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Long Protocol versus Short Protocol in Poor Responders

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Abstract: Aim: Comparison between long agonist protocol and short agonist protocol in poor responders females. **Methods:** A retrospective study done at El GALAA Teaching Hospital over a period of 10 years from January 2015 till end of 2024. Where 200 cycles of ICSI were performed for poor responders females divided into 2 groups: Group (A) 100 cases of poor responders females who received long protocol, And Group (B) 100 cases of poor responders females who received short protocol. Comparison between two groups done according to number of days of stimulation, number of oocytes retrieved, number of M2 oocytes, pregnancy rate. Both groups were on same maximum dose of HMG stimulation drug of 450 IU of same drug. **Results:** As regarding: Age was of statistically insignificant difference between both groups where mean of age of group A was 37.7 ± 4.5 year, And mean of age of group was 36.7 ± 4.9 year, And P value was 8%, So Age between both groups was statically insignificant as P value > 5%. Mean of days of stimulation was Group A was 13.7 ± 3 days, while Mean of group B was 11.6 ± 2.5 days, where P value was 0% so it is statistically significant between both groups as P value less than 5%. Number of oocytes retrieved was, Mean of group A was 1.8 ± 1.8 oocytes, while group B mean was 2.3 ± 2.2 oocytes, And P value was 5%, So Number of oocytes retrieved was statistically significant between both groups as P value was not more than 5%. Number of M2 oocytes was, Mean of Group A was 1.6 ± 1.5 M2, And mean of Group B was 2.5 ± 2.1 M2, where P value was 0 %, So Number M2 of oocytes retrieved was statistically significant between both groups as P value was not more than 5%. Pregnancy rate was, Mean of group A was 3% ± 0.17% oocytes, while group B mean was 4% ± 0.19% oocytes, And P value was 16%, So pregnancy rate was statistically insignificant between both groups as P value was more than 5%. **Conclusion:** In poor responders females short protocol was better than long protocol specially in number of days of stimulation, number of oocytes retrieved and number of M2 oocytes.
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Keywords: Protocol; Responders; female; oocyte

1. Introduction:

Defining poor ovarian responder (POR) has been a long standing challenge. 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).

The treatment of poor responders has challenged many in the field of assisted reproduction. A variety of ovarian stimulation protocols have been tried with some degree of success indicating different reasons for poor response. Many clinicians simply increase the gonadotropin daily dose despite the lack of supporting evidence (2).

The short down-regulation protocol (flare-up) has been reported to successfully improve ovarian response in poor responders. The initial agonistic flare-up that occurs with the short protocol may also aid follicular recruitment, which may theoretically reduce the gonadotropin requirement (3).

The short protocol is more suited to the profile of ovarian poor responders (4).

Aim of study:

To compare long protocol versus short protocol in Poor responders females

2. Patient and methods:

This is retrospective study was done in El Galaa Teaching Hospital over 10 years from January 2015 till end of 2024.

Where females who were Poor responders and received long protocol were compared with females who were Poor responders and received short protocol.

Inclusion criteria:

Females who were poor responders are defined according to 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)..

Exclusion criteria:

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

Females who were poor responders from January 2015 till end of 2024 were divided into 2 groups:

- Group A: 100 Females who were poor responders and received long protocol.
- Group B: 100 Females who were poor responders and received Short protocol

Comparison between two groups done according to number of days of stimulation, number of oocytes retrieved, number of M2 oocytes, pregnancy rate. Both groups were on same maximum dose of HMG stimulation drug of 450 IU of same drug.

3. Results:

As regarding the mean of age between the both groups (Group A: 100 Females who were poor responders and received long protocol. And Group B: 100 Females who were poor responders and received Short protocol), Mean of age of group A was 37.7 ± 4.5 year, And mean of age of group was 36.7 ± 4.9 year, And P value was 8%, So Age between both groups was statically insignificant as P value > 5% as shown in figure (1).

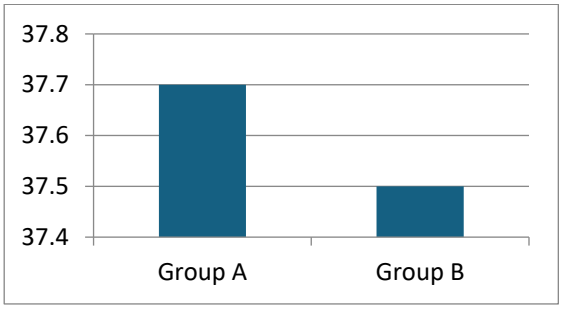

Figure (1): Age

As regarding number of days of stimulation, Mean of Group A was 13.7 ± 3 days, while Mean of group B was 11.6 ± 2.5 days, where P value was 0% so it is statistically significant between both groups as P value less than 5% as shown in figure (3).

