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# High dose letrozole in infertile women with unilateral tubal block: a preliminary report

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## Abstract

**Background:** Till now, there is no universal agreement on the best management of women with unilateral blocked tube. The aim of this study was to evaluate the use of high dose letrozole in infertile women with one blocked tube. This prospective non-randomized study was conducted at a university-affiliated infertility unit. It included 15 women with one blocked tube (*proximal or mid segmental block*) with a period of 1–6 years of infertility. Letrozole (10 mg/day for 5 days) was prescribed for all of them for a maximum of three cycles. The primary outcome was Live birth rate.

**Results:** Nine out of the 15 women conceived (60%). Live birth rate was 53% (8/15). All women had a good response to this regimen. None complained of side effects of this dose. No multiple pregnancies and/or congenital anomalies were reported.

**Conclusions:** This preliminary report showed that treatment of infertile women, with unilateral tubal block, with high dose letrozole is effective. To our knowledge, this is the first report in the English literature on the use of high dose of letrozole in such cases.

**Keywords:** Fallopian tube, IVF/ICSI, Letrozole, Unilateral tubal block

## Background

Tubal factor infertility is one of the most common causes of infertility. Its incidence is rising in both developed and developing countries due to rapidly increasing rate of sexually transmitted diseases (STDs) with subsequent pelvic inflammatory disease (PID) [1]. In addition, the epidemic of increasing C.S. rate is another contributing factor for increasing incidence of tubal factor infertility [2].

It has been estimated that tubal factor infertility accounts for about 35% of cases of infertility and more than 50% of cases of female infertility [3]. Treatment of infertile women with bilateral tubal block is clear and simple. However, management of infertile women with one occluded (obstructed) tube is more challenging and puzzling. There is no universal agreement on management of such women. Management options include

expectant management [4–6], surgical management and correction, and controlled ovarian stimulation (COS) combined with IUI or IVF/ICSI [5, 6]. A recent systematic review and meta-analysis showed that patients with proximal tubal block have similar pregnancy rates after COH-IUI when compared with those with bilateral patent tubes and unexplained infertility [6]. However, if the tubal block was distal, lower pregnancy rates are to be expected [6]. In this study, letrozole in a high dose was used in a trial to induce follicular growth both from both ovaries: the ipsilateral as well as the contralateral ovary of the blocked tube.

## Methods

This is a preliminary report of a prospective non-randomized study on 15 women who suffer from 1 to 6 years of infertility after being diagnosed with unilateral tubal block confirmed by hysterosalpingography (HSG) and/or laparoscopy. An approval was obtained from our Departmental Committee. All women gave their written

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**Table 1** Summary of the demographic and clinical characteristics of our population

Patient No.	Age	Parity	Infertility duration (years)	No. of stimulated cycles	Pregnancy	Outcome
1	27	2+3	5	1	Yes	Healthy girl
2	26	0	6	2	Yes	Healthy boy
3	26	0+2	1.5	2	Yes	Healthy girl
4	24	0+2	2	1	Yes	Healthy girl
5	28	1+0	2	2	Yes	Healthy boy
6	32	0+2	3	2	Yes	Healthy girl
7	27	1+1	3	3	Yes	Healthy girl
8	35	P1+5	3	1	Yes	Healthy girl
9	23	0+0	2	2	Yes	Blighted ovum
10	34	1+3	4	1	No	-----
11	24	0+1	3	1	Yes	-----
12	28	0+1	1.5	3	No	-----
13	25	0+1	2	3	No	-----
14	27	0+0	4	2	No	-----
15	30	P0+1	3	3	No	-----

informed consent for participation in the study. The experimental nature of the study was explained, in details, to all participants before embarking on more aggressive treatment. Inclusion criteria were as follows: (1) age between 20 to 35 years; (2) unilateral tubal block with patent second tube; (3) tubal block is corneal (proximal), mid-segmental; (4) absence of hydrosalpinx; (5) ovulatory women; and (6) normal semen parameters. Exclusion criteria were as follows: endometriosis ± endometriomas (if laparoscopy was performed), the presence of hydrosalpinx, male factor infertility, and known hepatic or renal impairment. Age of women enrolled in this study ranged between 23 and 35 years with the mean age of 27.7 years.

