Conference Paper

Characteristic of Poor Responder Patients and the Success Rate of Biochemical Pregnancy in the Administration of Adjuvant Recombinant Luteinizing Hormones in Yasmin Clinic, Jakarta

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Abstract

Introduction: Management for poor response patients is still a challenge for clinician engaged in Assisted Reproductive Technology. Various protocols have been proposed to improve the outcome for patients, though no RCT can provide the evidence based of success rate of one protocol among others.

Objective: Our purpose is to find the basic data of poor responder patients in Yasmin Clinic, Jakarta and to assess the IVF cycle outcome after the addition of recombinant Luteinizing Hormones.

Material and methods: This is a cohort retrospective study taken from medical records of IVF patients at Yasmin Clinic, Cipto Mangunkusumo Hospital between January 2012 to January 2015.

Result: Two hundreds and eighty-one poor response patients were selected for ART during January 2012 to January 2015, were divided into four main group. Control group received gonadotrophin protocol, while group II received additional recombinant Luteinizing hormones (rLH), Group III received additional Growth hormones (GH) and Group IV received additional rLH and GH both.

Discussion: Our study demonstrated the follicle count, the oocyte count and the cleavage rate were statistically significant difference between control group and LH group. Where the oocyte count and follicle count were significantly higher, but the cleavage rate with LH showed negative correlation compare with control group.

Conclusion: In this study we found that with adjuvant therapy with *recombinant Luteinizing Hormones,* produced higher follicles count and oocyte count.

Keywords: poor responder, diminished ovarian response, luteinizing hormone

1. Introduction

Management of poor responder patients is still a challenge for clinicians engaged in Asisted Reproductive Technology [1,2]. Various protocols have been given for improving outcomes for patients with poor responders, but the results are often disappointing, since any given protocol provides the end result with no significant different [2,3,4].

Poor response patient in the literature have diversity in terminology, characterized generally these patients respond minimal to the protocol of ovarian stimulation given, which is illustrated by the results of the low number of follicles, the low number of oocytes, the high failure cycle, in which will ultimately result in lower pregnancy success rates [1-7].

Poor response patient had a wide range of age [1,2]. Although associated with reduced ovarian reserve caused by aging process, poor responders can occur at a young age. Although egg donation is often suggested as an alternative, but different stimulation protocols should be done before it is offered in younger patients with poor response, since the optimal ovarian stimulation should be given first before proceed to the egg donation [1,2].

Various stimulation protocols offered for patients with poor response, such as by using high-dose gonadotrophin, estrogen, androgen administration, agents modulating androgen etc [3,4]. But there has been no RCTs or research can prove the success rate or superiority of one protocol among other in treatment of poor responder.

Infertility has become emerging problems in Indonesia, self-awareness for seeking help for fertility issues had increase in decade. Approximately 10% of population experiencing infertility issues [8]. Among those percentage, 9% - 24% are poor response patients [9]. There are limited basic data about the poor response patients in Indonesia. Likewise the best stimulation protocol or an additional protocol provided with the success rate.

2. Methods

2.1. Population and Sample

This retrospective cohort study was performed on Yasmin Clinic, Jakarta. Target population of this research was poor response patients underwent assisted reproductive treatment in Yasmin Clinic, Jakarta. The accessible population was poor response patients who came in between January 2012 to January 2015 and underwent assisted reproductive treatment in Yasmin Clinic (RSCM). The study was approved by ethics committee.

2.2. Data Collection

Data were collected from medical record. Inclusion criteria used in this research are all infertile patients who meet the Bologna criteria (EHSRE) for poor response patients in Yasmin Clinic. Exclusion criteria from this study are patients which failed to continue the stimulation nor stop the protocol and the ones with incomplete or loss of medical record data. All medical records from Yasmin Clinic between January 2012 to January 2015 were collected. We collected patients' demographic data, etiology of infertility, selected treatment for infertility, cleavage rate and chemical pregnancy as the outcome.

