



## Antagonist Protocol versus Short Protocol in Poor Responders

Wael Ahmed Ezzat Ammar

Fellow Obstetrics and Gynecology at El GALAA Teaching Hospital, Cairo, Egypt  
Email: [dr.waela3@gmail.com](mailto:dr.waela3@gmail.com)

**Abstract: Aim:** Here we try to compare antagonist protocol versus short protocol in females suffering from poor responders. **Methods:** This study is a retrospective study done in EL Galaa Assisted Reproductive Center in El GALAA Teaching Hospital over a period of 10 years from January 2015 till June 2025. In this study we recorded 200 poor responders' females underwent ICSI cycles where half of them were on antagonist protocol and other half were on short protocol; Group A: Antagonist protocol for 100 poor responder females. Group B: Short protocol for 100 poor responders' females. Both groups take the same starting maximum dose 450 IU of the same HMG drug. We recorded the results according to: number of days of stimulation, number of oocytes retrieved, number of M2 oocytes, pregnancy rate. **Results:** We recorded the following. Age mean in group A was  $39.23 \pm 2.17$ , and in group b was  $39.35 \pm 1.86$ , where p value was 0.67 i.e. > 5%, so age was statistically insignificant difference between both groups. BMI in group A mean was  $33.06 \pm 1.0$ , and group b mean was  $33.15 \pm 1.4$ , where p value was 0.6 i.e. > 5% s, so BMI was statistically insignificant difference between both groups. Days of stimulation group A mean was  $13.33 \pm 2.12$  days, group B mean was  $13.47 \pm 1.88$  days, P value was 0.62 i.e. > 5%, so days of stimulation was statistically significant between both groups. Number of oocytes retrieved group A mean was  $3.52 \pm 1.72$ , and group B mean was  $3.41 \pm 2.37$ , p value was 0.71 i.e. > 5% w, so number of oocytes retrieved was statistically significant between both groups. Number of M2 oocytes group A mean was  $1.31 \pm 1.4$  M2, and group B mean was  $1.25 \pm 1.73$  M2, P value was 0.79 i.e. > 5%, So number M2 of oocytes retrieved was statistically significant between both groups. Pregnancy rate for group A mean was  $0.05 \pm 0.21$  and group B mean was  $0.04 \pm 0.19$ , P value was 0.72 i.e. > 5%, so pregnancy rate was statistically insignificant between both groups. **Conclusion:** Comparison of Antagonist and short protocols in poor responders was statistically insignificant differences as regarding number of days of stimulation, number of oocytes retrieved, number of M2 oocytes and pregnancy rate.

[Wael Ahmed Ezzat Ammar. **Antagonist Protocol versus Short Protocol in Poor Responders** *Nat Sci* 2025,23(10):1-4]. ISSN 1545-0740 (print); ISSN 2375-7167 (online). <http://www.sciencepub.net/nature> 01. doi:[10.7537/marsnsj231025.01](https://doi.org/10.7537/marsnsj231025.01)

**Keywords:** Antagonist Protocol; Short Protocol; Poor Responders

### 1. Introduction:

It is very challenging to put a definition for poor responders for a long time ago. The European Society of Human Reproduction and Embryology organized a Campus Workshop in 2011 and published the "Bologna Criteria [BC] to Define Poor Responders" (1). POR was defined as the collection of three or fewer oocytes in two prior ovarian stimulation cycles (2), or collection of three or fewer oocytes in a single stimulation cycle from a woman who is over 40 years of age (3), collection of three or fewer oocytes in a single stimulation cycle and an abnormal ovarian reserve test (ORT: antral follicle count less than five to seven follicles or antimullerian hormone AMH < 0.5–1.1 ng/mL) (4), or presence of an abnormal ORT in a woman over 40 years of age (4).

Poor responders' management is very challenging. Different protocols in ICSI were used to overcome this challenge. Some advice to increase the dose of HMG(2).

In short protocol we depending on flare-up, which increase the response of the ovary in poor responders. This flare up helps follicular recruitment(3).

Poor responders may be suitable for short protocol(4).

In Antagonist protocol we starting HMG alone from day 2 or 3 of menstrual cycle then here in this study after 7 days of HMG we started the antagonist by Cetrotid 0.25 mg daily i.e. fixed antagonist protocol(5).

#### **Aim of study:**

Here we try to compare antagonist protocol versus short protocol in females suffering from poor responders.

