procedure (postpartum, postabortion, interval) has a significant effect on efficacy.

4. Assessment should be undertaken comparing complication rates of an abdominal procedure carried out between 3 days and 1 month post-partum to procedures performed within 72 h of delivery.

5. Operational research is needed: (i) to identify effective means of increasing the acceptability of local anesthesia by both service providers and clients; (ii) to develop indicators to measure and ensure quality of services in field situations, including mobile service delivery facilities; (iii) to test different approaches to training focused not only on technical aspects, but also on counselling and communication skills.

4. Transcervical delivery systems

Blind techniques for transcervical sterilization are preferable to visual techniques, and should be developed to be as independent of skill as possible. Radiographic and sonographic techniques are not useful at present. Hysteroscopy and fallopscopy for cannulation of the tubes are both feasible, but successful entry into the tubes is not achievable in more than 90-95% of cases, even in highly skilled hands. The technologies are not practicable for service delivery in developing country settings, but they are highly appropriate as developmental research tools.

Within China, a simple J-shaped tubal access cannula with a soft tip has been developed along with confirmation of tubal approximation using a fluid flow-back system. The system has been used on many thousands of women with reported success. However, the agents used for sterilization using this method of delivery, phenol and atabrine, have been associated with significant side effects, namely abdominal pain and fever, that have reduced the acceptability of the method.

Many biotechnology companies have refined technologies available for making delivery systems that are cheap and have memory and/or tactile properties that may improve the accurate location of a catheter tip to the tubal ostium.

Previous experience using small balloons to occlude the uterine cavity and cervix to facilitate the pumping of liquid agents of varying viscosity through the tubal ostium has been promising. One concern relates to the possibility that one or both tubes may not fill with the material.

Asherman's syndrome is a cause of infertility. Hysteroscopic and blind techniques for endometrial ablation, causing varying degrees of endometrial scarring, have resulted in high rates of infertility. A balloon system has been developed for endometrial ablation and may have merit for producing damage to the tubo-ovarian region and endometrium sufficiently for sterilization purposes. This system is blind and simple to use; it is potentially safe and free from the need for tubal sclerosing agents.

4. I. *Recommendations for research*

1. Research is needed to gain a better understanding of the physiology and pharmacology of the Fallopian tube in order to ensure a high success rate of transcervical delivery of sterilizing compounds to both tubes.

2. It is recommended that the delivery system, as used in China, be re-evaluated, and if necessary refined, as a promising blind system for the deposition of alternative chemicals, such as elemental iodine and newer compounds.

3. Research should continue to further develop balloon pump systems and to identify adjuvant treatment, such as DMPA, that might reduce uterine and tubal spasm. Atrophy of the **endomet-**

num also would facilitate access of materials into the tube through a relatively larger lumen. **Prior** to any field trials small, hysteroscopic studies of such drug effects would be cost effective to determine the degree of relaxation of the utero-tubal junction.

4. Research is needed to evaluate the heated balloon method for endometrial ablation in women seeking fertility regulation. Small studies with follow up by hysteroscopy and hysterosalpingography should be undertaken. At the same time there should be a retrospective evaluation of the pregnancy rate in women who have been subjected to endometrial ablation, by whatever method, for menstrual disorders. Despite the fact that many of these procedures will have been performed on women over the age of 35, such retrospective research would be of importance.

5. Other blind methods for endometrial ablation, such as the radiofrequency probe currently available, and a photodynamic system, under development, may warrant evaluation as potential devices for transcervical sterilization in the future.

5. **Chemicals for tubal occlusion**

A need exists in the world for a safe, effective, non-surgical method of sterilization, and research is required to develop such methods.

At this time the chemicals that are available for study are limited as are the methods whereby they may be delivered to the Fallopian tube reliably and consistently. These two limitations mean that there are real constraints to early success in the development of methods for non-surgical sterilization.

A catalog of those chemical substances that have been investigated in the past for use in transcervical sterilization, similar to that of **Richart [1]**, should be prepared, including quinacrine, iodine and methylcyanoacrylate (MCA).

Careful, standardized toxicological testing of all compounds with known or potential use as tubal occlusive agents should precede clinical studies which should be conducted in a step-wise fashion.

An estimated 70 000 women, in several developing countries, have been treated with one or more

installations of quinacrine pellets into the uterus. The protocols used for these studies, the method of installation, and the dose of quinacrine used have varied between centers. In some centers adjuvant treatment with non-steroidal anti-inflammatory drugs was given. Some toxicology testing of quinacrine applied locally was completed more than a decade ago, but the testing is considered to be inadequate by present day standards. In particular, the full range of genotoxicity studies that would be required by regulatory agencies has not been applied.

The precise mechanism of action of quinacrine on the Fallopian tube is poorly understood. Better understanding of the pharmacological action on the tissues of the tubal lumen might lead to the identification of other chemicals with similar action.

The consultation noted that MCA has passed all toxicology testing and that Phase I and II studies have been completed. A balloon-pump device for the instillation of MCA has been developed, but concern remains about the consistent delivery of the material to one or both tubes.

Consensus is needed on whether the high level of efficacy, already established for abdominal methods, should be applied to non-surgical methods, or whether some lesser efficacy would be acceptable.

5.1. Recommendations for research

1. The further study of quinacrine requires that the necessary toxicology testing (genotoxicity) be

completed and, if required, long-term animal carcinogenicity testing undertaken. Other animal tests, including tests for teratogenicity, would be needed if the initial animal carcinogenicity results are satisfactory.

2. Phase I and II human studies of intrauterine quinacrine, following properly designed and peer-reviewed protocols, should be initiated if the initial toxicology tests are satisfactory. Irrespective of the results of toxicology testing, retrospective studies of those women already treated with quinacrine must be continued and completed.

3. Additional research on quinacrine-induced tubal occlusion should include: (i) studies on the mechanism of action of quinacrine; (ii) the role of pretreatment with progestogens or other drugs; (iii) the effects of age and parity on efficacy; (iv) research to establish a standard method of use; (v) studies on the effect of quinacrine treatment on ascending genital infections.

4. Following the development of a stable solution of elemental iodine, appropriate animal studies should be completed to determine the efficacy of this substance in producing tubal closure.

5. Efforts to identify other chemicals that might be effective in creating tubal closure should be continued.

References

- [1] Richart RM. The use of chemical agents in female sterilization. In: Zatzchni GI, Shelton JD, Goldsmith A, Sciarra, JJ, editors, *Female Transcervical Sterilization*. Philadelphia: Harper & Row, 1983; 24.