

CORRELATIONS BETWEEN PSYCHOLOGICAL STRESSOR AND SEVERE PREECLAMPSIA (SPE)

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ABSTRACT

Pregnancy with severe pre-eclampsia may result from various types of stress, including psychological stress. Mechanism of psychological stressor that results in severe preeclampsia is unknown. The objective of this study was to disclose the mechanism from psychological stressor to severe preeclampsia. Results of homogeneous test to maternal age, age of pregnancy, maternal body weight dan laboratory data revealed no difference between S+ group and SPE+ group, S- group and SPE- group, and S+SPE+ group and S-SPE- group. Cortisol levels in S+ group and SPE+ group were not different ($p = 0.167$), so they were rendered to become one group of S+SPE+. Cortisol levels in group S- and SPE- were also not different ($p = 0.343$), therefore they were also rendered to be one group of S-SPE-. Biological data from S+SPE+ group and S-SPE- group was multivariately different ($p = 0.0001$). Biological data in S+SPE+ group and S-SPE- group revealed that the discriminator was cortisol, while IgG was not revealed. This indicated that SPE had a high cortisol level. Conceptual framework assisted with discriminator pattern revealed that the occurrence of SPE from psychological stressor is as follows: psychological stressor affects the hypothalamus to release corticotrophic releasing factor (CRF). The addition of CRF stimulates anterior pituitary gland that releases adenocorticotrophic hormone (ACTH), inducing adrenal cortex to release cortisol. Psychological stressor affecting the hypothalamus through autonomous nerve may enhance adrenal medulla to release catecholamine, which may inhibit the function of cortisol in monocyte. Monocyte/antigen presenting cells may affect Th to differentiate to become Th1 cell and Th2 cell. Th1 cell will also be inhibited, resulting in the inhibition of IFN gamma and IgG-produced B-cell. In conclusion, SPE mechanism due to psychological stressor can be explained by psychoneuroimmunological approach.

Keywords: psychoneuroimmunology, psychological stressor, SPE

INTRODUCTION

Severe preeclampsia (SPE) is a serious disease in obstetrics. Death occurring among pregnant women in the disease results from bleeding, preeclampsia, and infection. A number of theories explain causes of preeclampsia. One of those causes is psychological stressor (Lockwood, 1999) viewed from psychoneuroendocrinological approach. Various efforts have been taken to prevent SPE with less satisfactory results since the mechanism from psychological stressor to SPE has not been disclosed.

Psychological stressor stimulates adrenal cortex that releases cortisol inhibited by catecholamine (Fisher, 1999). In addition, hypothalamus may stimulate adrenal medulla through the autonomous nerve. Adrenal medulla will release catecholamine, which is more predominant to cortisol (Sikkema, 2001). Catecholamine may inhibit cortisol that enhances macrophage to release IL-4 and IL-12 (Daniel, 1998;

Rind, 2001). Here macrophage acts as an antigen presenting cell (APC). APC may express major histocompatibility complex (MHC) containing polypeptides that may be caught by T cell receptor (TCR) from Th cell, so that Th cell will be differentiated to become Th1 cell and Th2 cell (Chaturvedi, 1999). Th1 cell releases IFN γ and Th2 cell also releases IL-10. The effect of cortisol is inhibited by catecholamine, so that the formation of IFN γ and IL-10 is also inhibited, inhibiting subsequently the effect of IFN γ on B cell to release IgG (Gree-Johnson, 1996). Peripheral blood examination reveals that IgG in SPE is almost similar to that of normal pregnancy (Zheng, 1998, Pepple, 2000).

PATIENT AND METHODS

Study design

This study used Cohort retrospective design aimed to disclose relations between exposure and uncontrollable outcome. This study was undertaken in Dr Moewardi Hospital, Surakarta, from August 2002 to May 2003.

The design is as follows:

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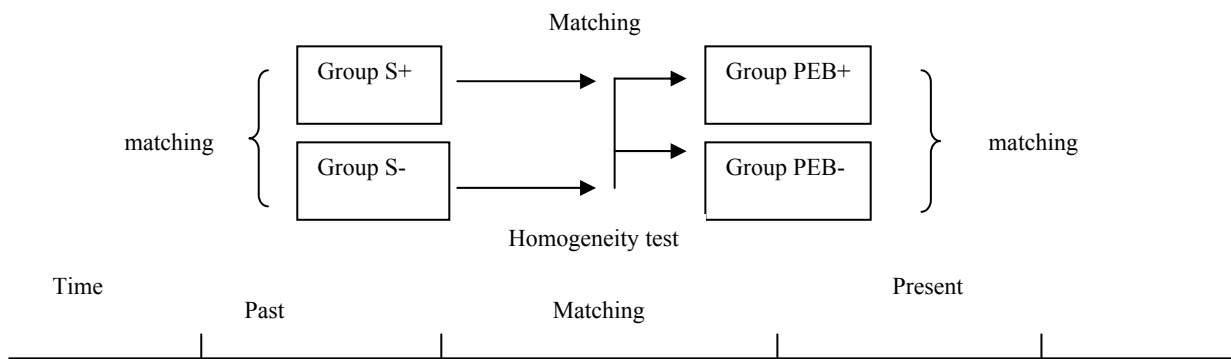


