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THE RELATIONSHIP OF THE GENERAL REACTION SCORE WITH THE NATURAL KILLER CELLS ACTIVITY AMONG WOMEN WITH AIRCRAFT NOISE EXPOSURE IN THE AREA OF ADI SOEMARMO AIRPORT SOLO

(Hubungan antara general reaction score dengan aktivitas sel NK pada wanita yang terpapar bising pesawat udara di sekitar Bandara Adi Soemarmo Solo)

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Abstract

Exposure to noise constitutes a health risk. There is sufficient scientific evidence that aircraft noise exposure can induce hearing impairment, hypertension and ischemic heart disease, annoyance, sleep disturbance, and decreased school performance. For other effects such as changes in the immune system and birth defects, the evidence is limited.The aims of the research is to find out the correlation of the general reaction score with The Natural Killer cell activity among women with aircraft noise exposure in the area of Adi Sumarmo Airport Solo**.** The research findings are expected to contribute to the scientific knowledge development and to give benefits for local government and among people in the area of Adi Sumarmo Airport in preventing the effect of aircraft noise. The research design was an analytical survey with a cross sectional approach, taking place at the Dibal and Gagak Sipat Village, Ngemplak Sub district, Boyolali District. The research was conducted from July 2008 to June 2009. The number of respondens was 39. They were divided into 3 groups; group 1 was exposed to 92.29 dB of noise level (13 respondents); group 2 was exposed to 71.79 dB of noise level (13 respondents); and group 3 was exposed to 52.17 dB of noise level (13 respondents). The samples were taken using simple random sampling. The data were analyzed by Pearson Correlation and Anova followed by Post Hoc Test using LSD test completed with Homogenous Subsets. The Anova test showed that there was significant differences in the general reaction score among all groups ($p = 0.000$). The Pearson correlation test showed that there was a negative association between the general reaction score with the Natural Killer cells activity ($r = - 0.613$; $p < 0.05$).

Key words: Aircraft noise, GRS, NK Cell activity, Adi Sumarmo Airport

Abstrak

Paparan bising pesawat udara dapat berisiko terhadap kesehatan. Terdapat banyak bukti yang menunjukkan bahwa paparan bising pesawat udara dapat menyebabkan gangguan pendengaran, hipertensi, penyakit jantung iskemik, ketergangguan (annoyance), gangguan tidur dan penurunan prestasi sekolah. Sedangkan efek terhadap perubahan pada sistem imun dan lahir cacat, bukti-bukti masih terbatas. Penelitian ini bertujuan untuk mengetahui hubungan antara general reaction score dengan aktivitas sel NK pada wanita yang terpapar bising pesawat udara di sekitar bandara Adi Sumarmo Solo. Penelitian ini diharapkan dapat memberikan manfaat bagi pengembangan ilmu pengetahuan dan bagi masyarakat serta pemerintah daerah khususnya dalam upaya pencegahan terhadap dampak paparan bising pesawat udara. Rancangan penelitian adalah survei analitik dengan pendekatan cross sectional, dengan mengambil lokasi di Desa Dibal dan Gagak Sipat, Kecamatan Ngemplak, Kabupaten Boyolali. Penelitian dilaksanakan dari bulan Juli 2008 sampai dengan bulan

Juni 2009. Jumlah keseluruhan sampel 39, terbagi dalam 3 kelompok ; kelompok 1 terpapar bising intensitas 92,29 dB (13 responden); kelompok 2 terpapar bising intensitas 71,79 dB (13 responden); kelompok 3 terpapar bising intensitas 52,17dB (13 responden). Pengambilan sampel dengan cara simple random sampling. Data dianalisis menggunakan uji Anova diikuti dengan Post Hoc Test metode LSD dilengkapi dengan Homogenous Subsets. Uji Anova menujukkan ada perbedaan yang signifikan antar kelompok terhadap general reaction score yang ditunjukkan dari nilai p=0,000. Uji Pearson Correlation menunjukkan ada hubungan yang negatif antara general reaction score dengan aktivitas sel NK (r = - 0,631; p < 0,05).

Kata kunci: Aircraft noise, GRS, Aktivitas sel NK, Adi Sumarmo Airport

INTRODUCTION

Around the International Airport of Adi Sumarmo Solo, Indonesia with a distance of less than 1,000 meters from the runway, the noise intensity of the high point activity ranges from 74.42 dB to 95.67 dB, measured with Weighted Equivalent Continuous Perceived Noise Level (WECPNL). It is reported that 65% of the inhabitants in the region suffered from sleep disturbance, hearing impairment and annoyance (Hartono, 2006). At the same region, Hartono found that the inhabitants exposed to the aircraft noise with the high intensity had higher number of lymphocytes compared to those exposed to lower intensity of aircraft noise.

