

Hematological and immunological effects of stress of air traffic controllers in northeastern Brazil

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Background: Several studies have shown that stress and emotional reactions can affect immune responses in animals and humans.

Objective: The aim of this study was to evaluate hematological and immunological effects of stress on air traffic controllers.

Methods: Thirty air traffic controllers and 15 aeronautical information service operators were evaluated. The groups were divided as information service operators with 10 years or more of experience ($AIS \geq 10$) and with less than 10 years in the profession ($AIS < 10$) and air traffic controllers with 10 years or more of experience ($ATCo \geq 10$) and with less than 10 years in the profession ($ATCo < 10$). Blood samples were drawn at 8:00 a.m. and 2:00 p.m. The paired t-test was used to compare monocyte and nitric oxide concentrations and ANOVA was used for the other parameters.

Results: The $ATCo \geq 10$ group presented a significantly lower phagocytosis rate of monocytes at 2:00 p.m. compared to 8:00 a.m. Moreover, the $ATCo \geq 10$ group presented lower hemoglobin, mean corpuscular hemoglobin concentration, platelet and leukocyte levels, and increased cortisol concentrations at 8:00 a.m. compared to the other groups. Additionally, this group had lower phagocytosis rate of monocytes, and hemoglobin, platelet, leukocyte, basophils and nitric oxide levels at 2:00 p.m. compared to the other groups.

Conclusion: Stress seems to greatly affect immune responses of air traffic controllers with more than ten years of experience.

Keywords: Stress, physiological; Burnout, professional; Leukocytes; Immunity; Occupational health; Brazil

Introduction

Air Traffic Control or ATC is a service provided by the air traffic controllers that guide pilots on the ground or in the air in order to guarantee safety, orderly and, when possible, faster traffic flow. The controllers establish indications of directions, headings, speed, rate of climb and rate of descent and flight authorizations according to aircraft operational features (airplane size, wake turbulence category and speed) and the air traffic conditions. These authorizations may be a reference for the route to be flown, altitude and/or speed requests by the pilots.⁽¹⁾ This activity possibly leads to stress, which may cause alterations in several physiological systems such as the nervous, endocrine and immunological systems, which interact with each other to regulate organism functions and control internal and external simulation.^(2,3)

Many studies demonstrate that stress and emotional reactions affect the immune system.^(4,5) The most common way to identify possible alterations in the immunological system is by complete blood counts, including the hematopoietic system, leukocyte profile or biochemical markers of stress.^(4,5) Some works^(5,6) have demonstrated that even before the feedback system, characterized by a constant turnover of cells, which need constant replication to maintain the leukocyte, platelet and erythrocyte populations, stress can affect the number and quality of these cells.⁽⁷⁾ However, when comparing blood counts, certain variables that affect the blood system, such as the time of collection due to alterations in the circadian rhythm, and the presence of viruses and infections such as in tonsillitis, must be taken into account.⁽⁸⁾

Stress can cause the release of catecholamines or cortisol, deregulating circadian rhythm, and different to what happens during infections, this stimulation is not self-limiting, persisting while stress lasts. In some individuals herpes may appear, in others allergies worsen, while in others, autoimmune diseases appear, such as multiple sclerosis or lupus, or preexisting symptoms worsen.^(2,9)

As stress may be predominantly physical or psychological, in air traffic control stress may last for a long time mainly due to the fear of facing varying conditions and small incidents may persist in the mind for days or even weeks.^(10,11) The persistence of stress, i.e. chronic stress, whether physical or emotional, may cause an imbalance in the main defenses, that is between the humoral and cellular immune systems. It is well known that the humoral immune system is responsible for antibody production and defense against extracellular organisms such as bacteria and the cellular immune system is responsible for defense against viruses, fungi and cancer cells. However with external aggression, such as stress, although both systems participate, it is the most competent one that prevails in the body's defense.⁽¹²⁾

