

Is there a benefit from routine follicular flushing for oocyte retrieval?

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Summary

The object of this study was to determine the optimum number of follicular flushing for a maximum number of oocytes to be retrieved. This was a prospective study, based at a private *in vitro* fertilization centre (Brentwood Fertility Centre, The Essex Nuffield Hospital, Brentwood, Essex UK). Patients attending the IVF centre for assisted reproductive technology were studied. We counted the number of oocytes obtained with each flushing after primary aspiration of the follicle. Some 40% of the oocytes were retrieved with primary aspiration without follicular flushing, while up to 82% of oocytes were retrieved with two flushes and 97% of oocytes were retrieved in up to four flushes. Only 3% of the remaining oocytes were retrieved with 5th and 6th flush. The optimum number of follicular flushing was four times, in order to achieve maximum number of oocytes without compromising the duration of retrieval and number of oocytes retrieved.

Introduction

Once *in vitro* fertilization (IVF) was established as a successful clinical procedure, at the end of the 1970s and, continuing partly, until the mid-1980s, laparoscopic oocyte retrieval was the method of choice for oocyte collection (Steptoe and Edwards 1970). Ultrasonically directed follicular aspiration for oocyte retrieval was first described in 1981 (Lenz *et al.* 1981). The use of a vaginal ultrasound transducer guided aspiration of follicles was subsequently described by Wickland *et al.* (1985) and Feichtinger and Kemeter (1986) and this approach is today the most widely used method of oocyte retrieval for IVF (Tan *et al.* 1990). The question of flushing during oocyte retrieval has been reviewed with doubtful benefits. Prospective studies in 1980s and 1990s came out with differing conclusions. Studies by Scott *et al.* (1989) and Kingsland *et al.* (1991) have suggested no benefit in the routine practice of follicular flushing. However, these were small studies with relatively few patients.

Many fertility specialists still use follicular flushing during egg collection. A recent survey of Australian assisted reproduction units revealed that more than 50% use flushing of follicles in addition to direct aspiration of the fluid during oocyte retrieval. The rationale behind this is that flushing offers an advantage to the patient with a large number of oocytes being collected and thus a higher potential for pregnancy (Knight *et al.* 2001).

With these various results available, we carried out this study at Brentwood Fertility Centre, Essex Nuffield Hospital, Brentwood, Essex UK to analyse the number of oocytes retrieved by aspiration with or without follicular flushing.

Materials and methods

The patients were collected prospectively from June 2001 to September 2002. They all had assisted reproductive techniques, including IVF/ICSI at Nuffield Hospital.

Controlled ovarian hyper stimulation was achieved either by long- or short-cycle protocol. Buserelin SC daily injection or suprecur three-times-daily nasal spray (Shire Pharmaceuticals Ltd, Harts, UK) were used for desensitization and downregulation of the pituitary gland. Urinary gonadotrophin (Menopur, Ferring Pharmaceutical, UK, Langley, Berks) or Recombinant FSH (Gonal F, Serono Pharmaceutical Ltd, Feltham, Middlesex) were used for subsequent stimulation.

All the patients were followed up by transvaginal ultrasound scanning on alternate days starting 7 days from the commencement of ovarian stimulation. Induction of final follicular maturation was achieved with human chorionic gonadotropin (hCG) and oocyte retrieval was performed after 36–38 hours under ultrasound guidance.

Heparinized normal saline was used for follicular flushing. Flushing was performed with a Cook ovum aspiration 16-gauge double lumen needle (Cook, Limerick, Ireland). We employed a single entry into the ovary and the needle tip was manipulated to enter the follicles without withdrawing the needle outside the ovary to minimize ovarian trauma and post retrieval bleeding. The needle lumen was flushed and primed with flushing solution before insertion of the needle. A three-way tap was used to allow the circulation of 2 ml of heparinized normal saline through the empty follicle after aspiration of follicular fluid until an oocyte was retrieved or deemed not to be present. During flushing, the needle tip was rotated in a circular pattern to help to dislodge the oocyte from the follicular wall. The maximum number of flushes performed was six. All follicles 14 mm and more were flushed. The pressure was maintained at 170 mmHg throughout the procedure and egg collection was performed by two consultants.

The duration of egg collection procedures was determined by the number of follicles in any given IVF treatment cycle and therefore the duration was slightly longer (approximately 10 min) in the flushing group compared with no flushing. There was no difference in

the number of follicles obtained following different treatment regimes (long- or short-cycle).