There is sufficient scientific evidence that the noise has influences on ischemic heart disease, hypertension, hearing impairment, sleep disturbance, duodenum and gastric disorders. For other effects such as changes in the immune system, the evidence is limited (Passchier-Vermeer and Passchier, 2000; Cheng Zheng and Ariizumi, 2007).

The noise of high intensity is more annoying than that of low intensity. The intermittent noise is more annoying than the continuous one (Stansfeld and Matheson, 2003). Women are more sensitive to responding noise than men (Melamed et al., 1992). Among the intermittent noise, the aircraft noise is significantly more annoying. The chronic exposure to noise is thought to bring about significant impacts if it happens for more than a year (Miedema and Vos, 1998; Passchier-Vermeer and Passchier, 2000).

One of the noise impacts is stress (Haines et al., 2001; Passchier-Vermeer and Passchier, 2000). In response to a stressor, physiological changes are set into motion to help an individual cope with stressor. However chronic activation of these stress responses, which include the hypothalamic- pituitary-adrenal (HPA) axis and the sympathetic-adrenal-medullary (SAM) axis, result in chronic production of glucocorticoid hormone and catecholamines. Glucocorticoid receptors expressed on a variety of immune cells bind cortisol and interfere with the function of NF-kB, which regulates the activity of cytokine producing immune cells. Adrenergic receptors bind epinephrine and norepinephrine and activated cAMP response element binding protein, inducing the transcription of genes encoding for variety of cytokines. The changes in genes expression mediated by glucocorticoid hormones and catecholamines can dysregulate immune system. Lymphocytes, NK cells, macrophages and granulocytes, exhibit receptors for many neuroendocrine product of the HPA and SAM axis, such as cortisol and catecholamines which can cause changes in cellular trafficking, proliferation, cytokine secretion, antibody production and cytolytic activity (Ader, 2000; Dobbin et al., 1991; Glaser and Kiecolt-Glaser; 2005; Padgett and Glaser, 2003; Ronald, 2003).

General reaction score (GRS) was a rating scale with a questionnaire to measure the annoyance level due to the aircraft noise to the inhabitants who were exposed to it for years. The rating scale used to measure the annoyance level was a questionnaire which was arranged

and tested in terms of validity and reliability by Bullen and Hede (1982).

Natural Killer (NK) cells are important components of the innate immune systems, owing to their cytokines and chemokines production and ability to lyse target cells without prior sensitization. Human NK cells comprise ±15% of all lymphocytes and are defined phenotypically by their expression of CD56 and CD 16, lack of expression of CD3 ($CD56^+CD16^+CD3^-$) (Cooper et al, 2001). Among many indices of immune function, NK activity and NK cells subsets have been of interest to researchers because NK cells are known to be important in host defense against viral diseases and they appear to play a significant role in protection against neoplastic growth (Megan et al., 2001; Morikawa et al., 2005). The NK cells are also one of the leukocyte subsets, which are responsive to the physiological stress and psychological stress (Suzui et al., 2004).

Based on the above elaborations, this research aims at finding out the correlation of the general reaction score with the Natural Killer cell activity among women with aircraft noise exposure in the area of Adi Sumarmo Airport Solo.

METHODS

Subjects

This research is an observational analytic with cross sectional design. Subject of the research were the inhabitants around the runway of Adi Sumarmo International Airport Solo, Indonesia. Population of the research were all of the inhabitants of Dibal village and Gagak Sipat village, Ngemplak sub-district, Boyolali regency who fulfilled the following criteria:

Inclusion criteria:

Female, married, housewife, aged 20-40 years old, living in the area at least 1 year.

Exclusion criteria:

Consuming non-herbal or herbal medicines, being pregnant, suffering from hearing loss, suffering from infectious disease (cold, flue, and diarrhea) and suffering from diabetes mellitus.

The respondents who fulfilled the criteria were selected through a simple random sampling technique. The total number of respondents was 39 and were divided into 3 groups based on the distance of their living area from the runway:

Group 1 : respondents whose living area is less than 500 meters from the tip of the runway with the noise intensity of 92.29 dB measured with the scale of WECPNL .

Group 2 : respondents whose living area is between 500 and 1,000 meters from the tip of the runway with the noise intensity of 71.79 dB measured with the scale of WECPNL.

Group 3 : respondents whose living area is greater than 1,000 meters from the tip of the runway with the noise intensity of 52.17 dB measured with the scale of WECPNL.