### 2. Patient and methods:

This study is a retrospective study done in EL Galaa Assisted Reproductive Center in El GALAA

Teaching Hospital over a period of 10 years from January 2015 till June 2025.

In this study we recorded 200 poor responders' females underwent ICSI cycles where half of them were on antagonist protocol and other half were on short protocol; Group A: Antagonist protocol for 100 poor responder females. Group B: Short protocol for 100 poor responders' females.

Both groups take the same starting maximum dose 450 IU of the same HMG drug.

We recorded the results according to: number of days of stimulation, number of oocytes retrieved, number of M2 oocytes, pregnancy rate.

#### Inclusion criteria:

Poor responders females (POR) were defined according to the "Bologna Criteria [BC] to Define Poor Responders" (1). Poor responders were defined as the collection of three or fewer oocytes in two prior ovarian stimulation cycles (2), Or collection of three or fewer oocytes in a single stimulation cycle from a woman who is over 40 years of age (3), collection of three or fewer oocytes in a single stimulation cycle and an abnormal ovarian reserve test (ORT): antral follicle count less than five to seven follicles or antimullerian hormone AMH < 0.5–1.1 ng/mL (4), or presence of an abnormal ovarian reserve test in a woman over 40 years of age (4).

#### Exclusion criteria:

- Presence of male azoospermia
- Presence of intrauterine adhesions.
- Presence of any uterine anomalies.
- Presence of uterine intramural or submucous myoma.
- Presence of any medical disorders.

In short protocol group we started from day 2 or day 3 of menstrual cycle by one ampule decapeptyl 0.1 mg s.c. then from next day half ampule decapeptyl 0.1 mg plus HMG daily.

In Antagonist protocol we starting HMG alone from day 2 or 3 of menstrual cycle then here in this study after 7 days of HMG we started the antagonist by Cetrotid 0.25 mg daily i.e. fixed antagonist protocol. Both groups receiving the maximum stimulation dose 450 IU of the same HMG drug.

### 3. Results:

We recorded the following

Age mean in group A was  $39.23 \pm 2.17$ , and in group b was  $39.35 \pm 1.86$ , where p value was 0.67 i.e. > 5% so age was statistically insignificant difference between both groups (Figure 1).

BMI in group A mean was  $33.06 \pm 1.0$ , and group b mean was  $33.15 \pm 1.4$ , where p value was 0.6 i.e. > 5% s, so BMI was statistically insignificant difference between both groups (Figure 2).

Days of stimulation group A mean was  $13.33 \pm 2.12$  days, group B mean was  $13.47 \pm 1.88$  days, P value was 0.62 i.e. > 5%, so days of stimulation was statistically significant between both groups (Figure 3).

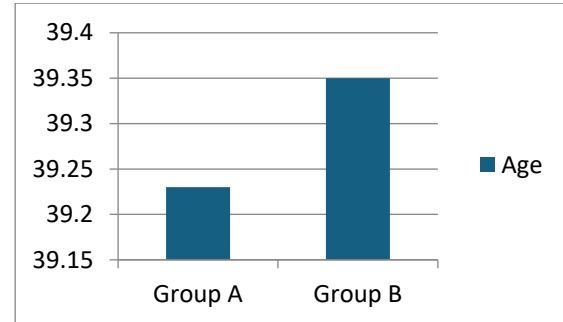


Figure (1): Age.

