Advances in Contraception, 1998; **14**: 81–90.
© 1998 Kluwer Academic Publishers. Printed in the Netherlands

Quinacrine sterilization: an assessment of risks for ectopic pregnancy, birth defects and cancer

E. KESSEL

Department of Public Health and Preventive Medicine, Oregon Health Sciences University, Portland, Oregon 97201, USA

Abstract

Quinacrine sterilization (QS) involves transcervical insertion of quinacrine pellets using a modified Copper T IUD inserter. Pellets are placed at the fundus in the proliferative phase of the menstrual cycle. Efficacy is presently estimated at 1 pregnancy failure per 100 women at 2 years. Early complications are lower for QS than surgical sterilization and this is also true for risk of ectopic pregnancy with newer insertion protocols. The risk of birth defects is very low, when estimated from a model with reasonable assumptions for probability of insertion in a pregnant uterus or within 30 days of conception, probability of such exposed pregnancy being carried to term, and probability of quinacrine exposure to the fetus causing a birth defect. Although quinacrine is a mutagen it is unlikely to be a carcinogen. Concentrations of quinacrine in the uterus after transcervical insertion are higher than for oral administration for only a matter of a few hours, although this brief exposure is adequate to cause injury to the tubal epithelium, leading to inflammation and an occluding scar. Oral administration of quinacrine is accepted as non-carcinogenic. Each site of use of QS must make its own risk/benefit assessment. The benefits of any contraceptive that can raise contraceptive prevalence is greatest for developing countries.

Sterilization, especially for women, is the most prevalent type of contraception today [1]. Unmet need for contraception varies greatly among different countries and within them. This is particularly true for female sterilization, which accounts for 40% of contraception in China [2], but only 3% in Indonesia [3] and Vietnam [4] and 1% in Egypt [5]. Both cultural and technical factors are responsible for this wide variation. But it is generally agreed that the technical requirements of surgical female sterilization are important reasons for failure to satisfy the demand for voluntary sterilization. Development of a safe, 95% effective method of non-surgical female sterilization that could be performed on an outpatient basis, even by non-physicians,

is vital for meeting this worldwide need [6]. The quinacrine pellet method, as developed by Zipper *et al*. [7], is at present the leading candidate for doing so. It involves transcervical insertion of quinacrine to the uterine fundus in the proliferative phase of the menstrual cycle. Generally 2 monthly insertions of 252 mg are given. Quinacrine causes inflammation and an occlusive scar on the proximal tubes. While use of quinacrine sterilization (QS) is spreading and has reached over 100 000 cases [8] without a fatality, concerns remain. These mainly relate to risks of ectopic pregnancy, birth defects and cancer. We review present knowledge regarding these risks.

Ectopic pregnancy

It was a reasonable theoretical concern that quinacrine might partially damage the tubes leading to incomplete closure and increased risk of ectopic pregnancy. Actual experience has shown the risk of ectopic pregnancy for QS to be equal to and probably lower than that for surgical sterilization. The ectopic risk per 1000 woman-years for surgical sterilization in the United States was reported as 0.7–0.8 [9], compared with 0.89 in Namha Province, Vietnam [10]. However, the pregnancy failure rate of QS with newer protocols is about half that reported in the Vietnam trials, suggesting that the risk of ectopic pregnancy is lower for QS than for surgical sterilization. As ectopic pregnancy is closely related to efficacy [11], the improvement in efficacy of QS compared with surgical sterilization is shown in Figure 1. Older QS protocols gave a 10-year pregnancy rate of 8 per 100 women [12] compared with 1.8 for surgical sterilization [13]. Recent studies [14,15] using a newer protocol [16] show failures of about 1 per 100 women at 2 years giving an estimate of approximately 3.5 at 10 years.

In a study of surgical sterilization failures where segments of tubes were examined when removed by minilaparotomy, it was found that a probable cause of ectopic pregnancies after surgical sterilization was fistula formation [17]. Unreported in this series were a few QS failures which showed at least one normal tube in each failure. This suggested that if the quinacrine reaches the tube it closes it completely in a high proportion of cases. This would be consistent with the lower risk of ectopics with QS.