Figure 1. The design of the study

Group S+ : with psychological stressor
 S- : without psychological stressor
 Group PEB+ : with PEB
 PEB- : without PEB

ewit+ and udem+
 3. Age of pregnancy more than 28 weeks
 4. Informed consent to involve in the study.
 5. Single pregnancy

Sample criteria :

This study observed pregnancy with psychological stress (S+), pregnancy with SPE (SPE+), pregnancy without psychological stress (S-), and pregnancy without SPE (SPE-). Sample criteria were as follows: maternal age (year), pregnancy age (week), maternal body weight (kilogram), psychological stressor and all patients were at their first pregnancy. Psychological stressor was indicated by the presence of high cortisol level (normal 5 - 25 mg/100 ml).

Inclusion criteria:

1. First pregnancy with good psychical condition.
2. Blood pressure higher than 160/90 mmHg,

Exclusion criteria:

1. Hemorrhagic ante partum
2. Early rupture of the membrane
3. Pregnancy with infection
4. Cephalopelvic disproportion'
5. Fetal death
6. Pregnancy with DM

RESULTS

Data analysis

- 1.a. Cortisol in S+ group with SPE+ group

Table 1.a. Cortisol in S+ group with SPE+ group

Hormonal data	S+ group (n=12)		PEB+ group (n=12)		p	s
	X	SD	X	SD		
Cortisol (ug/100 ml)	48.958	11.524	41.492	14.078	0.167	TS

Above data demonstrate no difference between cortisol in S+ group and that in PSE+ group ($p = 0.167$).

- 1.b. Cortisol in S- group with SPE- group

Table 1.b. Cortisol in S- group with SPE- group

Hormonal data	S- group (n=12)		PEB- group (n=12)		p	s
	X	SD	X	SD		
Cortisol (ug/100 ml)	17.608	5.694	20.700	9.413	0.343	TS

Above data also demonstrate no difference between cortisol in S- group with SPE- group ($p = 0.343$)

1.c. Biological data from S+SPE+ group with S-SPE- group

Table 1.c. Biological data from S+SPE+ group with S-SPE- group

Hormonal data	S+PEB+ group (n=24)		S-PEB- group (n=24)	
	X	SD	X	SD
IgG (gr/l)	1.036	0.332	0.984	0.375
Cortisol (ug/100 ml)	45.225	13.147	19.163	7.769
Multivariate, $p = 0.0001$				

Biological data on S+SPE+ and S-SPE- assessed using multivariate test revealed no difference ($p = 0.0001$)

2. Discriminant analysis from biological data on S+SPE+ group and S-SPE- group

Table 2. Discriminator analysis on biological data of S+SPE+ group and S-SPE- group

Differential data	Wilk's Lambda	Significance
Cortisol (ug/100 ml)	0.397	0.0001

Results of discriminant analysis of biological data on S+SPE+ group and S-SPE- group revealed one differential data, i.e., cortisol.

3. Fisher's coefficient value

Table 3. Value of Fisher's coefficient

Biological data	S+PEB+ group	S-PEB- group
Cortisol (ug/100 ml)	0.388	0.164

After being subjected to discriminant analysis, one appearing biological data, cortisol, also revealed regression model, Fisher's linear discriminant, which is also found in each group.

4. Contribution of discriminator pattern function of S+SPE+ group and S-SPE-

Table 4. Contribution of discriminator pattern function of S+SPE+ group and S-SPE- group

Biological data	S+PEB+ group (n=24)	S-PEB- group (n=24)
Cortisol (ug/100 ml)	17.547	3.147

Table 4 reveals contribution of discriminator pattern function of S+SPE+ group and S-SPE- group obtained from the multiplication of Table 1.c with the Fisher's coefficient. In Fisher's coefficient, the value of IgG was 0 (zero). Based on Table 4 we could create contribution

of discriminator pattern function of S+SPE+ and S-SPE- groups (Figure 2).

