Matrix metalloproteinases in serum and follicular fluid of women treated by in vitro fertilization

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Introduction

Conception, implantation of the embryo and subsequent development is a comprehensive range of complex processes. An important participant in these processes is the immune system.

A key step to a successful pregnancy is the implantation of the embryos (nidation). Immunological implantation failure, is not only responsible for repeated fetal loss, but also for a large part of sterility and unsuccessful embryo transfers.

Matrix metalloproteinases (MMPs) are a family of key enzymes, which degrade the extracellular matrix during tissue remodeling (including follicular development, embryo development, ovulatory process cell morphology, changes in the cell structure and function of reproductive organs).

Aim

In our study, we focused on determining the concentration of matrix metalloproteinases 2 and 9 in the follicular fluid and serum of women undergoing in vitro fertilization (IVF) and the enzymes' possible link to the success of IVF treatment.

Method

Fifty eight women evaluated for infertility were divided into two cohorts based on the success of IVF treatment. The first cohort consisted of 29 women who had become pregnant as a result of IVF treatment, but whose pregnancy had been aborted. The second cohort consisted of 29 women whose treatment was not successful (did not become pregnant). The ages of women in the study ranged from 24 to 43 years with a median of 32.0 (IQR 30.0 – 35.0) years.

The concentrations of MMP-2 and MMP-9 were measured in follicular fluid and serum by means of commercially available ELISA-kits (Quantikine®, R&D Systems, USA).

The results are expressed as median and in the interquartile range (IQR). Statistically significant differences between the groups of women were tested using a nonparametric test (Mann-Whitney). For all statistical tests, the chosen significance level was 5% ($\alpha = 0.05$).

Results

Table 1.: Results and a comparison of the concentration matrix metalloproteinases (ng/ml).

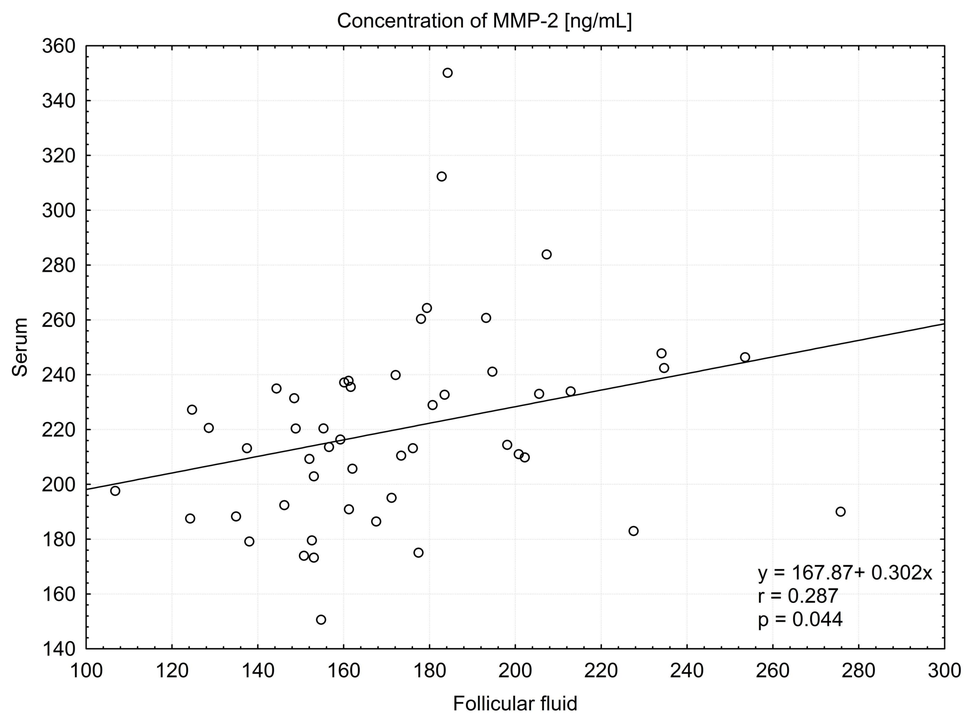
			Result of IVF		p-value
			Pregnant	Non-pregnant	
MMP-2	Follicular fluid	Median (IQR)	179.1 (154.2 - 200.1)	161.2 (152.0 - 179.4)	0.106
	Serum	Median (IQR)	213.6 (191.8 - 246.4)	220.4 (192.4 - 237.7)	0.480
MMP-9	**Follicular fluid**	**Median (IQR)**	**9.6 (6.0 - 17.0)**	**7.1 (4.6 - 10.7)**	**0.003**
	Serum	Median (IQR)	880.4 (691.2 - 976.3)	743.7 (592.0 - 948.3)	0.127

This study shows that women undergoing IVF treatment have, at the time of ovulation, approximately the same concentrations of MMP-2 in the follicular fluid and in the serum. On the other hand, these women have significantly lower concentrations of MMP-9 in follicular fluid than in serum ($p < 0.0001$).

A statistical analysis revealed that there is a correlation between the MMP-2 concentrations in serum and in follicular fluid ($p = 0.043$). However, there is no correlation for the concentrations of MMP-9. ($p = 0.954$).

This study also found no correlation between the number of follicles and the concentration of MMPs.

Figure 1.: Correlation of MMP-2 concentration in serum and in follicular fluid.



Conclusion

The concentration of MMP-2 and the concentration of MMP-9 (serum) do not play a key role in the initial stage of pregnancy.

The results show that the concentration of MMP2 in serum, MMP2 in follicular fluid, and MMP9 in serum can serve as predictors of successful IVF treatment. MMP-9 is likely to play a role in the breakdown of ECM during follicle growth and development, in follicle migration, in ovulation, and in controlling other cell functions, including the cell cycle. This study also demonstrated that a low concentration of MMP-9 in follicular fluid is a good predictor of successful IVF treatment.

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