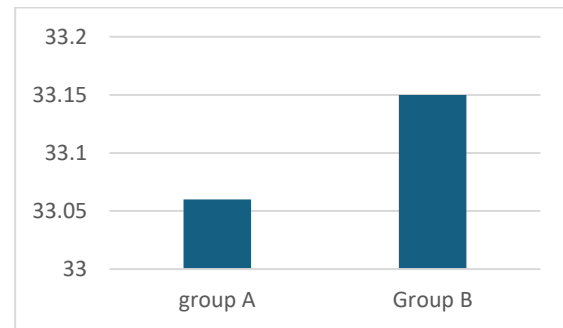


Figure (2): BM

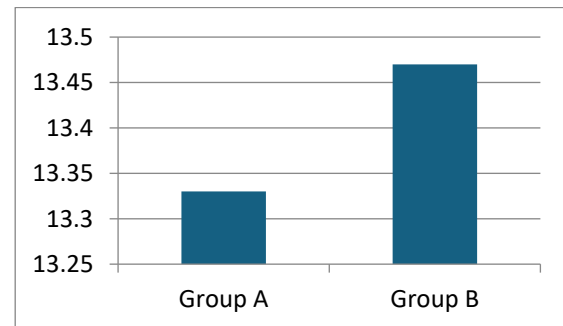
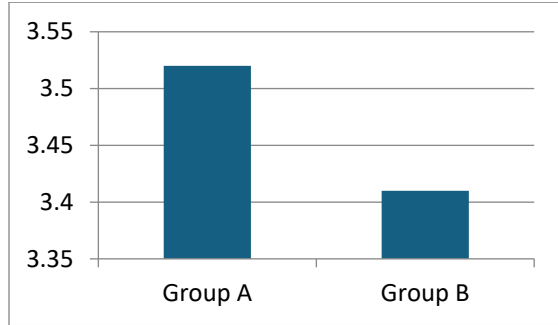


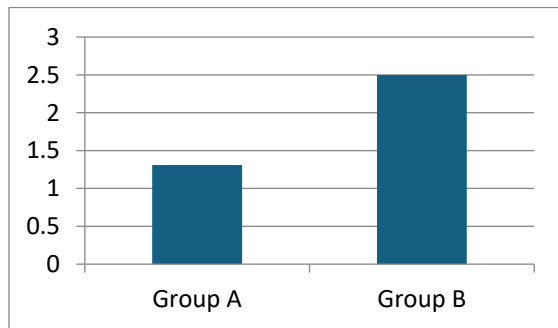
Figure (3): Number of days of stimulation

Number of oocytes retrieved group A mean was  $3.52 \pm 1.72$ , and group B mean was  $3.41 \pm 2.37$ , p value was 0.71 i.e. > 5% w, so number of oocytes retrieved was statistically significant between both groups (Figure 4).



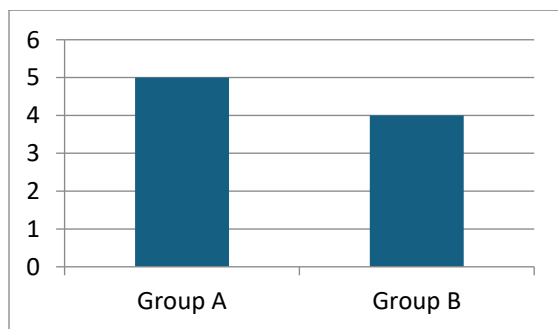
**Figure (4):** Oocytes retrieved

Number of M2 oocytes group A mean was  $1.31 \pm 1.4$  M2, and group B mean was  $1.25 \pm 1.73$  M2, P value was 0.79 i.e.  $> 5\%$ , So number M2 of oocytes retrieved was statistically significant between both groups (Figure 5).



**Figure (5):** M2 oocytes

Pregnancy rate for group A mean was  $0.05 \pm 0.21$  and group B mean was  $0.04 \pm 0.19$ , P value was 0.72 i.e.  $> 5\%$ , so pregnancy rate was statistically insignificant between both groups (Figure 6).



**Figure (6):** Pregnancy rate%

#### 4. Discussion:

This study was retrospective study done in El Galaa Assisted Reproductive Center in El Galaa Teaching Hospital from January 2015 till June 2025.

In this study we recorded 200 poor responders' females underwent ICSI cycles where half of them were on antagonist protocol and other half were on

short protocol; Group A: Antagonist protocol for 100 poor responder females. Group B: Short protocol for 100 poor responders' females.

Both groups take the same starting maximum dose 450 IU of the same HMG drug.

Where we found that Comparison of Antagonist and short protocols in poor responders was statistically insignificant differences as regarding number of days of stimulation, number of oocytes retrieved, number of M2 oocytes and pregnancy rate

Our results agree with other studies done as, study done by Tarek et al. (5).

Our recorders agreed with results of other study as Surrey et al. (1); Ferraretti et al. (2); Polyzos and Devroey (3) Lie et al. (6); Li et al. (7) and Sunkara et al. (10).

While Adel et al. (13) found that Antagonist protocol is better than short protocol in poor responders.

Chatillon-Boissier et al. (11) and Chatillon-Boissier et al. (12) concluded that there were no differences between protocols in poor responders.