The following diagram describes SPE incidence experienced by patients with psychological stressor

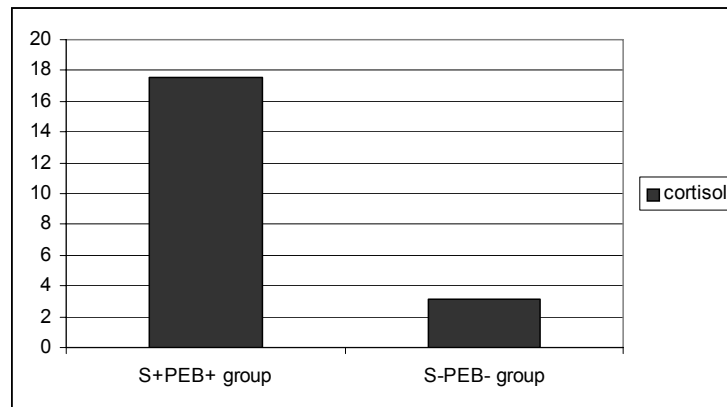


Figure 2. Diagram of contribution of discriminator pattern function of S+SPE+ and S-SPE- groups

DISCUSSION

Psychological stressor may result in stress that is indicated by increasing level of cortisol. Cortisol in S+ group was not different from that in SPE+ group ($p = 0.167$, Table 1.a), so both groups were rendered to become one group, i.e., S+SPE+ group. Cortisol in S-group and that in SPE- group was not different ($p = 0.343$, Table 1.b), therefore, both groups were also rendered to become one group, i.e., S-SPE- group. These groups were compared to each other, and multivariately it was found that both were different ($p = 0.0001$, Table 1.c).

Discriminant analysis was done to above table (Table 1.c), resulting in one discriminator, i.e., cortisol. One discriminator showed difference between S+SPE+ group and S-SPE- group (Setyawan, 1996).

Discriminant analysis was undertaken to obtain discriminator data between S+SPE+ group and S-SPE- group. The difference of these variables were used to obtain contribution of discriminator pattern function in the incidence of SPE due to stress as appears in Fisher's coefficient (Table 3). Each group has function contribution of discriminator (Sharma, 1996). In this case there were two groups, i.e., S+SPE+ group and S-SPE- groups, so that there were two values of Fisher's coefficient (Table 3). The diagram of discriminant pattern of S+SPE+ group and S-SPE- group (Figure 2).

The incidence of SPE due to psychological stressor

Psychological stressor may stimulate hypothalamus in perceptive way. Hypothalamus will release corticotropin releasing factor (CRF) and CRF will stimulate pituitary tissue. This tissue will subsequently release adreno corticotropin hormone (ACTH) and ACTH will

stimulate adrenal cortex tissue that may release cortisol, which will subsequently be inhibited by catecholamine (Fischer, 1999).

Additionally, through the autonomous nerve, the hypothalamus may stimulate adrenal medulla tissue, which will release catecholamine, which is more predominant than the cortisol (Haller, 1997; Reister, 1999; Sikkema, 2001). Catecholamine may stimulate macrophage to release IL-4 and IL-12 (Daniel, 1998; Rhind, 2001).

Cytotrophoblast is an antigen that expresses antigen which may be phagocytosized by the macrophage so that it may release Class II MHC that may be bound by TCR from Th cells. These cells will differentiate into TH1 and Th2 cells (Chaturvedi, 1999). In SPE, cytokine produced by Th1 cells increases and that produced by Th2 cells is reduced (Saito, 1999). IL-12 will stimulate the release of Th1 cells, and IL-4 stimulates the release of Th2 cells (Saito, 1999). The release of Th1 cells is more predominant than the release of Th2 cells (Elenkov, 2000) so that IFN γ is more predominant to IL-10 (Darmochwal, 1999). IFN γ stimulates the cell B to proliferate to become plasma cells to release IgG (Romagnani, 1997).

IFN γ and IgG will be inhibited by the catecholamine (Green-Johnson, 1996). IL-10 stimulates the release of IgG from plasma cells. Results of peripheral blood examination showed that IgG in SPE was almost equal to that in normal pregnancy (Zheng, 1998; Pepple, 2000).

IFN γ -stimulated macrophage may release IL-1 β and TNF α , which will stimulate endothelium in decidual spiral arteriole to release adhesive molecules (Heyl, 1999). Adhesive molecule acts as adhesive between macrophage and endothelium, resulting in

DTH process in decidual spiral arteriole, which is narrowed in SPE (Hefler, 1999; Lyall, 1999). Damaged extravillous cytotrophoblast invasion due to DTH process in spiral artery is the pathogenesis of SPE occurrence (Leszczynska, 2000; Reister, 2001).

CONCLUSION AND SUGGESTION

This study has disclosed psychological stressor in SPE mechanism. Pregnant women should therefore prevent or reduce psychological stressor.

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