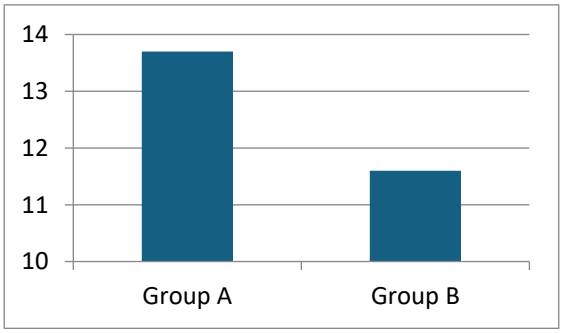

Figure (3): Number of days of stimulation

As regarding number of oocytes retrieved, Mean of group A was 1.8 ± 1.8 oocytes, while group b mean was 2.3 ± 2.2 oocytes, And P value was 5%, So Number of oocytes retrieved was statistically significant between both groups as P value was not more than 5% as shown in figure(2).

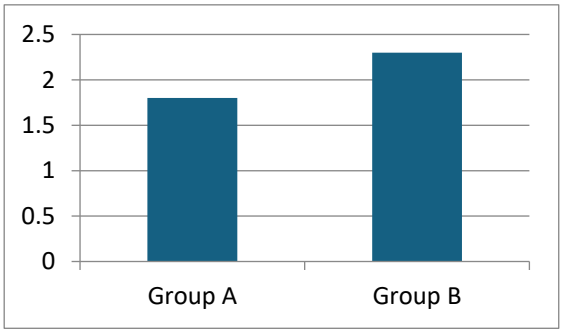

Figure (2): Oocytes rtrived

As number of M2 between both groups, Mean of Group A was 1.6 ± 1.5 M2, and mean of Group B was

2.5 ± 2.1 M2, where P value was 0 %, So Number M2 of oocytes retrieved was statistically significant between both groups as P value was not more than 5% as shown in figure (4).

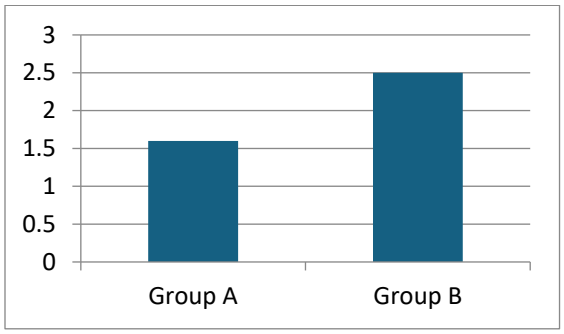

Figure (4): M2 oocytes

As regarding pregnancy rate between both groups, Mean of group A was 3% ± 0.17% oocytes, while group b mean was 4% ± 0.19% oocytes, And P value was 16%, So pregnancy rate was statistically insignificant between both groups as P value was more than 5% as shown in figure(5)

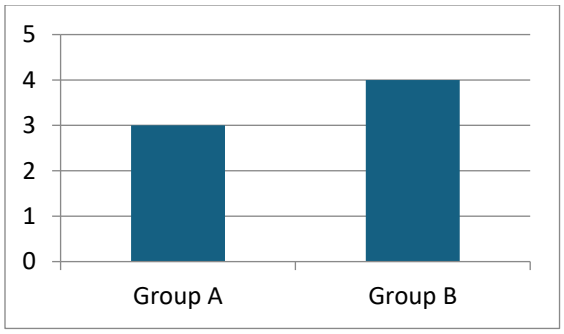

Figure (5): Pregnancy rate%

4. Discussion:

Our study was retrospective done in El Galaa Teaching Hospital from January 2015 till end of 2024, where 200 poor responders females were performed ICSI cycles with same drug of stimulation and same maximum dose of stimulation, These poor responders females arranged in to 2 groups, Group A 100 poor responder female received long agonist protocol by starting down regulation from day 18 of previous cycle for 14 days by daily half ampoule of decapeptyl 0.1 mg then after down regulation stimulation started. Second group (group B): 100 poor responders female received short protocol where starting from day 2 by one ampoule Decapeptyl 0.1 mg then from 3rd day half ampoule of decapeptyl 0.1mg with stimulation drug.

From our results we can observe that Age and pregnancy rate was insignificant statistically difference between long and short protocol in poor responders.

While Short protocol in poor responders was better than long protocol in poor responders as regarding: days of stimulation which was less with short protocol with statistically significant difference, number of oocytes was higher in short protocol with statistically significant difference. Number of M2 oocytes was higher in short protocol with statistically significant difference.

Our results agree with other studies done as, study done by **Mauries et al. (8), Kdous Moez, et al. (5) And Schimberni et al. (9) 2016** which concluded that short protocol is better than long protocol in poor responders**.**

Also our results agreed with results of other study as **Surrey et al. (1); Ferraretti et al. (2); Polyzos and Devroey (3).**

Lie et al (6) 2020 and Li F, et al. (7) concluded that long protocol was better than short protocol for young age poor responders. And, there was no statistically significant difference in old age poor responders.

While **Sunkara et al (10)** found that Long protocol is better than short protocol in poor responders where short is associated with less number of oocytes.

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

Conclusion:

In poor responders females short protocol was better than long protocol specially in number of days of stimulation, number of oocytes retrieved and number of M2 oocytes.

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