Birth defects

Teratology is another risk to be considered for QS. There is little concern about systemic levels of quinacrine in this regard in light of its safety with extensive oral use. Concern is rather for higher concentrations that would exist in a pregnant uterus if accidentally inserted there. There are some animal data for both cynomolgus monkeys and rats showing that exposure of the fetus at the time of embryogenesis leads to resorption or abortion, especially in early gestation, but there was no evidence of treatment-related malformations [18]. There is no human experience reported to date for accidental quinacrine insertion in pregnancy, although a

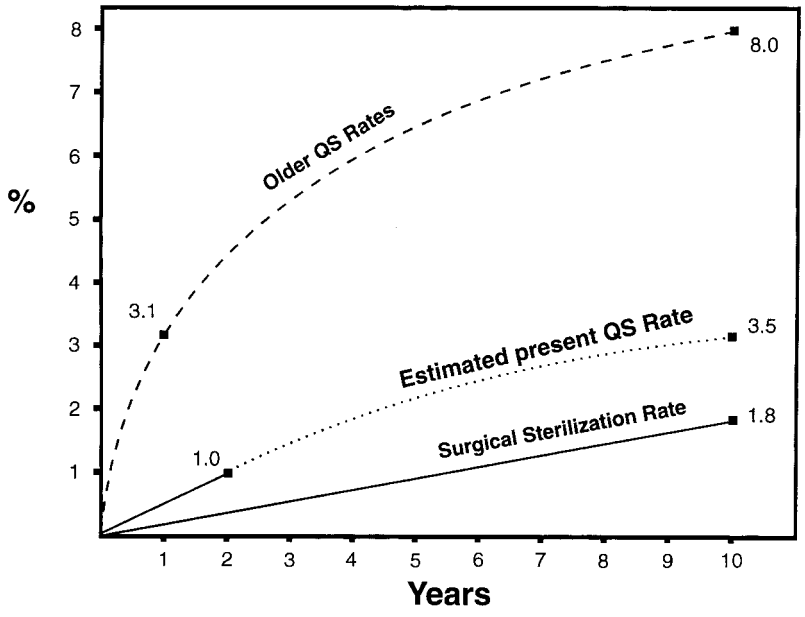

Figure 1. Comparison of pregnancy failure rates of surgical tubal occlusion with older and recent (estimated) quinacrine sterilization rates

systematic surveillance by pediatric examinations of all QS failure cases carried to term is in progress where quinacrine insertions occurred within 30 days of conception or after conception. It will take several years to accumulate a significant number of cases in this surveillance. In the large Vietnamese trial only a single case was found [10] resulting in a normal infant.

Some approximation of risk of a birth defect can be made however using a model with reasonable assumptions. The needed assumed rates pertain to the following:

1. Probability of insertion in a pregnant uterus or within 30 days of conception when some quinacrine may remain in uterine tissue.

2. Probability of such an exposed pregnancy being carried to term.

3. Probability of quinacrine exposure to the fetus causing a birth defect.

Because each of these probabilities is independent, we know from probability theory that to estimate the probability of a birth defect it is necessary to successively multiply each of the three probabilities. As an illustration, if the first listed

probability is assumed as one in 2000, or 0.0005, the second one in 10, or 0.1 and the third one in 50, or 0.02 then the estimated risk of a birth defect is 0.000001 or one in one million QS cases. This would have to be considered in any risk–benefit analysis. While the third factor is as yet unknown, the other two will vary for different locations, the first being related to clinician skill, and the second to availability of abortion.

Carcinogenicity

Because quinacrine is a mutagen there has been concern about its potential carcinogenicity, i.e. cancer-causing potential. Mutagenicity is determined by a standard set of in-vitro/in-vivo short-term tests which can identify genotoxicity involving as endpoints DNA damage and chromosomal/mutational damage. In reviewing established, probable, and possible human carcinogens it is found that a high proportion – in the range of 80–90% – are found to be genotoxic in short-term mutagenicity tests. In other words, the sensitivity of these short-term tests is high. For this reason toxicologists warn that any agent with unknown carcinogenic potential may represent a hazard to humans [19]. Carcinogenic potential can be known from human experience or rodent carcinogenicity tests.