Variables	Median ± Standar Deviasi	N (%)
Age	39 ± 5,406	
Duration of infertility	8 ± 4,783	
Additional etiology		
Endometriosis		64 (22,8)
Endometrial polyps		39 (13,9)
Fibroid		17 (6)
Ovarian cyst		4 (1,4)
Bilateral tubal occlusion		9 (3,2)
Unilateral tubal occlusion		4 (1,4)
Bilateral non patent tube		9 (3,2)
Unilateral non patent tube		6 (2,1)
Adenomyosis		16 (5,7)
Hydrosalping		14 (5)
OAT		17 (6)
Azoosperm		10 (3,6)
Astenozoosperm		9 (3,2)
Oligozoosperm		12 (4,3)
Oligosperm		18 (6,4)
Hyperprolactin		5 (1,8)

TABLE 1: Demographic characteristics of patients.

Cycles were cancelled in the presence of <1 developing follicle. eggs retrieval was performed after administration of HCG. Insemination was performed by either conventional IVF or ICSI. Fertilization then assessed 16 hours after insemination and embryo's cleavage was evaluated at 24-hours interval by recording cell number and then classified as grade I – III (poor – good).

2.3. Data Analysis

Statistical analysis of obtained data was analyzed by means of Statistical Package for the Social Sciences (SPSS) for Windows version 11.0 software. Differences between each variables were analyzed using Chi-square to compare the chemical pregnancy rate between selected therapy and to asses the cleavage rate within them.

3. Result

From January 2012 to January 2015, there were 324 patients meet the criteria of poor response based on our inclusion criteria. From all 324, we were having 43 patients as

Variables	LH		GH		LH+GH		Control	
	Median ± SD	N (%)	Mean/ Median ± SD	N (%)	Median ± SD	N (%)	Median ± SD	N (%)
Number of patients		118		28		47		88
Age	39 ± 4,623		39 ± 8,025		40 ± 4,186		39 ± 5,914	
Duration of infertility	9 ± 4,679		9,86		8 ± 4,631		7 ± 4,837	
Additional etiology								
Endometriosis		29 (24,6)		6 (21,4)		6 (12,8)		23 (26,1)
Endometrial polyps		23 (19,5)		1 (3,6)		2 (4,3)		13 (14,8)
Fibroid		10 (8,5)		0 (0)		2 (4,3)		5 (5,7)
Ovarian cyst		1 (0,8)		0 (0)		0 (0)		3 (3,4)
Bilateral tubal occlusion		3 (2,5)		2 (7,1)		3 (6,4)		1 (1,1)
Unilateral tubal occlusion		2 (1,7)		0 (0)		0 (0)		2 (2,3)
Bilateral non patent tube		3 (2,5)		1 (3,6)		2 (4,3)		3 (3,4)
Unilateral non patent tube		4 (3,4)		1 (3,6)		0 (0)		1 (1,1)
Adenomyosis		10 (8,5)		0 (0)		1 (2,1)		5 (5,7)
Hydrosalping		9 (7,6)		1 (3,6)		1 (2,1)		3 (3,4)
OAT		14 (11,9)		1 (3,6)		0 (0)		2 (2,3)
Azoosperm		1 (0,8)		1 (3,6)		3 (6,4)		5 (5,7)
Astenozoosperm		2 (1,7)		4 (14,3)		2 (4,3)		1 (1,1)
Oligozoosperm		5 (4,2)		1 (3,6)		3 (6,4)		3 (3,4)
Oligosperm		9 (7,6)		1 (3,6)		6 (12,8)		2 (2,3)
Hyperprolactin		3 (2,5)		0 (0)		0 (0)		2 (2,3)

TABLE 2: Distribution of therapy given and demographic data.

	LH	GH	LH+GH	Control
Number of patients	118	28	47	88
Follicles count	6 ± 4,015	8 ± 6,523	5 ± 4,621	3 ± 3,954
Oocyte count	4 ± 2,923	5 ± 4,634	4 ± 3,695	2 ± 2,406
Number of patients experienced degenerative oocyte	11	2	3	6
Mean of embryo transferred	2 ± 0,977	2,58	2 ± 0,984	1 ± 0,868

TABLE 3: Outcome data of research samples.

P value				
	Kontrol	LH	Seizen	LH+Seizen
Kontrol		0,000	0,006	0,016
LH	0,000		0,298	0,999
Seizen	0,006	0,298		0,404
LH+Seizen	0,016	0,999	0,404	

TABLE 4: Outcome data of statistic difference in number of mean follicles count.