#### Conclusion:

Comparison of Antagonist and short protocols in poor responders was statistically insignificant differences as regarding number of days of stimulation, number of oocytes retrieved, number of M2 oocytes and pregnancy rate.

GOTHI Review and Approval Certificate Number: HG000088(23/11/2022)

#### References

- Ferraretti AP, La Marca A, Fauser BC, et al. ESHRE consensus on the definition of "poor response" to ovarian stimulation for in vitro fertilization: the Bologna criteria. *HuReprod* 2011; 26:1616–24.2011
- Polyzos NP and Devroey P. A systematic review of randomized trials for the treatment of poor ovarian responders: is there any light at the end of the tunnel? *FertilSteril*2011;96:105861.e7. 2011
- Surrey E, Bower J, D, et al. Clinical and endocrine effects of a microdoseGnRH agonist flare regimen administered to poor responders who are undergoing in vitro fertilization. *FertilSteril* 2014;69:419 –24.2014
- Nikolettos N, Al-Hassani S, Felberbaum R, et al Gonadotrophinreleasing hormone antagonist protocol: a novel method of ovarian stimulation in poor responders. *Eur J Obstet Gynecol Reprod Biol* 2001 Aug;97(2):202-7.2001
- Tarek K Al-Hussaini, Ahmed Aboelfadle Mohamed, Ayman Askar, et al: Ovarian stimulation in patient oriented strategies

- encompassing individualised oocyte number 4 category; antagonist versus short agonist protocols, *J Hum Reprod Sci.* Sep 29;16(3):212-217.2023
6. Li F., Ye T., Kong H., Li J., Hu L., Jin H., Su Y., Li G.: Efficacies of different ovarian hyperstimulation protocols in poor ovarian responders classified by the POSEIDON criteria. (2020) *Aging*, 12 (10), pp. 9354 - 9364, Cited 25 times (2020)
  7. Li F., Niu A., Feng J., Wang C., Feng X., Zhang Y., Chen Y.: Comparison of different ovarian hyperstimulation protocols efficacy in poor ovarian responders classified by Poseidon criteria. (2021) *Chinese Journal of Reproduction and Contraception*, 41 (9), pp. 770 - 775, 2021
  8. Mauries C., Ranisavljevic N., Mollevi C., Brunet C., Hamamah S., Brouillet S., Anahory T.: "Short agonist stop" protocol, an ovarian stimulation for poor responders in in vitro fertilization (IVF). (2022) *Frontiers in Endocrinology*, 13, art. no. 1056520, 2022
  9. Schimberni M., Ciardo F., Schimberni M., Giallonardo A., De Pratti V., Sbracia M.: short gonadotropin-releasing hormone agonist versus flexible antagonist versus clomiphene citrate regimens in poor responders undergoing in vitro fertilization: a randomized controlled trial (2016) *European review for medical and pharmacological sciences*, 20 (20), pp. 4354 – 4361. 2016
  10. Sunkara S.K., Coomarasamy A., Faris R., Braude P., Khalaf Y.: Long gonadotropin-releasing hormone agonist versus short agonist versus antagonist regimens in poor responders undergoing in vitro fertilization: A randomized controlled trial (2014) *Fertility and Sterility*, 101 (1), pp. 147 - 153, 2014
  11. Chatillon-Boissier K., Genod A., Denis-Belicard E., Felloni B., Chene G., Seffert P., Chauleur C.: Prospective randomised study of long versus short agonist protocol with poor responder patients during in vitro fertilization [Étude prospective randomisée protocoles agonistes long versus court chez les patientes mauvaises répondeuses en fécondation in vitro] (2012) *Gynecologie Obstetrique et Fertilité*, 40 (11), pp. 652 - 657, 2012
  12. Chatillon-Boissier K., Genod A., Denis-Belicard E., Felloni B., Chene G., Seffert P., Chauleur C.: Prospective randomised study of long versus short agonist protocol with poor responder patients during in vitro fertilization [Étude prospective randomisée protocoles agonistes long versus court chez les patientes mauvaises répondeuses en fécondation in vitro] (2012) *Gynecologie Obstetrique et Fertilité*, 40 (11), pp. 652 - 657, 2012
  13. Adel Aly Elbogdady and Amal Helmy: GnRH agonist short protocol versus GnRh antagonist flexible protocols in poor responders undergoing in vitro fertilization treatment. *Al Azhar International Medical Journal*, Article 10, volume1, issue3, 2020.

8/25/2025