In the past, attempts to extrapolate human cancer risk have relied heavily on tumor findings and the high sensitivity of short-term mutagenicity tests [19]. The latter have assumed importance as results are known quickly and inexpensively compared to the traditional 2-year bioassays in rodents. As quinacrine is a known mutagen, it has suffered from a past lock-step approach of reliance on mutagenicity tests which alone do not consider more recent guidelines for carcinogenic risk assessment [20]. These newer guidelines require a risk characterization that summarizes and integrates scientific findings of known cancer risk, effect of dose and degree of exposure. Newer guidelines incorporate advances in science which can change risk assessment over time as these advances may reduce uncertainties associated with extrapolations from high doses to low doses, from one route of exposure to another and from experimental animals to humans. The limitations of standard toxicology tests may also be revealed in the process.

The main concerns of cancer risk of QS pertain to quinacrine's known mutagenicity, its presence in the uterus during an inflammatory process with rapid cell division [21] and lack of a rodent carcinogenicity study with intrauterine administration. These concerns can now be submitted to a risk assessment and finally a risk characterization.

There is no direct evidence of quinacrine carcinogenicity in humans or animals. A huge experience exists for oral administration with no reports of increased risk of cancer. Quinacrine was used as an antimalarial by millions of soldiers in World War II at higher doses than needed for QS and for prolonged periods of time without reported evidence of carcinogenicity. Quinacrine is approved for management of giardiasis and millions of children have been so treated. It appears from this that if any increased cancer risk does exist it is probably low [22]. The near equivalent of a

rodent carcinogenicity study was performed in 1945 [23] involving daily oral administration at maximum tolerated dose for the life of rats. No evidence of increased risk of cancer was noted. There is even evidence in an experimentally induced cancer in rats that quinacrine may protect against that cancer [24]. Follow-up of early QS cases in Chile [25] for up to 14 years to detect cancer showed an observed to expected ratio of 1.44 with 95% confidence limits of 0.84 to 2.30. The report concludes that there is no evidence of increased risk of cancer.

In the study of short-term mutagenicity tests on agents in the International Agency for Research on Cancer (IARC) Monographs consisting of known human carcinogens, possible human carcinogens and agents with limited evidence of carcinogenicity in animals, the sensitivity of the tests was in the order of 80–90% [19]. A limitation of these short-term tests for mutagenicity should be noted. The common indices to measure performance of a screening test are sensitivity, specificity and accuracy defined as follows:

$$\text{Sensitivity} = \frac{\text{number of carcinogens positive in test}}{\text{total number of carcinogens}} \times 100$$

$$\text{Specificity} = \frac{\text{number of non-carcinogens negative in test}}{\text{total number of non-carcinogens}} \times 100$$

$$\text{Accuracy} = \frac{\text{number of correct test results}}{\text{number of agents tested}} \times 100$$

The IARC Monographs have too few known non-carcinogens to estimate specificity. But, specificity is needed to know the rate of false positives in short-term mutagenicity tests, which would be 100% minus specificity. The International Union of Pure and Applied Chemistry (IUPAC) has provided a chemical classification of compounds [26], some of which have known results for short-term mutagenicity tests such as the Salmonella assay and rodent carcinogenicity studies for which sensitivity, specificity and accuracy have been calculated [27]. These indices are shown in Table 1 for broad chemical class categories. Quinacrine is a nitrogen organic compound and this class has a low specificity of 36%, giving it a false positive rate of 64% using animal carcinogenicity results as a standard. Quinacrine may very well be among these false positives, as are many commonly consumed products such as broiled hamburger [28] and roasted coffee [29].