In this context, when an imbalance occurs, it can cause an excessive production of one or more soluble proteins, denominated cytokines. These proteins have the function of communicating between macrophages and specific cells in order to change the line of defense from innate to adaptive in situations of pathogen invasions (bacteria) and also to induce dilation of capillary blood vessels in the region of the invasion. This in turn increases blood flow making the skin hot thereby facilitating further vascular dilation with larger spaces between endothelial cells permitting more plasma to leak into the connective tissues, increasing the pressure on nerve endings and as a result causing pain.⁽¹³⁾

In this case, the nervous system is also important to regulate defense mechanisms by releasing endorphins that not only decrease pain but also act on the immune system. Alpha-endorphin is immunosuppressive and beta-endorphin is immunostimulant. Stressful situations affect the regulation of endorphin and cytokine secretion thereby having direct consequences on immunity.⁽⁸⁾ Elevated cortisol levels stimulate thymocyte apoptosis and may cause lymphocytopenia, neutrophilia and monocytopenia.⁽⁴⁾ Monocytes should be analyzed, not only in respect to quantity but in the functional effect, as they are phagocytic cells and in this case, pathogen elimination happens by microorganism encompassment and degradation.⁽¹³⁾

Some works^(5,14) demonstrate reductions in the phagocytosis rate of monocytes. Although these studies were on animal models, the relationship between the observed immunological and neuroendocrine systems suggests that physiologic alterations in response to stress have repercussions on the efficiency of organic defense mechanisms.⁽¹⁵⁾

There are also studies^(16,17) associating nitric oxide (NO) to stress. NO is an inorganic gas with a very short half-life that is involved in many physiological mechanisms including neurotransmission, vasodilatation, cytotoxic activity of the immune system and platelet function.⁽¹⁶⁾ In animal models, considerable reductions in L-arginine were observed during and after stress. L-arginine is a basic amino acid precursor of NO synthesis.⁽¹⁷⁾

Thus, this work aimed at investigating the effects of chronic stress on cells of the hematopoietic system including leukocytes, on the phagocytosis rate of monocytes and on the NO levels in air traffic controllers of the Recife Area Control Center (ACC), Pernambuco, Brazil.

Methods

Subjects

A total of 45 flight protection professionals were evaluated, including 30 air traffic controllers (ATCo) and 15 aeronautical information service operators (AIS) who were included as a control group. Notwithstanding shift work, the AIS perform a different role to that of the controllers. The specification of this function will be presented below. All professionals belong to the Third Integrated Center of Air Defense and Air Traffic Control (CINDACTA III) and the Aeronautical Command (COMAER) in Recife, Brazil. More specifically, the ATCo are from the ACC. The participants were subjected to the evaluations (blood collection) at CINDACTA III under standard conditions at 8:00 a.m. and at 2:00 p.m., that is, at the start and end of their shifts, in a building with central air conditioning and a temperature of $22 \pm 2^\circ\text{C}$. Only male air traffic controllers were included in this study; inactive controllers were excluded as were women because there are few.

Air traffic control activity specifications

Air traffic control is provided by three units of control: Tower (TWR), Approach Control (APP) and ACC. The controllers of the Tower are responsible for traffic during landing and takeoff and also for the movement of people and vehicles in the maneuver area; they monitor roads used for local circulation. In terms of vertical division, the tower has jurisdiction on all traffic flying at altitudes up to 2000 feet.

APP is responsible for the intermediary phase of the flight. In large capitals, there are usually areas mapped out called terminals that consist of route letters and are defined in manuals available to airmen. These areas cover a side approach with a distance of 40 nautical miles or slightly over. The APP has jurisdiction over traffic that flies between 2000 and 14,000 feet.

The ACC usually controls a much larger air space than the above-mentioned sectors. The ACC Recife, for example, controls aircraft in the whole of Northeast Brazil flying at 14,000 feet or above (Figure 1).

