

Effect of Circadian Rhythm Changes on Innate Immunity Response

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ABSTRACT

The adaptation failure of circadian rhythm cause work stress for the night shift workers. The research aims to prove that the work stress will affect the innate immunity, by the concept of psychoneuroimmunology. The research was done by using quasi-experimental research design and similar working unit workers who have never been in night shift work as control. Samples were selected among male workers, unmarried, 20–25 years old with good health status and no psychological disturbances. Responses of cortisol hormone was used as stress indicator, and cellular response of monocyte, lymphocyte, neutrophil, and natural killer (NK) cell were used as immune response indicators. Data were collected during 5 (five) working days. This study shows that cortisol hormone and neutrophil cell are the important indicators in the circadian rhythm among workers. Two profiles appear in the group studied. The first is considered adaptive to circadian rhythm. The second group, unadaptive group, is a group where the work stress occurs and this is showed by the high of cortisol response with low response of neutrophil cell. Circadian rhythm changes can play as a stressor for rotating shift worker.

Key words: *circadian rhythm, night shift, cortisol, psychoneuroimmunology, immune response*

INTRODUCTION

The adaptation failure of circadian rhythm cause work stress for the night shift workers. However, incident of upper respiratory tract infection occur among the workers in the factory using three shifts is more prevalent compared to factory using only two shift rotating work schedule (East Java Department of Manpower Regional Office, 1996). The similar incident may also be found in the other studies on occupational health, which shows that the incidence of upper respiratory tract infection is related to night shift work (Zuskin, 1995). The above incidence indicates that the change of circadian rhythm may decrease immune status of workers. However, its mechanism is still unknown.

Mechanism of the disease of immunologic status due to change of circadian rhythm is still unknown. Such mechanism is important to be unraveled, because if it is not anticipated, there will be a decrease of physical quality of workers for approximately the next 5 years. Stress due to the change of circadian rhythm suffered by night shift workers is acute and repetitive, and may lead to chronic disease (Stites, 2000; Roitt, 1994). Because workers are vulnerable to exposure of various chemical and physical factors, they are susceptible to suffer from occupational disease (Bos N, 1995; Prawirakusuma, 2000). To improve productivity among the worker, it's necessary to build and increase body defense against such predisposing factors of occupational diseases.

To disclose the mechanism of the decrease of immune response, the paradigm of pathobiology was used

to study the indication of disorder in the homeostatis system due to the change of circadian rhythm. Body has an ability to maintain homeostasis through regulation system of neurohormones appropriate to its pathway (Bear, 1996; Felig, 1995). One concept from the paradigm of pathobiology is psychoneuroimmunology, a science that studies change of immune response caused by the occurrence of behavioral change mediated by immunomodulator (Carlson, 1994; Felig, 1995; Pinel, 1995).

Psychoneuroimmunological concept showed that hypothalamus pituitary adrenal (HPA) axis may induce secretion of Corticotropin releasing hormone (CRH) which may stimulate pituitary anterior to secrete Adrenocorticotropin hormone (ACTH), and through hypothalamus pituitary adrenal (HPA) axis, cortisol hormone is secreted (Felig, 1995). Therefore, these hormones were used to be an indicator of circadian rhythm changes among night shift workers.

Immune system consists of innate and adaptive immunity system (Roitt, 1995; Stites, 2000; Tristram, 2003). For the first step, the variable studied was immune competent system at the stage of innate immunity. Immune competent response can be seen from the response of neutrophil, monocyte, lymphocyte and natural killer (NK) cells, while stress can be indicated by cortisol hormone.

Based on some evidences that mentioned above, this research was carried out to study the effect of circadian rhythm changes on innate immunity response. The results can be used as reference to make the profile of night shift working.

METHOD

This was a quasi-experimental study by using pre-test post-test control groups design. The experiment group was night shift workers and the control group was non-shift workers. The sample size was 15 persons, with the three inclusion criterias such as male worker of 20–25 years old, unmarried, has been working for 1–5 year and good health condition.

Variables used were cortisol hormone as indicator of stress and innate immunity components, consisted of monocyte, lymphocyte, neutrophil and natural killer (NK) cells. Data collected was then analyzed statistically in several steps. The first step was to describe of cortisol hormone and innate immunity pre and post examination. The second step was multivariate analysis of variance to identify the difference between those groups and the third step was the discriminant analysis to identify.

RESULT

Profile of Cortisol Hormone and Innate Immunity

The first step of study was done to describe of cortisol hormone and innate immunity before and after examination. Data described in figure 1.