Regarding dose and duration of exposure to quinacrine in QS it is worth comparing it to oral quinacrine administration where there is little concern of carcinogenicity. First, it is known that quinacrine is rapidly absorbed from the gut [30] or endometrium [31] resulting in early high plasma levels. With a single administration plasma levels rapidly decline, as seen in dogs [30], cynomolgus monkeys [31] and humans [32]. This rapid decline is not due to excretion or degradation but redistribution to other tissues based on circulation to the tissues, as seen in Table 2 for monkeys at 24 hours [31]. By 28 days quinacrine was not

Table 1. The sensitivity, specificity and accuracy values for the combined class and chemical class groupings of a Salmonella/carcinogenicity data base

Chemical class category	*Carcinogen/ Salmonella tests number*	*Sensitivity (%)*	*Specificity (%)*	*Accuracy (%)*
All classes combined	220	77	64	75
Nitrogen organics	87	85	36	77
Halogen organics	52	63	91	69
Sulfur organics	24	76	57	71
Oxygen organics	27	70	100	74
Hydrocarbons	12	92	0	92

Source: Reference 27

Table 2. Tissue plasma ratio of quinacrine 24 h after intravascular administration of 30 mg quinacrine to cynomolgus monkeys

Tissue	*Ratio*	*Tissue*	*Ratio*
Lung	1676:1	Ovary	219:1
Adrenal	1345:1	Hypothalamus	200:1
Kidney	1211:1	Endometrium	184:1
Pancreas	1041:1	Cerebellum	171:1
Liver	994:1	Uterine cervix	158:1
Spleen	904:1	Midbrain	138:1
Heart	723:1	Isthmus (oviduct)	131:1
Bone marrow	445:1	Ampulla (oviduct)	94:1
Lymph node	378:1	Skeletal muscle	68:1
Myometrium	258:1		

Source: Reference 31

detectable. Among women in a phase I study [32] mean plasma levels peaked at 3 h after intrauterine administration averaging 46.3 ng/ml and then dropped to below 20 ng/ml in the 4th hour. Only about 1% of the total dose of quinacrine (250 mg) was excreted in the first 48 h, which is similar to oral administration [30]. The decline in plasma levels can only be due to redistribution to all tissues. Quinacrine concentration in uterine tissue after a few hours is a result of this redistribution rather than a residual remaining after insertion. Tissue concentrations of quinacrine in both

animal and human studies showed great individual variation. With repeated oral administration, as for malaria prophylaxis, much higher tissue levels are achieved and can even tinge the skin yellow in Caucasians [30]. Tissue concentrations are higher in QS than with oral use in malaria prophylaxis for a brief period of a few hours. This brief high intrauterine exposure is, however, adequate to initiate an inflammatory reaction in the lining of the proximal tubes that leads to an occlusive scar regardless of subsequent quinacrine exposure. It is analogous to a flash burn of the skin which, if third degree, proceeds to inflammation and a scar. The endometrium is partially spared in this process due to its higher concentration of zinc [33]. The inflammatory process is hardly started in the tube in an interval of a few hours. The prolonged use of quinacrine for months and years as a malaria suppressant is likely to have produced greater uterine exposure to quinacrine for women military personnel in the Pacific theater in World War II than is produced with QS. Wounded or injured soldiers continued quinacrine malaria prophylaxis. Of the many thousands so exposed there is no report of increased risk of cancer.

The absence of a rodent carcinogenicity study for intrauterine quinacrine administration is unfortunate but hardly the sole basis for judging carcinogenicity in humans. Even if a decision could be made on dose and number of insertions in the mouse or rat, the limitations of rodent carcinogenicity studies should not be forgotten. The concurrence between mouse and rat carcinogenicity studies is only 75% suggesting that the carcinogenicity results from animal studies are for specific mammalian species and not for mammals as a group [34]. Rodent carcinogenicity studies are conducted at near toxic doses of the test chemical, for the life of the rodent, which can cause chronic mitogenesis similar to that in chronic inflammation, which is known to be a cause of some human cancers [35]. It is not surprising that a high proportion of chemicals so tested are carcinogens in test animals at this dose [35]. QS involves a lower therapeutic dose for a brief period, resulting in an acute inflammation for which there is no evidence of carcinogenicity.

In making a risk characterization of carcinogenic risk of QS we note the extensive oral use of quinacrine at higher doses than needed for QS that produced prolonged higher tissue concentrations than for QS with no report of increased carcinogenic risk. The limited time of higher intrauterine quinacrine exposure for QS, of a matter of a few hours, is before most rapid cell division in the inflammatory process leading to an occlusive scar. The known low specificity of short-term mutagenicity tests on organic nitrogen components strongly suggests quinacrine is one example of a false positive test in view of the extensive human experience with this drug. These assessments lead to a characterization of QS as not likely to have an increased risk of carcinogenicity, probably not higher than for oral administration. The present toxicokinetic finding of lower quinacrine concentrations in uterine tissue than for repeated oral administration, except for a brief period of a few hours, supports this description. As QS cases continue internationally, long-term follow-up of a large number of women can give a definitive answer to carcinogenic risk as was the case for oral contraceptives.

