

# Clinical management of functional ovarian cysts: a prospective and randomized study

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**Most ovarian cysts in women of reproductive age are physiological (functional) and patients have been treated for years with oral contraceptives to obtain the resolution of these cysts. Expectant management has been suggested to have the same effectiveness as hormonal treatment but such suggestions come from studies including all kinds of cysts. The objective of the present study was to assess the resolution of functional ovarian cysts, observed after ovulation induction, with expectant management and hormonal treatment and also to determine the period of time necessary for the resolution of the cysts. For this purpose, 53 patients with ovarian cysts, observed by transvaginal ultrasound within the first 5 days of a cycle after ovulation induction, were randomized to have expectant management (group A) or to receive oral contraception (group B) for one cycle. If the cyst persisted, the patient was followed for another cycle, without any treatment. Within the 50 women who completed the trial, a complete resolution of the cysts was observed in 19/25 (76%) and 18/25 (72%) in groups A and B respectively. On the other hand, all the persistent cysts disappeared after a second cycle without any treatment. In conclusion, expectant management is as effective as oral contraceptives for the resolution of functional ovarian cysts induced by ovarian stimulation. However, studies with a larger number of cases are needed to increase the power of the results and to obtain a firm conclusion.**

*Key words:* functional cysts/ovarian cysts/physiological cysts

## Introduction

The vast majority of ovarian cysts in women of reproductive age are physiological (functional), either follicular cysts or cystic corpus luteum (De Wilde *et al.*, 1989). The presence of this kind of cyst is a frequent finding in patients undergoing ovulation induction and ultrasound follicular growth monitoring (Steinkampf *et al.*, 1990). As it is not advisable to perform ovarian stimulation under these conditions, patients

must be followed up, with or without hormonal treatment, until the resolution of the cyst.

For years, gynaecologists have prescribed oral contraceptives, containing a variety of oestrogen and progestin combinations, for the resolution of functional ovarian cysts (Vessey *et al.*, 1987) and to distinguish between them and pathological cysts of the ovary (Spanos, 1973). On the other hand, randomized controlled trials in women undergoing ovulation induction suggest that ovarian cyst resolution is not affected by oral contraceptives (Steinkampf *et al.*, 1990; Ben-Ami *et al.*, 1993), although both studies cited included not only functional cysts, but also pathological adnexal masses. Despite the results reported by the latter studies, the use of combined oestrogen and progestin preparations has become a common and accepted clinical practice in women having ovarian cysts in which the sonographic characteristics are benign (Lipitz *et al.*, 1992).

The purpose of the present study was to assess the spontaneous resolution of genuine functional ovarian cysts in women undergoing ovulation induction (cysts induced by ovarian stimulation), to determine whether the prescription of oral contraceptives has benefits over expectant management and to define the period of time necessary for the resolution of the cysts.

## Material and methods

### Protocol

In all, 54 women with ovarian cysts  $\geq 15$  mm diameter, found in a transvaginal ultrasound within the first 5 days of the cycle, were prospectively recruited for the study. All of them underwent ovarian stimulation with clomiphene citrate, human menopausal gonadotrophin or both in the previous cycle, as part of an infertility treatment because of mild male infertility factors or unexplained infertility (MacKenna, 1995). All the patients had a normal transvaginal ultrasound within the first 5 days of the cycle in which they received ovulation induction. All women recruited had previous regular menstrual cycles with normal ovulation, detected by follicular growth monitoring and serum progesterone, measured in the mid-luteal phase.

Patients recruited for the study, except one who did not enter the randomization because of a previous history of gastric intolerance to oral contraceptives, were followed-up by transvaginal ultrasound for one or two cycles to verify the resolution of the ovarian cyst.

### Assignment

After consent was obtained, 53 patients were randomized, either to have an expectant management for one cycle (group A: 27 women) or to receive oral contraception (ethinyl oestradiol 0.05 mg and levonorgestrel 0.25mg) for 21 days (group B: 26 women). Treatments were alternated every other week. A transvaginal ultrasound was repeated within the first 5 days of the next cycle, after women had

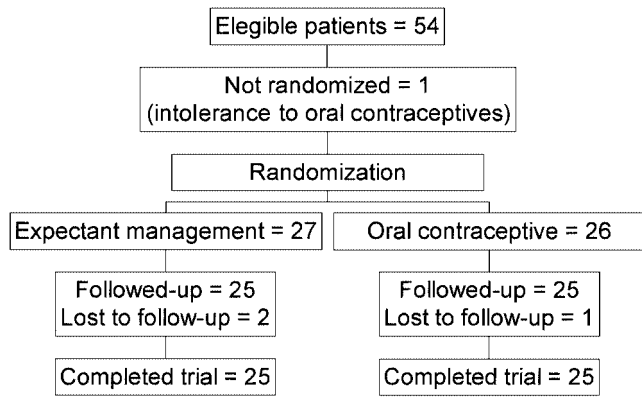


Figure 1. Trial profile.

their period following a spontaneous cycle or 3 weeks of oral contraceptive. If persistence of the cyst was observed, the patient had another cycle without any treatment and the ultrasound was performed again within the first 5 days of the next cycle.