Results

The total number of patients was 141 with an average age of 34 years (range 24–47 years). The total number of follicles aspirated was 1,489 and numbers of flushes counted were from no flush to up to six flushes. A total of 487 eggs were obtained with primary aspiration without flushing from 501 follicles (33.6% of all follicles). Of these 501 follicles, 14 were empty and as no granulosa cells were identified they were not flushed further. With one flush, 30 oocytes were retrieved from 34 follicles (2.3%); with two flushes, 486 oocytes from 496 follicles (33.3%); with three flushes, 54 oocytes from 63 follicles (4.2%); and with four flushes, 126 oocytes were retrieved from 145 follicles (9.8%). While 32 follicles (2.2%) were flushed five times with only 13 oocytes, and with a 6th flush only 21 oocytes were retrieved from 218 follicles (14.6%) (see Table I).

The total number of oocytes retrieved was 1,217 from 1,489 follicles. A total of 487 oocytes (40% of total oocytes) were retrieved from 501 follicles with primary aspiration without flushing. The percentage of oocytes retrieved with one flush was 2.5% of total oocytes and with two flushes, eggs were retrieved in 40%. The percentage with three, four, five and six flushes were 4.5%, 10.3%, 1.0% and 1.7% of total oocytes, respectively (see Table I).

The number of eggs collected was 20% more when flushing was adopted compared with the no flushing group.

The fertilization rates were compared in the centre between follicular flushing and no flushing groups; 58% achieved fertilization in the flushing group compared with 55% in the no flushing group. The overall pregnancy rate was 26% compared with 20% in the no flushing group and the live birth rate was 20% vs 13%.

Discussion

Ultrasound guided transvaginal needle aspiration of oocytes has become the most preferred method of egg collection for IVF/ICSI. This has improved the collection rate from 19.8% (Mettler *et al.* 1982) and 46% (Mao *et al.* 1987) per follicle, with laparoscopic methods to between 52% (Lenz and Lauristen 1982) and 64% (Lenz 1984) and recently, 82.6% (Baber *et al.* 1988). Follicles have been flushed in the expectation of collecting more oocytes.

Table I. Follicles aspirated and oocytes retrieved by number of flushes

Flushes	Follicles aspirated		Oocytes retrieved		Cumulative (%)
	n	(%)	n	(%)	
No. flushes	501	33.6	487	40	40
1	34	2.2	30	2.5	42.5
2	496	33.3	486	40	82.5
3	63	4.2	54	4.5	87
4	145	9.7	126	10.3	97.3
5	32	2.1	13	1	98.3
6	218	14.6	21	1.7	100
Total	1,489	100	1,217	100	

Studies have suggested that neither aspiration of follicular fluid alone, nor aspiration with flushing have advantages over each other. The technique may depend on the preferences of the surgeons. There have been no differences found in the pregnancy rates between aspiration alone and utilizing follicular flushing (Scott *et al.* 1989).

In our study, about 40% of oocytes were retrieved with aspiration only. With the first four flushes a further 57.3% of oocytes were obtained, giving 97.3% of the total oocytes obtained. The fifth and sixth flushes only added another 2.7% of oocytes.

Number of oocytes retrieved, fertilization rate and pregnancy rate were higher when follicular flushing was performed.

There are a number of theoretical advantages of aspiration over flushing, such as reduction in the operating time, anaesthetic agent and also in the operating cost. There is however, a potential risk of pelvic infection with increased risk of damage to the oocyte and patient tissue. These theoretical risks were not however encountered, except for a slight increase in operating time, but there was no change in the anaesthetic regimen.

Follicular flushing *per se* does not appear to damage the oocytes (Lenz and Lauristen 1982).

A number of studies have shown a range of outcomes regarding fertilization and pregnancy rates (Waterstone and Parsons 1992; Knight *et al.* 2001). The time required for oocyte retrieval will be shorter if no flushing is performed. For the patients with a good number of follicles the chances of achieving pregnancy may not alter without flushing, but for patients with few follicles, it is desirable to collect every oocyte, as only one extra oocyte may affect the outcome.

In conclusion, flushing up to four times would not make a difference to operating and anaesthetic time, with minimum implication for the cost. However, it would allow a maximum number of oocytes, especially in patients with very few follicles, up to 85% of oocytes to be retrieved with four flushes.

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