The risk–benefit assessment

The conclusion drawn from the above is that the risks of QS are low or non-existent for the main concerns of ectopic pregnancy, birth defects and cancer. Such risks, if they exist, must be balanced against the potential benefits of QS, which by raising contraceptive prevalence can prevent unwanted pregnancies and lower maternal mortality and morbidity. There are those who feel that standards for approval of contraceptives should be the same throughout the world, regardless of the economic status of the region, and that if an exception is made for QS it may lead to a slippery slope of risky adventures in contraceptive development. They desire some uniform low risk acceptable to all societies. But as Dr. Tore Godal, Director of the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Disease, insists, there is no such thing as one global standard specifying some global level of low risk. Rather, in each local case, a rational analysis of risk against benefit is needed [36]. He provides examples from trials of treatments of tropical diseases. The same applies to any preventive measure, including contraception. The difference is that in therapy the patient is known, whereas in prevention we are only aware of the number of patients benefited or at risk.

Of course, risks and benefits change over time and for various local situations. While risks of QS are somewhat similar, benefits vary greatly. Benefits are highest where contraceptive prevalence is disappointing and/or maternal morbidity and mortality are unacceptable. This is the situation in many developing countries. For industrialized countries there is the savings in operative mortality. Other mortality savings would depend on what QS is substituting for in a society with high contraceptive prevalence [37]. Many of these women continue on temporary methods only because they lack the financial resources for sterilization. But the financial savings over the billion dollar cost of surgical sterilization in the United States would be significant.

Each locality must conduct its own risk–benefit assessment for use of QS. The reproductive health benefits of QS or any measure to raise contraceptive prevalence are considerable. QS is another option that should be available to all well informed women as a right and a means of protecting their health and family.

References

1. Sadik N. The State of World Population 1997. United Nations Population Fund, New York, 1997.
2. State Family Planning Commission. Population and Family Planning in China. Beijing, 1997.
3. Central Bureau of Statistics (CBS) [Indonesia] and State Ministry of Population/National Family Planning Coordinating Board (NFPCB) and Ministry of Health (MOH) and Macro International Inc. (MI). 1995. Indonesia Demographic and Health Survey 1994. Calverton, Maryland: CBS and MI, p. 76, Table 5.2.2.
4. General Statistical Office. 1994 Inter-Censal Demographic Survey. Statistical Publishing House, Hanoi, May 1995.
5. National Population Council (NPC) and Macro International Inc. (MI). Egypt Demographic and Health Survey 1996. Calverton, Maryland: NPC and MI; 1997.
6. Klitsch M. Sterilization without surgery. Int Fam Plann Perspect 1982;8:101–4.