Control group activity specifications (Aeronautical Information Operators)

The AIS, despite also having shift work, have very different jobs to those of ATCo. AIS organize publications that involve flight protection in the form of Aeronautics Command Instructions (ICAs), including the ICA 100-12, which describes air traffic regulation throughout Brazil.



Figure 1 – Area Control Center (ACC), Recife, Pernambuco, Brazil
Recife ACC belongs to the third Integrated Center of Air Defense and Air Traffic Control (CINDACTA III) of the Aeronautical Command (COMAER)

Additionally, they guide pilots and operational flight dispatchers during the preparation of flight plans and provide important news related to flight security called Notice to Airman (NOTAM). These NOTAM contain information about restricted, dangerous or prohibited areas related to air combat training of Brazilian Air Force, Army and Navy fighters, all of which have defined areas in Brazilian air space.

Study groups

The subjects were divided into four groups: 30 to 45-year-old AIS operators with at least ten years experience (AIS>10, Control 1 – n = 8); 18 to 29-year-old AIS operators with less than ten years in the profession (AIS<10, Control 2 – n = 7); 30 to 45-year-old ATCo with at least ten years experience (ATCo>10 – n = 15) and 18 to 29-year-old ATCo with less than ten years in the profession (ATCo<10 – n = 15).

All participants had university degrees. The decision to elect ten years experience as the parameter for group division was based on an earlier doctoral thesis.^(18,19) In this study, the information was collected by a questionnaire that contained data related to the prevalence of headaches, anxiety, depression, hypertension, infections and viruses that were significantly worse after ten years in the profession.

Evaluations

This work was approved by the Commandant of CINDACTA III and by the Research Ethics Commission of the Federal University in Pernambuco (homologated on November 1st, 2006).

Peripheral blood was collected in plastic vacutainer tubes (4 mL) with EDTA anticoagulant.

The blood samples were drawn at the beginning

(8:00 a.m.) and end (2:00 p.m.) of the shift for the following laboratory exams: complete blood count, phagocytosis rate of monocytes, nitric oxide produced by monocytes stimulated in a culture and cortisol levels.

Methods

The complete blood count was performed using a Coulter cell counter in the Laboratory of Clinical Analyses and Blood Diseases (LIAC), Recife, Brazil. The other exams were carried out in the Keizo Asami Laboratory (LIKA) in UFPE. To evaluate the phagocytosis rate, monocytes (1×10^6) and *S. cerevisiae* (1×10^7) yeast were incubated in a RPMI culture at 37°C and 5% CO₂ for one hour (Figure 2).



Figure 2 – The phagocytes rate, monocytes (1×10^6 in a RPMI culture) and *S. cerevisiae* (1×10^7) yeast were incubated in an incubator (37°C, 5% CO₂) for one hour

Statistical analysis

All data were analyzed by ANOVA and Tukey (post-hoc) except for NO data which was evaluated by the paired t-test. All data are expressed as means \pm standard error, with a p-value < 0.05 being considered significant.

Results

Hemoglobin count

The ATCo \geq 10 group had a significantly lower hemoglobin count (14.44 \pm 0.23 g/dL) at 8:00 a.m. compared to the ATCo<10 group (14.81 \pm 0.24 g/dL; p-value < 0.05), the AIS \geq 10 group (15.33 \pm 0.37 g/dL; p-value < 0.05) and the AIS<10 group (15.47 \pm 0.24 g/dL; p-value < 0.05). Reference values for adults are from 11.0 to 18.5 g/dL.

The ATCo \geq 10 group had a significantly lower hemoglobin count (14.35 \pm 0.22 g/dL) at 2:00 p.m. compared to the ATCo<10 group (14.93 \pm 0.26 g/dL; p-value < 0.05), the AIS \geq 10 group (15.05 \pm 0.36 g/dL; p-value < 0.05) and the AIS<10 group (15.36 \pm 0.31 g/dL; p-value < 0.05).