**Statistical analysis**

As previous studies reported no differences between groups very similar to groups A and B (Steinkampf et al., 1990; Ben-Ami et al., 1993), a sample size calculation was not conducted a priori. However, in order to detect the clinical relevance of the results, a statistical power calculation was performed (power test). Student’s *t*-test was used to compare patients’ characteristics,  $\chi^2$ -test and Fisher’s exact test, as appropriate, were used for statistical analysis and comparison between the group with and without oral contraceptives. The level of statistical significance was  $P < 0.05$ .

**Results**

**Participants flow and follow-up**

From the 54 patients initially recruited for the study, only one was eliminated because of previous gastric intolerance to oral contraceptives. The remaining 53 women were randomized, 27 in group A and 26 in group B. However, three patients were lost to follow-up, two in group A and one in group B, so that only 25 women in each group completed the trial (Figure 1).

**Analysis**

The mean (SE) age of patients in group A and B was 33.5 (2.3) and 34.2 (1.9) years respectively (not significant). The mean (SE) duration of infertility in groups A and B was 3.85 (0.35) and 3.47 (0.69) years respectively (not significant). The mean (SE) diameter of the cysts in group A and B was 24.3 (1.5) and 28.1 (2.0) mm respectively (not significant).

In group A, 19 of the 25 (76%) patients had a complete resolution of their cysts within the first cycle and in group B, 18 of the 25 (72%) women showed a complete resolution of their cysts when the ultrasound was performed after one cycle receiving oral contraception (Table I). Values in group A and B were not significantly different; however, the statistical power required to detect a significant difference between the groups, for 25 cases in each group, was only 5%. A total of 2500 cases in each group would be needed to increase this statistical power to 90%.

**Table I.** Resolution of ovarian cysts after one cycle of either expectant management (group A) or oral contraception (group B)

	Group A	Group B
Resolution (%)	19/25 (76) <sup>a</sup>	18/25 (72)
Persistent cysts (%)	6/25 (24) <sup>a</sup>	7/25 (28)

<sup>a</sup>Not significantly different from group B.

**Table II.** Persistent cysts after one cycle of either expectant management (group A) or oral contraception (group B), grouped according to the cyst diameter

Cyst diameter (mm)	Group A	Group B
15–19	1/7 <sup>a</sup>	2/4
20–24	3/9 <sup>a</sup>	4/7
25–29	1/3 <sup>a</sup>	0/6
>30	1/6 <sup>a</sup>	1/8

<sup>a</sup>Not significantly different from group B.

Table II shows the number of patients having persistent cysts after one cycle of either expectant management or oral contraception, depending on the cyst diameter: groups A and B were not significantly different. All women with persistent cysts in both groups (13 patients) had a complete resolution of the ovarian mass after a second cycle of expectant management, without any treatment.

**Discussion**

Most ovarian cysts in both groups resolved within one cycle of either expectant management (group A) or oral contraception (group B), irrespective of the cyst diameter, although the numbers were too small to reach a firm conclusion about this relationship (Table II). The results observed in this study are in agreement with previous reports (Steinkampf et al., 1990; Ben-Ami et al., 1993), suggesting that expectant management has the same effectiveness as oral oestrogen/progestin therapy for the treatment of functional ovarian cysts generated in cycles with ovulation induction. Therefore, it seems unnecessary to prescribe the latter treatment to patients having a functional cyst, unless they are women with anovulatory cycles who need oral contraceptives to induce the next period and start a new cycle of ovulation induction.

Moreover, all patients having persistent cysts had a complete resolution of the ovarian mass after one more cycle, without any treatment. This is in disagreement with the findings of Ben-Ami et al. (1993) and Steinkampf et al. (1990), who followed ovarian cysts after ovulation induction and found persistent cysts after 8 and 9 weeks respectively. Those patients underwent a laparoscopy and pathological adnexal masses, including endometriomas, hydrosalpinges, dermoid cysts and para-ovarian cysts were found, confirming that the initial findings did not correspond to functional cysts. This was not observed in the present study because an ultrasound was performed before starting with ovulation induction, confirming that both ovaries were normal, which seems to be a good

practice in order to avoid wasting time with ovulation induction when patients need laparoscopy. Therefore, the results reported correspond to the resolution of functional cysts in women undergoing ovulation induction. However, as the number of patients included in this report is low, and the statistical power of the results obtained from the comparison between group A and B is only 5%, a larger number of cases is needed to obtain stronger and definitive clinical conclusions.

Although these results cannot be generalized to spontaneous cycles, it is likely that in women having normal ovulatory cycles, spontaneous resolution of functional cysts also occurs within 2 months of expectant management. After that period of time a laparoscopy should be performed if a persistent cyst is observed because of the high probability of finding a pathological rather than a functional cyst.

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*Received on April 10, 2000; accepted on August 18, 2000*