Impact of Filgrastim on blastocyst transfers in egg recipients cycles with previously implantation failure according to KIR genotyping

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1. Objective

To compare ongoing pregnancy rate (OPR) in blastocyst transfers in egg recipients cycles with previously implantation failure according to killer cell immunoglobulin-like receptor (KIR) genotyping. And to evaluate the effect of filgrastim in this group.

2. Methods

It is a retrospective study that evaluated 442 embryo transfers in egg recipients cycles performed from January 2020 to March 2024. The Inclusion criteria were: transfer of at least one blastocyst graded as 3BB or better, from donated oocytes from a donor aged < 32 years old. Exclusion criteria were severe adenomyosis and no information on the evolution of the pregnancy until at least 14 weeks. The patients were initially divided into 3 groups, according to the KIR genotyping test: KIR AA, KIR Bx (AB or BB) and without KIR information. Patients with KIR test had at least one implantation failure as egg recipient, while those without KIR evaluation had no previous failures as a recipient (Control Group). Group 1 (KIR AA) and Group 2 (KIR Bx) were divided into two groups according to whether or not filgrastim was used. The protocol of filgrastim use was: filgrastim 300 mcg/ml – 0.25 ml subcutaneously every other day from the day of embryo transfer and maintained until 8 weeks of pregnancy. Outcomes were compared between groups using the chi square test or Fisher's test.

3. Results and Discussion

Of the 442 patients, 41 were KIR AA, 123 were KIR Bx and 278 did not have KIR information. KIR AA patients and KIR Bx had similar pregnancy rate (PR) and clinical pregnancy rate (CPR) but KIR AA women had higher clinical miscarriage rate (CMR) (p=0.0396) and lower OPR (not signicant) than KIR Bx (Table 1). Comparing to patients without implantation failure and without Kir information, both KIR AA and Bx had lower PR, CPR and OPR and KIR AA had higher CMR, all of than significant ($p < 0.05$) (Table 1).

Table 1. Outcomes according to KIR

	KIR AA	KIR Bx	Control
N	41	123	278
Pregnancy Rate	58,54%	62,60%	76,26%
Clinical pregnancy Rate	36,59%	39,84%	67,99%
Clinical Miscarriage Rate	26,67%	6,12%	2,12%
Ongoing Pregnancy Rate	26,83%	37,40%	66,55%

When we separated groups 1 and 2 according to the use of filgrastim, we observed that KIR AA patients without filgrastim had extremely low OPR (only 5%), significant lower than KIR Bx patients without filgrastim (29.55%, p< 0.05) (Table 2 and 3).

In patients with KIR AA, the use of filgrastim increased the OPR from 5% to 47.62% (p<0.05). In patients with KIR BB, OPR increased from 29.55% to 57.14% with the use of filgrastim (p< 0.05). When we compared OPR between KIR AA and KIR Bx who used filgrastim, no significant difference was observed (p= 0.4890) (Table 2 and 3).

Patients with KIR AA who used filgrastim had significantly higher CPR and OPR than those who did not use it (Table 2).

Table 2. Outcomes in KIR AA Group

	Without Filgrastin	With Figrastin	p
N	20	21	
Pregnancy Rate	45,00%	71,43%	p = 0.0860
Clinical pregnancy Rate	**15,00%**	**52,14%**	**p = 0.0088**
Clinical Miscarriage Rate	66,67%	16,67%	p = 0.1538
Ongoing Pregnancy Rate	**5,00%**	**47,62%**	**p = 0.0036**

Patients with KIR BB also had higher CPR and OPR than those who did not use it, in addition to a higher PR (Table 3).

Table 3. Outcomes in KIR Bx Group

	Without Filgrastin	With Figrastin	p
N	88	35	
Pregnancy Rate	**57,95%**	**74,29%**	**p< 0.0001**
Clinical pregnancy Rate	**32,95%**	**57,14%**	**p = 0.0134**
Clinical Miscarriage Rate	10,34%	0	p = 0.2760
Ongoing Pregnancy Rate	**29,55%**	**57,14%**	**p = 0.0043**

When comparing KIR AA and KIR BB who used filgrastim with the control group, we found no statistical difference in PR, CPR and OPR between the groups. We only found higher CMR in KIR AA patients, even with the use of filgrastim (p: 0.0430).

Regarding the number of embryos transferred in KIR AA patients, 32 underwent single embryo transfer (SET) while 9 underwent double embryo transfer (DET). In the group with SET, the POR was 25%, not statistically different from the POR with DET (33%).

4. Conclusion

Egg recipients with previous implantation failure and KIR AA have very low OPR even with good quality blastocyst transfer and this rate is lower than patients with KIR Bx. The use of filgrastim seems to significantly increase OPR for recipients with implantation failure with both KIR AA and KIR BB, although better benefit was observed in KIR AA group. Considering the very low OPR found in KIR AA recipients without filgrastim use, KIR genotyping and filgrastim use may be considered in cases of implantation failure. Nevertheless, this is a retrospective study and a randomized study with a larger number of patients is necessary to reach definitive conclusions. definitive conclusions.

5. References

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