Mean corpuscular hemoglobin concentration

The ATCo \geq 10 group had a significantly lower mean corpuscular hemoglobin concentration (MCHC) (44.10 \pm 0.60%) only at 8:00 a.m. compared to the ATCo<10 group (44.46 \pm 0.66%; p-value < 0.05), the AIS \geq 10 group (45.00 \pm 0.94%; p-value < 0.05) and the AIS<10 group (46.20 \pm 0.74%; p-value < 0.05).

Table 1 - Comparison of hemoglobin and mean corpuscular hemoglobin concentration

Group	Collection time	Hemoglobin g/dL Mean \pm SEM	MCHC % Mean \pm SEM
AIS \geq 10 n = 8	8:00 a.m.	15.33 \pm 0.37	45.00 \pm 0.94
	2:00 p.m.	15.05 \pm 0.36	44.84 \pm 0.85
AIS<10 n = 7	8:00 a.m.	15.47 \pm 0.24	46.20 \pm 0.74
	2:00 p.m.	15.36 \pm 0.31	46.26 \pm 0.86
ATCo<10 n = 15	8:00 a.m.	14.81 \pm 0.24	44.46 \pm 0.66
	2:00 p.m.	14.93 \pm 0.26	44.67 \pm 0.63
ATCo \geq 10 n = 15	8:00 a.m.	14.44 \pm 0.23* \downarrow	44.10 \pm 0.60* \downarrow
	2:00 p.m.	14.35 \pm 0.22* \downarrow	43.73 \pm 0.59

AIS \geq 10 = AIS with \geq 10 years experience; AIS<10 = AIS with < 10 years experience; ATCo \geq 10 = ATCo with \geq 10 years experience; ATCo<10 = ATCo with < 10 years experience ANOVA and Tukey (post-hoc) tests were used SEM = standard error; *p-value < 0.05

White blood cell count

Total leukocyte count

The ATCo \geq 10 group had a significantly lower total leukocyte count (5.393 \pm 0.272 \times 10⁹/L) at 8:00 a.m. compared to the ATCo<10 group (5.947 \pm 0.240 \times 10⁹/L; p-value < 0.05), the AIS \geq 10 group (6.388 \pm 0.540 \times 10⁹/L; p-value < 0.05) and the AIS<10 group (6.871 \pm 0.690 \times 10⁹/L; p-value < 0.05). Reference values for the total leukocyte count are from 3.5 to 13.0 \times 10⁹/L in adults.

The ATCo \geq 10 group had a significantly lower total leukocyte count (5.733 \pm 0.311 \times 10⁹/L) at 2:00 p.m. compared to the ATCo<10 group (6.180 \pm 0.271 \times 10⁹/L; p-value < 0.05),

the AIS \geq 10 group (6.388 \pm 0.505 \times 10⁹/L; p-value < 0.05) and the AIS<10 group (7.243 \pm 0.767 \times 10⁹/L; p-value < 0.05).

Monocyte count

The ATCo \geq 10 group presented a statistically significant reduction in the monocyte count in blood drawn before (0.905 \pm 0.05 \times 10⁹/L) and after (0.799 \pm 0.033 \times 10⁹/L, p-value < 0.05) their shifts. The other groups did not present any significant differences.

Table 2 - Comparison of white blood cell count in flight protection professionals

Group	Collection time	Leukocytes (\times 10 ⁹ /L) Mean \pm SEM	Monocytes (\times 10 ⁹ /L) Mean \pm SEM
AIS \geq 10 n = 8	8:00 a.m.	6.388 \pm 0.540	0.914 \pm 0.068
	2:00 p.m.	6.388 \pm 0.505	0.888 \pm 0.078
AIS<10 n = 7	8:00 a.m.	6.871 \pm 0.690	0.734 \pm 0.071
	2:00 p.m.	7.243 \pm 0.767	0.733 \pm 0.084
ATCo<10 n = 15	8:00 a.m.	5.947 \pm 0.240	0.820 \pm 0.065
	2:00 p.m.	6.180 \pm 0.271	0.799 \pm 0.042
ATCo \geq 10 n = 15	8:00 a.m.	5.393 \pm 0.272* \downarrow	0.905 \pm 0.050
	2:00 p.m.	5.733 \pm 0.311* \downarrow	0.799 \pm 0.033* \downarrow