7. Zipper J, Cole LP, Goldsmith A, Wheeler R, Rivera M. Quinacrine hydrochloride pellets: preliminary data on a nonsurgical method of female sterilization. Int J Gynaecol Obstet. 1980;18:265–9.
8. Kessel E. 100,000 quinacrine sterilizations. Adv Contracept. 1996;12:69–76.
9. Peterson HB, Xia Z, Hughes JM, Wilcox LS, Taylor LR, Trussell V. The risk of ectopic pregnancy after tubal sterilization. N Engl J Med. 1997;336:762–7.
10. Hieu DT, Tan TT, Tan DN, Nguyet PT, Than P, Vinh DQ. 31 781 cases of non-surgical female sterilisation with quinacrine pellets in Vietnam. Lancet. 1993;342:213–7.
11. Franks AL, Beral V, Cates W, Hogue CJR. Contraception and ectopic pregnancy risk. Am J Obstet Gynecol. 1990;163:1120–3.
12. Sokal DC, Zipper J, King T. Transcervical quinacrine sterilization: clinical experience. Int J Gynecol Obstet. 1995;51(suppl):556–69.
13. Peterson HB, Zhisen X, Hughes J, et al. The risk of pregnancy after tubal sterilization: finding from the U.S. Collaborative Review of Sterilization. Am J Obstet Gynecol. 1996;174:1161–70.
14. Soroodi-Maghaddam S. Preliminary report on a clinical trial of the quinacrine pellet method for nonsurgical female sterilization in Iran. Int Fam Plann Perspect. 1996; 22:122–3, 127.
15. Bairagi NR, Mullick BC, Kessel E, Mumford SD. Comparison of the efficacy of intrauterine diclofenac and ibuprofen pellets as adjuvants to quinacrine nonsurgical female sterilization. Adv Contracept. 1995;11:303–8.
16. Institute for Development Training. Female voluntary non-surgical sterilization: The quinacrine method. Module 12 of Training Course in Women's Health. Institute for Development Training, Chapel Hill, 1996.
17. Rock JA, Parmley TH, King TM, Laufe LE, Su BC. Endometriosis and the development of tuboperitoneal fistulas after tubal ligation. Fertil Steril. 1981;35:16–20.
18. Blake DA, Dubin NH, Blasé MC, Parmley TM, Stetten G, King TM. Teratologic and mutagenic studies with intrauterine quinacrine hydrochloride. In: Zatuchni GI, Shelton JD, Goldsmith A, Sciarra JJ, eds. Female Transcervical Sterilization. Philadelphia, Harper and Row, 1983, p. 71–88.
19. Bartsch H, Malaveille C. Prevalence of genotoxic chemicals among animal and human carcinogens evaluated in the IARC Monograph Series. Cell Biol Toxicol. 1989;5(2):115–27.
20. Wiltse J, Dellarco VL. U.S. Environmental Protection Agency Guidelines for carcinogenic risk assessment: Past and future. Mutation Res. 1996;365:3–15.
21. Cohen SM, Ellwein LB. Cell proliferation in carcinogenesis. Science. 1990;249:1007–11.
22. Tice RR, Griffith J, Recio L. An evaluation of the mutagenicity and carcinogenicity of quinacrine. Family Health International 1990. Research Triangle Park, NC. pp. 27.
23. Fitzhugh OG, Nelson AA, Calvery HO. The chronic toxicity of quinacrine (atabrine). J Pharmacol Exp Ther. 1945;85:207–21.
24. Dabancens A, Zipper J, Guerrero A. Quinacrine and copper, compounds with anticonceptive and antineoplastic activity. Contraception. 1994;50:243–51.
25. Sokal DC, Zipper J, Guzman-Serani R, Aldrich TE. Cancer risk among women sterilized with transcervical quinacrine hydrochloride pellets, 1988–1991. Fertil Steril. 1995;64:324–34.
26. Cahn RS, Dermer OC. Introduction to Chemical Nomenclature, 5th ed. Butterworths, London, 1979, 245 pp.
27. Claxton LD, Stead AG, Walsh D. An analysis by chemical class of Salmonella mutagenicity tests as predictors of animal carcinogenicity. Mutation Res. 1988; 205:197–225.
28. Commoner B, Vithayathil AU, Dolara P, Nair S, Madyastha P, Cuca GC. Formation of mutagens in beef extract during cooking. Science. 1978;201:913–16.
29. Fujita Y, Wakabayashi K, Nagao M, Sugimura T. Implication of hydrogen peroxide in the mutagenicity of coffee. Mutation Res. 1985;144:227–30.
30. Shannon JA, Earle DP Jr, Brodie BB, Taggart JV, Berliner RW. The pharmacological basis for the rational use of atabrine in the treatment of malaria. J Pharmacol Exp Ther. 1944;81:307–30.
31. Dubin NH, Parmley TH, DiBlasi MC et al. Pharmacology of quinacrine hydrochloride with emphasis on its use as a tubal occluding agent. In: Zatuchni GI, Shelton JD, Goldsmith A, Sciarra JJ, eds. Female Transcervical Sterilization. Philadelphia, Harper and Row, 1983. pp. 60–70.
32. Laufe LE, Sokal DC, Cole LP, Shoupe D, Schenken RS. Phase I prehysterectomy studies of the transcervical administration of quinacrine pellets. Contraception. 1996;54:181–6.
33. Patek E. Quinacrine hydrochloride: Review and mode of action of an antimalarial, used as an occlusive agent for transvaginal human sterilization. Acta Obstet Gynecol Scand. 1979;58:561–4.
34. Gold LS, Bernstein L, Magaw R, Slone TH. Interspecies extrapolation in carcinogenesis: prediction between rats and mice. Environ Health Perspect. 1989;211–19.
35. Ames BN, Gold LS. Too many rodent carcinogens: mitogenesis increases mutagenesis. Science. 1990;249:970–1.