P value				
	Kontrol	LH	Seizen	LH+Seizen
Kontrol		0,001	0,012	0,005
LH	0,001		0,347	0,730
Seizen	0,012	0,347		0,806
LH+Seizen	0,005	0,730	0,806	

TABLE 5: Outcome data of statistic difference in number of mean oocyte count.

the drop out due to incomplete medical report and cycle cancellation. Demographic and infertility characteristic of patients are summarized in Table 1.

Poor response patients were given several different therapies, used gonadotrophin only; we used this group as a control, several added *Luteinizing hormones, Growth hormones* and even combination between two. Table 2 showed distribution of therapy given to poor response patients. We also obtained data for follicles and oocyte numbers, number of patients experienced degeneratives oocyte and mean of embryo transferred, listed in Table 3.

We classified mean of follicle count in each group and calculated the difference between groups, we found the follicle count in LH groups shows significant higher compare with control group, Table 4. We also classified oocyte count in each groups and searched for the difference between groups, and once again LH groups showed significant higher number of oocyte counts than control groups, as listed in Table 5.

We calculated the cleavage rate of each groups and also the chemical pregnancy rate in each groups and find the most suitable therapy for poor response patients. The cleavage rate was statistically significant different between control group and LH group (p value 0,004), where control group give the positive correlation with cleavage rate,

Cleavage rate	Good	Poor	Total	p
LH	27	80	107	0,004
Control	37	45	82	
Total	64	125	189	
RR 1,788 (CI 95% 1,194 – 2,679)				

TABLE 6: Comparison of cleavage rate between LH and control groups.

Cleavage rate	Good	Poor	Total	p
GH	7	19	26	0,1
Control	37	45	82	
Total	44	64	108	
RR 1,676 (CI 95% 0,852 – 3,297)				

TABLE 7: Comparison of cleavage rate between GH and control groups.

Cleavage rate	Good	Poor	Total	p
LH+GH	26	18	44	0,649
Control	37	45	82	
Total	63	63	126	
RR 1,103 (CI 95% 0,719 – 1,692)				

TABLE 8: Comparison of cleavage rate between LH+GH and control groups.

while we found no difference between other groups and also in chemical pregnancy we found no differences. Here are the data of the outcome results.

4. Discussion

Various protocols have been proposed to improve the outcome for patients, although no RCT can provide the evidence based of success rate of one protocol among others [1-4,17]. we did not differ our patients into young and old poor responders, since it is generally accepted that both groups have diminished number of follicle in the ovary [1].

Our study demonstrated the follicle count and the oocyte count were statistically significant difference between control group and LH group. Our findings was similar with previous study which stated that with LH pretreatment could increase the number of collected oocyte compare with control [2]. Our study showed supplementation with r-LH giving higher follicles count and oocyte count.

Our study demonstrated the cleavage rate were statistically significant difference between control group and LH group. However, other cleavage rate comparison between groups were statistically similar. The use of LH is suggested by several

Chemical pregnancy	Yes	No	Total	P
LH	52	46	98	0,112
Control	32	46	78	
Total	84	92	176	
RR 0,773 (CI 95% 0,559 – 1,070)				

TABLE 9: Comparison of chemical pregnancy between LH and control groups.

Chemical pregnancy	Yes	No	Total	P
GH	14	10	24	0,136
ontrol	32	46	78	
Total	46	56	102	
RR 0,703 (CI 95% 0,457 – 1,081)				

TABLE 10: Comparison of chemical pregnancy between GH and control groups.

Chemical pregnancy	Yes	No	Total	P
LH+GH	21	21	42	0,345
Control	32	46	78	
Total	53	67	120	
RR 0,821 (CI 95% 0,548 – 1,228)				

TABLE 11: Comparison of chemical pregnancy between GH and control groups.

studies which reporting a higher embryo ploidy rate and a lightly higher pregnancy rate [12], although in our study we only found the correlation with chemical pregnancy.

The chemical pregnancy success rate between control group, LH group, GH group and LH+GH group showed no statistically different.

5. Conclusion

In this study we found that with adjuvant therapy with *recombinant Luteinizing Hormones,* produced higher follicles count, oocyte count and cleavage rate. A larger trial and comprehensive trial need to be prepared to assess contributing factors to increase the pregnancy rate in assisted technology reproductive methods.

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