AIS \geq 10 = AIS with \geq 10 years experience; AIS<10 = AIS with < 10 years experience; ATCo \geq 10 = ATCo with \geq 10 years experience; ATCo<10 = ATCo with < 10 years experience ANOVA and Tukey (post-hoc) tests were used SEM = standard error; *p-value < 0.05 § inter-group data analyzed using the paired t-test, *p-value < 0.05

Cortisol

The ATCo \geq 10 group had significantly higher cortisol levels (9.61 \pm 1.12 μ g/dL) at 2:00 p.m. compared to the ATCo<10 group (5.93 \pm 0.53 μ g/dL; p-value < 0.05), the AIS \geq 10 group (6.49 \pm 0.57 μ g/dL; p-value < 0.05) and the AIS<10 group (7.96 \pm 0.74 μ g/dL; p-value < 0.05). Reference values for cortisol in adults are from 5.00 to 25.00 μ g/dL.

Platelets

The ATCo \geq 10 group had a significantly lower platelet count (202 \pm 13 \times 10⁹/L) at 8:00 a.m. compared to the ATCo<10 group (226 \pm 10 \times 10⁹/L; p-value < 0.05), the AIS \geq 10 group (273 \pm 9 \times 10⁹/L; p-value < 0.05) and the AIS<10 group (221 \pm 20 \times 10⁹/L; p-value < 0.05). Reference values for platelets in adults are from 150 to 450 \times 10⁹/L.

The ATCo \geq 10 group had a significantly lower platelet count (210 \pm 12 \times 10⁹/L) at 2:00 p.m. compared to the ATCo<10 group (233 \pm 12 \times 10⁹/L, p-value < 0.05), the AIS \geq 10 group (271 \pm 9 \times 10⁹/L, p-value < 0.05) and the AIS<10 group (229 \pm 18 \times 10⁹/L, p-value < 0.05).

Phagocytosis rate of monocytes

The ATCo \geq 10 group had a lower phagocytosis rate of monocytes (22.80 \pm 0.28) in the blood collected at 2:00 p.m. compared to the ATCo<10 group (26.07 \pm 0.68; p-value < 0.05), the AIS \geq 10 group (27.13 \pm 0.44; p-value < 0.05) and the AIS<10 group (25.86 \pm 1.14; p-value < 0.05) (Figure 3).

Table 3 - Comparison of cortisol and platelet levels of flight protection professionals

Group	Collection time	Cortisol $\mu\text{g/dL}$ Mean \pm SEM	Platelets ($\times 10^9/\text{L}$) Mean \pm SEM
AIS \geq 10 n = 8	8:00 a.m.	9.21 \pm 1.12	273.038 \pm 9.065
	2:00 p.m.	6.49 \pm 0.57	271.038 \pm 9.057
AIS $<$ 10 n = 7	8:00 a.m.	10.71 \pm 0.36	221.014 \pm 20.038
	2:00 p.m.	7.96 \pm 0.74	229.29 \pm 18.80
ATCo $<$ 10 n = 15	8:00 a.m.	10.77 \pm 1.07	226.067 \pm 10.059
	2:00 p.m.	5.93 \pm 0.53	233.007 \pm 12.21
ATCo \geq 10 n = 15	8:00 a.m.	9.91 \pm 0.77	22.08 \pm 13.097* \downarrow
	2:00 p.m.	9.61 \pm 1.12* \downarrow	210.038 \pm 12.095* \downarrow