36. Godal T. Fighting the parasites of poverty: public research, private industry, and tropical diseases. Science. 1994;264:1864–6.
37. Kawachi I, Colditz GA, Hankinson S. Long-term benefits and risks of alternative methods of fertility control in the United States. Contraception. 1994;50:1–16.

MS received 6 Apr. 98.
Accepted for publication 28 Apr. 98.

Resumen

La esterilización mediante quinacrina (QS) comprende la colocación transcervical de gránulos de quinacrina utilizando un dispositivo de colocación DIU Copper T. Los gránulos se colocan en el fundus en la fase proliferativa del ciclo menstrual. La eficacia se estima actualmente en 1 fallo por embarazo por cada 100 mujeres al cabo de 2 años. Las complicaciones tempranas registran un nivel inferior en la QS que en la esterilización quirúrgica, y esto es igualmente válido para el riesgo de embarazo ectópico con protocolos de colocación más nuevos. El riesgo de defectos de nacimiento es muy bajo al estimarse en base a un modelo con suposiciones razonables de probabilidad de colocación en un útero grávido o dentro de los 30 días de la concepción, probabilidad de que tal embarazo se lleve a término y probabilidad de exposición de quinacrina al feto que provoque un defecto de nacimiento. Si bien la quinacrina es mutágena, es poco probable que sea carcinógena. Las concentraciones de quinacrina en el útero después de la colocación transcervical son mayores que con la administración oral durante unas pocas horas, si bien esta exposición breve basta para causar lesiones al epitelio tubario, que producen inflamación y una cicatriz de oclusión. La administración oral de quinacrina es aceptada como no carcinógena. Cada emplazamiento donde se utilice la QS debe hacer su propia evaluación del riesgo/beneficio. Los beneficios de cualquier anticonceptivo que pueda aumentar la tasa de prevalencia anticonceptiva son mayores para los países en desarrollo.

Resumé

La stérilisation à la quinacrine (SQ) nécessite l'insertion transcervicale de pellets de quinacrine à l'aide, après modification, d'un instrument normalement utilisé pour insérer des DIU Copper T. Les pellets sont déposés au fond de l'utérus au cours de la phase proliférative du cycle menstruel. L'efficacité est actuellement estimée à 1 grossesse pour 100 femmes au bout de 2 ans. La SQ entraîne moins de complications précoces que la stérilisation chirurgicale et moins également de risques de grossesses ectopiques lorsqu'on applique les nouveaux protocoles d'insertion. Les risques de malformations à la naissance sont minimes si on les estime en fonction d'un modèle comportant des hypothèses raisonnables quant à la probabilité d'insertion dans un utérus gravide ou dans les 30 jours qui suivent la conception, quant à la probabilité que des grossesses ainsi exposées soient portées à terme, et quant à la probabilité que l'exposition du foetus à la quinacrine entraîne des défauts à la naissance. Si la quinacrine est mutagène, elle n'est probablement pas carcinogène. Les concentrations de quinacrine dans l'utérus après l'insertion transcervicale sont plus élevées que dans le cas de l'administration par voie buccale, mais pendant quelques heures seulement, encore que cette brève exposition soit suffisante pour occasionner des lésions à l'épithélium des trompes, provoquant une inflammation et une cicatrisation occlusive. Il est admis que l'administration de quinacrine par voie buccale n'est pas carcinogène. Le choix de la méthode de SQ doit est subordonné à une évaluation des risques et des avantages respectifs. Les avantages d'une méthode contraceptive susceptible de renforcer le pouvoir contraceptif priment dans les pays en développement.