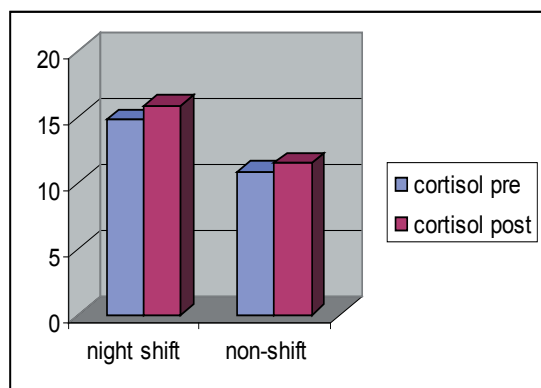


Figure 1. Mean Value of Cortisol Hormone in Pre and Post-Examination (5 Days Shift)

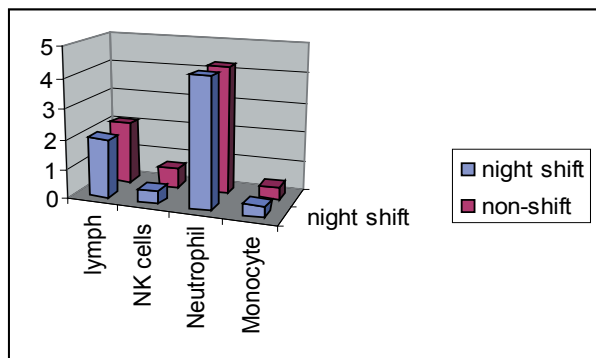


Figure 2. Mean Value of Immune System Components (Lymphocyte, NK Cells, Neutrophil, and Monocyte) in Pre-Examination.

Univariate analysis revealed that the level of cortisol hormone was different between experiment group (night shift) and control group (non shift) with sign of F 0,000. The mean value of cortisol was higher among the experiment group compare to control group.

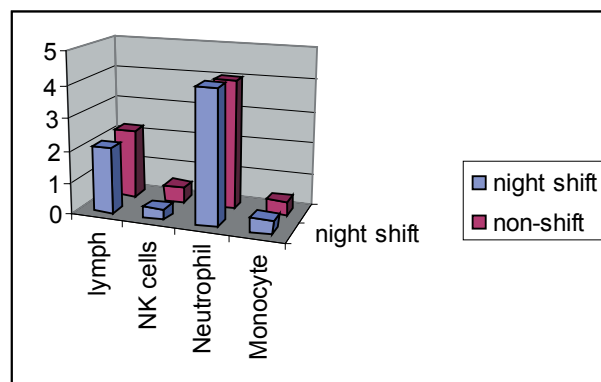


Figure 3. Mean Value of Immune System Components (Lymphocyte, NK Cells, Neutrophil, and Monocyte) in Post-Examination (5 Days Shift)

Table 1. Mean Value of the Immune System Component in Pre and Post-Examination

Immune System Component	Night Shift		Non Shift	
	Pre	Post	Pre	Post
Lymphocyte	2.061	1.979	2.206	2.099
NK cells	0.429	0.337	0.668	0.504
Neutrophil	4.302	4.165	4.277	4.022
Monocyte	0.359	0.424	0.399	0.436

There was a significant difference of the indicator lymphocyte, NK cells, neutrophil and monocyte, between night shift and non shift workers.

Multivariate Analysis of Variance

Second step was multivariate analysis on the response of immunologic defense was done to the variables of cortisol, lymphocyte, monocyte, NK cells and neutrophil in the four group formed. This analysis was done to identify the difference of those groups. Results showed that there was a significant difference among those four group (Wilks sign of F 0,001). Univariate analysis revealed that the differential variable was cortisol (sign of F 0.000). It could be concluded that the grouping based on cortisol was caused by the difference of ability to accept treatment between night shift and non shift workers. To find visual description of those four groups based on cortisol hormone differentiation, discriminant analysis was used.

Discriminant analysis

Discriminant analysis was done due to above groupings and data scale from dependent variables of cortisol

hormone was changed into ordinal scale. Results obtained showed that the differential variable of those groups were cortisol hormone (sign 0.0000) and neutrophil. Discriminant analysis revealed coefficient of discriminant function (Fisher's linear discriminant function) of each group as seen in table 4.