The noise measurement

The noise was measured using Sound Level Meter (Extech Model 407735, Japan) and was rated based on WECPNL as follows:

$$WECPNL = dB\ (A) + 10 \log N - 27$$

$$N = N_1 + 3N_2 + 10N_3$$

dB (A) : the average decibel score of each peak level of aircraft activity in a day.

N : The number of arrival and departure of aircrafts in 24 hours.

N_1 : The number of arrival and departure of aircrafts between 07.00 and 19.00 Western Indonesia Time

N_2 : The number of arrival and departure of aircrafts between 19.00 and 22.00 Western Indonesia Time

N_3 : The number of arrival and departure of aircrafts between 22.00 and 07.00 Western Indonesia Time

The result of measurement in the scale of dB (A) was then converted into WECPNL in accordance with the number of aircrafts passing over the areas for 24 hours.

General Reaction Score

General reaction score (GRS) was a rating scale with questionnaire to measure the annoyance level due to the aircraft noise to the inhabitants who were exposed to it for years. The rating scale used to measure the annoyance level was questionnaire which was arranged and tested in terms of validity and reliability by Bullen and Hede (1982).

Natural Killer cells activity

The activity (cytotoxicity) of NK cells was measured by using a non-radioactive method, which was a modification of procedure conducted by Andalib et al. (2006). Peripheral blood of 10 cc was taken by using syringe, and placed in the venoject tube which contained saturated solution of Heparin. The lymphocytes were separated by using Ficoll-Hypaque gradient technique (Lymphoprep; Norway). Lymphocytes were isolated, washed, and brought to a concentration of 5 x 10^5 cells/ ml in RPMI 1640+10% FCS (Gibco, Germany).

The ATCC-K562 erythromyelocytic leukemia cell line (target cell) maintained in continuous suspension culture in RPMI 1640+10% of FCS, supplemented with L-glutamine, 100 µg/ml streptomycine and 100 U/ml Penicillin. A working solution was prepared by adding 0.5 µg/ml propidium iodide (PI, Sigma) in RPMI 1640+10% FCS. The lymphocytes (as effectors) and K562 (as target) cell lines were mixed and cultured in the same tube with the effectors. Target ratio was effectors to targets 50:1 respectively. Briefly: the tubes containing the mixed cells were centrifuge for 7 minutes at 250 x g at room temperature, then kept in 37°C for 10 minutes in the water bath, then the tubes were resuspended.

In the working solution, a concentration of 1 x 10^5 cells/ml was prepared to avoid recycling of NK cells. The samples were then incubated for 1.5 hours in the incubator at 37°C, 5% of CO_2, then the cells concentration brought to 1 x 10^6 cells/ml and was ready for running for flow-cytometry. The result of the measurement was read twice by two different observers. In order to monitor the spontaneous death rate, the only target cells (without effector cells) were incubated accompanied with the processing. The final concentration of 1 x 10^5 cells/ml has been used as control. The cells were analyzed with a FAC Scalibour flow-cytometry. The activity of NK cells were calculated based on the percentage of dead target cells (K562) in the tube which contained effector cells, subtracted by the percentage of dead target cells in the control tube (without effector cells), divided by the total number of cells (100%), and subtracted by the dead target cells in the control tube (without effector cells).

RESULTS AND DISCUSSION

The data of noise intensity level are shown according to the scale of WECPNL, general reaction score, and the activity of NK cells of each group is presented in Table 1 below.

Tabel 1: The results of noise intensity level measured with WECPNL, general reaction score and the activity of NK cells of each group.

No.		Group I	Group II	Group III	p-value
1.	The intensity level (dB) General	92.29	71.49	52.17	
2.	reaction score	8.30 ± 1.70[a]	4.85 ± 2.03[b]	3.21 ± 1.23[c]	0.000
3.	The activity of NK cells (%)	12.50 ± 3.25[a]	17.20 ± 3.06[b]	22.33 ± 6.30[c]	0.000

Notes: The different letters [a], [b], and [c] at one row show that there is a real difference in the test with ANOVA, followed by *Post Hoc Test* with $\alpha = 0.05$.

The result of measurement on the intensity levels of the aircraft noise with WECPNL was not much different from that of measurement on the intensity levels of the aircraft noise with WECPNL conducted by Hartono (2006) and Hartono et al. (2007), where the intensity levels in area 1, 2, and 3 were 92.29 dB, 71.49 dB, and 52.17 dB respectively. From the results of the measurement, it can be seen that the three areas had significantly different intensity levels.