Twelve out of 15 patients had one of their tubes removed (unilateral salpingectomy) because of tubal pregnancy through either laparoscopy or laparotomy. One patient had her tube removed because of a tubo-ovarian abscess through laparotomy. The last two patients had unilateral corneal block mostly due to PID.

All women received letrozole (Femara, Novartis, UK Ltd 2.5 mg) in the dose of two tablets twice daily (10 mg/day) for 5 days starting on the third cycle day for three consecutive cycles. Serial ultrasound folliculometry was performed starting on day 10 to ensure adequate follicular growth, to count number of follicles in each ovary, and to determine from which side follicles are growing. Ovulation was triggered using 5000 IU of HCG, once one or more follicles reached 18 mm in mean diameter. The primary outcome is live birth rate. Secondary outcomes were multiple pregnancies, ovarian hyperstimulation syndrome (OHSS), and side effects of the medication.

## Results

Nine out of the 15 women conceived (60%). One pregnancy ended in an embryonic pregnancy and a miscarriage, giving an 8/15 (53%) live birth rate. The remaining eight women gave birth to healthy babies. Three women got pregnant during the first stimulated cycle and five during the second stimulated cycle whereas the last patient conceived during the third stimulated cycle (Table 1).

All women had a good response to this regimen without any incidence of ovarian hyperstimulation. None complained of any side effects of this dose. No incidence of multiple pregnancies or congenital anomalies was encountered in these women.

## Discussion

In developing countries with limited resources, every effort should be done to treat infertile couples before resorting to the more expensive options including COS + IUI and/or IVF/ICSI. In this preliminary report, letrozole, an aromatase inhibitor, in the dose of 10 mg/day was used as a last trial before proceeding to other options in women who suffer from infertility with unilateral blocked tube after allowing enough time for pregnancy to occur by ovum transmigration. Ovum transmigration was reported to be a frequent event occurring in both intrauterine and ectopic pregnancies [7]. Ross et al., in their retrospective study, showed that one-third of pregnancies result from transperitoneal migration of ova in women with one fallopian tube [7]. Letrozole has been used for ovulation induction for nearly two decades [8]. Letrozole in doses as high as 12.5 mg per day has been reported [9]. Letrozole in high doses

resulted in increased follicular growth and ovulation without adversely affecting the endometrium [9]. The rationale in this study is that superovulation with high dose letrozole might ensure follicular growth and ovulation from both ovaries including the ovary related to the patent tube as well as the contralateral ovary of the blocked tube. Letrozole was chosen to avoid the anti-estrogenic effect of clomiphene citrate on both endometrium and cervical mucus in particular because a high dose was tried. A satisfactory live rate of 53% was achieved in this study. To our knowledge, this is the first report in the English literature on the use of high dose of letrozole in such cases.

### Limitations

Very small sample size—our population was a group of young aged women regularly ovulating and expected good responders. If no pregnancy occurs, they still have enough time to go for other options including IVF. Randomized controlled studies are needed to validate the results of this report and to examine the safety and possibility of evaluating different, possibly lower doses of letrozole.

### Conclusions

This preliminary report with a small sample size showed that treatment of young infertile women, with unilateral tubal block, with high dose letrozole is effective. To our knowledge, this is the first report in the English literature on the use of high dose of letrozole in such cases. In countries with limited resources, if the results of this report are validated by randomized controlled trials, this will be a less expensive treatment option.

### Abbreviations

STDs: Sexually transmitted diseases; C.S.: Cesarean section; COS: Controlled ovarian stimulation; PID: Pelvic inflammatory disease; OHSS: Ovarian hyperstimulation syndrome

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### Author's contributions

Single author. The author read and approved the final manuscript.

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### Availability of data and materials

Data are available.

### Declarations

#### Ethics approval and consent to participate

Full name of the ethics committee: Medical Ethics Committee, Faculty of Medicine, Assiut University. IRB no.: 17300509. All women gave their written informed consent for participation in the study.

#### Consent for publication

Not applicable

### Competing interests

The author declares that he has no competing interests.

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