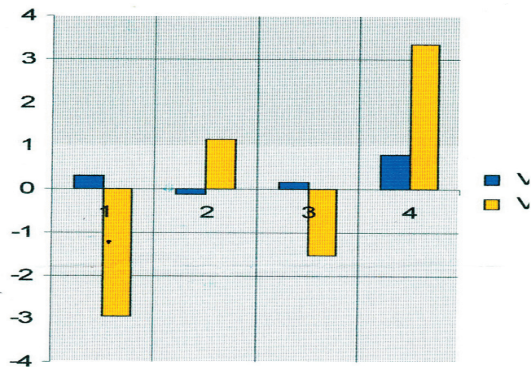


Figure 4. Profile of Response of Neutrophil Cell and Response of Cortisol in
 V1 = response of neutrophil cell
 V2 = response of cortisol hormone
 Profile 1 and 2 → studied groups
 Profile 3 and 4 → control groups

DISCUSSION

The higher level of cortisol among experiment group compare to control group it is means to explain that the night shift workers experience more stress compared to non-shift workers. The rhythm of cortisol hormone was similar with the pattern of alertness. Alertness at night was in lower level, but it increase to higher level in the morning or during the day. The pattern showed a similar rhythm with photoperiod received by individual (Felig, 1995; Phillips, 1999). These were the profile of the immune system component in pre and post examination. Reduced immune response due to stressor may give a description of profile decrease lymphocyte, NK cells, neutrophil and monocyte responses.

The fourth profile showed that the contribution of cortisol was high (Figure 4). This indicated that even though they were not exposed to the change of circadian rhythm, the presence of physical activity and occupational environment affected the increase of cortisol hormone (Setyawan, 1996), and this condition was continually accepted (chronic). In this case, physical activity and occupational environment were signal received by pineal gland limbic hypothalamus so that HPA axis may induce secretion of cortisol hormone.

The fourth profile indicated the phenomenon of higher cortisol contribution and neutrophil. This phenomenon indicated that cortisol was not directly influential to the circulation of neutrophil. This explanation was based on the results of analysis factor of all strong interaction grouped variable which may indicate that the higher level of neutrophil was not influenced by cortisol but caused by interaction with other variable. To identify variable that interacted with neutrophil, whole groupings in all sub groups were observed. The formation of such groupings indicated strong interaction among those variable.

Response of cortisol hormone in profile 2 was lower than that in profile 4. This might be caused by the night physical activity that induced inhibition of signal to pineal gland and amygdale by signal from suprachiasmatic nucleus which is regulator of the rhythm of body function so that inhibition of the response of cortisol hormone occurred in the night. Consequently, body function was reduced (Bear, 1996; Carlson, 1994; Pinel, 1993).

The rhythm of cortisol hormone was similar with the pattern of alertness. Alertness at night was in lower level, but it increase to higher level in the morning or during the day. This pattern showed a similar rhythm with photoperiod received by individuals (Felig, 1995).

The influence of circadian rhythm was managed by each individual using their own effort. Among night shift workers, what occurred to them was learning process and short term and long term memory, because there were night afternoon and morning shift and each was done for 5 days. This was different than a permanent shift in which a worker always worker in night shift. Adaptation easily

Table 2. Coefficient of Discriminant Function (Fisher's Linear Discriminant Function)

Groups	Night Shift Workers		Non Shift Workers	
	1	2	3	4
Neutrophil	0.7853508	-0.4797822	0.5773918	0.6213353
Cortisol	-0.9366527	0.5859878	-0.6717540	0.8809972

Table 3. Mean Value of Cortisol Hormone Variables, Multiplied by Discriminant Coefficient

Groups	Night Shift Workers		Non Shift Workers	
	1	2	3	4
Mean of Neutrophil	0.296	-0.106	0.166	0.803
Mean of Cortisol	-2.946	1.157	1.510	3.341

occurred in such permanent shift, which was manifested not only as the change of biological function, but also social support from the people and family (Phillips, 1999).

In non-permanent night shift workers, there was a short at long term adaptation process that can be studied using coping mechanism and such process might lead to habituation. Mechanism of the emergence of habituation was the decrease of synaptic transmission in sensory neurons due to the decrease of neurotransmitter counts released by pre-synaptic terminal (Notosoedirdjo, 1998).

CONCLUSION

It has been proved that the decrease of immunologic defence among night shift workers can be explained using psychoneuroimmunological concept. The change of circadian rhythm can be accepted as stressor and can also be adapted. Reduced immune response due to stressor may give a description of the profile of decreased neutrophil response. Among shift workers with good adaptation the response of cortisol hormone decrease, while the response of neutrophil increase. The decrease of cortisol hormone response among groups with good adaptation showed the successful of coping mechanism in forming a coping strategy. Presence of chronic physical stressor among control groups may be adapted by the body, so that it does not influence immunologic defence, because it has been adaptation through coping mechanism.

It has been proved that the role of cortisol hormone and neutrophil cells as variable to differentiate adaptable

and un-adaptable groups, indicates that acute stressor influence response of acute inflammatory cells among night shift workers.

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