The result of the measurement for each area as stated above was then followed with the measurement of general reaction score (GRS) towards the 39 respondents. GRS represented annoyance level measurement with questionnaire towards the community around the airport exposed to aircraft noise for years. The result of measurement shows that there was difference between the groups tested with ANOVA followed with Post Hoc Test ($\alpha = 0.05$) as indicated by the value of $p = 0.000$. Based on the results of the measurement, a conclusion is drawn that the group of respondents in area 1 with the intensity level of 92.29 dB underwent higher general annoyance than those in area 2 with the intensity level of 71.49 dB and those in area 3 with the intensity level of 52.17dB. Similarly, the group of respondents in area 2 underwent higher general annoyance level than those in area 3 (seen in figures 1 below).

In Table 1, it can be seen that the activity of NK cells of the respondents of groups 1, 2, and 3 were 12.50%, 17.20%, and 22.33% respectively. The results of the measurement of the activity of NK cells show that there was a significant average difference of the activity of NK cells among the three groups as shown by the value of $p = 0.000$ ($\alpha = 0.05$). After the measurement was followed with Post Hoc Test, there was a significant average difference of the activity of NK cells between group 1 and group 3, between group 2 and group 3, and between group 1 and group 2 as shown by the value of $p < 0.05$.

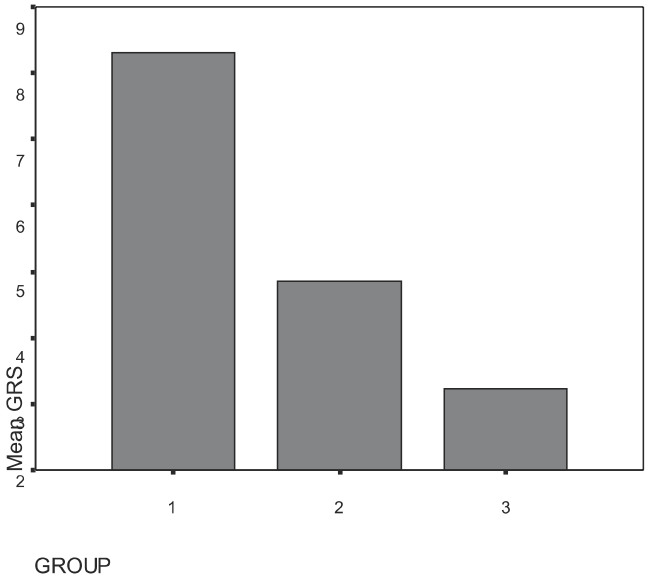

Fig.1. General reaction score in the subjects group according to the tertile distribution of aircraft noise exposure (Anova ; p = 0.000). Group 1, respondents whose living area is less than 500 meters from the tip of the runway with the noise intensity of 92.29 dB. Group 2, respondents whose living area is between 500 and 1,000 meters from the tip of the runway with the noise intensity of 71.79 dB. Group 3, respondents whose living area is greater than 1,000 meters from the tip of the runway with the noise intensity of 52.17 dB.

The test of Pearson's product moment correlation shows that there was a negative correlation between the GRS and the activity of NK cells as shown by the value of $p < 0.05$ and correlation coefficient (r) = – 0.613 (seen in Table 2 below). The negative sign indicates the reverse correlation, meaning that if GRS is high, the activity of NK cells is low, and reversely if GRS is low, the activity of NK cells is high.

The detailed information of the activity of NK cells of each group (analyzed with a FACScalibour flow-cytometry) can be seen in Figures 2, 3, and 4 below.

The exposure of aircraft noise with the intensity level (92.29 dB measured with WECPNL) will be responded as a stress as shown by the high GRS. This is in compliant with the theories that the response to noise may partly depend on the characteristics of sound. These include intensity, frequency, complexity of sound and duration (whether intermittent or continuous noise). The high intensity level of the noise is more annoying than the low intensity level (Passchier-Vermeer and Passchier, 2000; Shon, 1994; Spreng, 2000; Stansfeld and Matheson, 2003; Sobotova, 2006).

Table 2: Pearson's correlation coefficient between general reaction score and activity of NK cell

variables	General reaction score	NK cells activity
General reaction score	1	- 0.613*
NK cells activity	- 0.613*	1

*$p < 0.05$

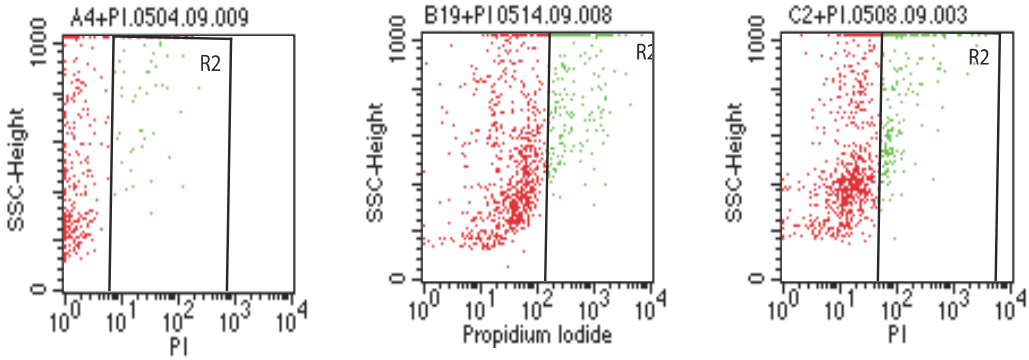

Fig. 2 Fig. 3 Fig. 4

Fig. 2 : The comparison between the living target cells (K562) labeled in red color and the dead target cells (K562) labeled in green color of group 1.

Fig. 3 : The comparison between the living target cells (K562) labeled in red color and the dead target cells (K562) labeled in green color of group 2.

Fig. 4 : The comparison between the living target cells (K562) labeled in red color and the dead target cells (K562) labeled in green color of group 3.

It is known that the continuous recurrent noise will be responded as stress (psychologically and physiologically), which may activate hypothalamus, increase the efferent activity of *nervus vagus* and stimulate anterior *hypophysis* (Ader, 2000; Ganong, 2003; Guyton and Hall, 2006). Psychological stress can upregulate the expression of corticotropine-releasing hormone (CRH) through the hypothalamus, which leads to production adreno-corticotropin hormone (ACTH). ACTH stimulates the adrenal cortex to increase levels of glucocorticoid hormones. Furthermore, the cells at the medulla of adrenalic glands secrete epinephrine and (EPI)-norepinephrine (NE). Several findings of studies with animal models show that the increase of glucocorticoid and catecholamine (epinephrine and norepinephrine) due to the stress in a long term resulted in the decrease of the activity of NK cells. (Glaser and Kiecolt-Glaser, 2005; Kiecolt-Glaser et al., 2002; Morikawa et al., 2004; Nagao et al., 2000; Padgett and Glaser, 2003; Ronald, 2003; Suzui et al., 2004).

The activity of NK cells influenced by TNF, interferons (IFN) α, β, and γ which cause the increase of the cytolytic function of NK cells. INF- α brings about higher increase to the cytolytic functions than IFN- γ. Other lymphokines also produce effects on NK cells. IL-12 and IL-2 in a synergic way increase the cytotoxicity of NK cells. NK cells are also able to lyse cells with the aid of IL-2. On the one hand IL-2 is a potent induction factor for the cytokine production by NK cells. On the other hand, IL-2 is also a growth factor for NK cells and plays a role to increase the cytotoxicity and migration of NK cells (Cooper et al., 2001; Rodella et al., 1998).

The increase of cortisol level and catecholamine levels due to the stress in a long term will inhibit the activity of NF-kB (NF-kappa Beta). Due to such inhibition, several cytokines generated by NK cells (INF-α, INF-β, IFN-γ, IL-10, GM-CSF, and TNF- β) and IL-2, IL-4 generated by T cells will decrease in term of their production. The decrease of the levels of cytokines TNF, INF, IL-2 and IL-12, which is caused by the inhibition of the activity of cortisol and norepinephrine (NE) will cause the cytolytic activity of NK cells to decrease (Biron et al., 1990; Cooper et al., 2001; Kehrl et al., 1990; Megan et al., 2001[a]).

These results are similar to those reported by Andalib et al. (2006) in a study on 45 women suffering from chronic stress due to recurrent spontaneous abortion. Their study showed that there was a high level of stress in women with recurrent spontaneous abortion, and such a stress condition resulted in decreased activity of NK cells. Similar results were also reported by Morikawa et al. (2005); Suzui et al. (2004); and Nagao et al.(2000).

CONCLUSION

Based on the analysis of the data, a conclusion is drawn that the exposure of aircraft noise with the intensity level of 71.49 dB on above measured with WECPNL will be responded as a stressor as shown by the high GRS among women around Adi Sumarmo International Airport, Solo. The aircraft noise stress in a long term resulted in the decrease of the activity of NK cells. The increase of the intensity level to 92.29 dB will decrease the activity of NK cells.

RECOMMENDATION

Based on the results of the research, preventive measures are needed to deal with the aircraft noise so that it will not produce more bad impacts towards the inhabitants around Adi Sumarmo International Airport, Solo. One of the efforts that should be considered is to relocate the inhabitants to safer settlements.

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