AIS $>$ 10 = AIS with \geq 10 years experience; AIS $<$ 10 = AIS with $<$ 10 years experience; ATCo $>$ 10 = ATCo with \geq 10 years experience; ATCo $<$ 10 = ATCo with $<$ 10 years experience

ANOVA and Tukey (post-hoc) tests were used
SEM = standard error; *p-value $<$ 0.05

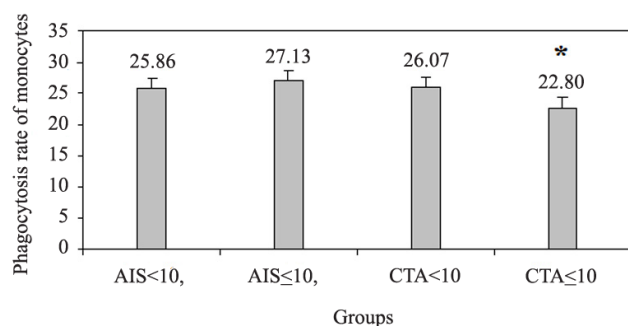


Figure 3 – The phagocytosis rate of monocytes of blood collected at 2:00 p.m. Data expressed as means

Nitric oxide

The ATCo \geq 10 group had low NO levels only in blood collected at 2:00 p.m. (0.180 \pm 0.07 before and 0.024 \pm 0.005 after stimulation using lipopolysaccharide, p-value $<$ 0.05).

Discussion

This work showed that ATCo of ACC Recife with more than ten years experience in the profession had higher cortisol levels and lower phagocytosis rates of monocytes, nitric oxide concentrations and platelet counts. This study also found lower total leukocyte, total basophil and total hemoglobin counts compared to the other groups.

The immunological system responds differently to each stimulus⁽²⁰⁾ and is composed of numerous cell types and soluble mediators that are influenced by neuroendocrine regulation and other factors. The communication between the central nervous system and the immunological system occurs through the hypothalamus-pituitary-adrenal (HPA) axis. The components of this are the paraventricular hypothalamic nucleus secretor of the corticotrophin releasing hormone (CRH); the anterior pituitary gland secretor of the adrenocorticotrophic hormone (ACTH); and the adrenal glands that secrete glucocorticoid. Parallel to

the HPA axis is the locus coeruleus norepinephrine sympathetic nervous system axis (LC-NA-sympathetic). Both these axes act synergically.⁽⁸⁾

Within physiologic limits, the HPA axis is stimulated in the hypothalamus during stress through serotonin (5-HT), acetylcholine (Ach), arginine vasopressin (AVP) and inflammatory cytokines (TNF- α , IL-1 and IL-6) produced at sites of inflammation. Activation of the axis results in the production of CRH and increases AVP secretion which together activate the release of ACTH by the pituitary gland. This hormone stimulates the production of cortisol by adrenal glands.⁽²¹⁾

The increase of cortisol in this study was only observed in the ATCo \geq 10 group at the end of seven working hours. The presence of cortisol over long periods can cause an imbalance such as hyperactivity or hypoactivity of the HPA axis or even at the molecular level such as in glucocorticoid receptors.⁽²²⁾

Increases in cortisol seem to suggest that these subjects are in highly stressful conditions related to the profession. These results mean that the HPA axis functions more with consequent reduction, albeit not necessarily total suppression, of the immune system. In this case, the increased risk of infections is considerable.⁽²²⁾

The various cell types (monocytes, lymphocytes, natural killer cells and granulocytes) react differently to stress. Macrophages, for example, seem to be sensitive to the effects of stress due to glucocorticoid receptors.⁽²³⁾ The way that monocytes act against infection is by phagocytosis. There are still few published works on monocyte phagocytic activity and research on the effect of stress on humans. However, similar to the way many medications are tested, there are studies on experimental models of animals^(4,5) that investigate this direct relationship between stress and the monocyte phagocytosis rate.

It was observed in this study that monocyte phagocytosis in the ATCo \geq 10 group was lower than the other groups. Monocytes originate from undifferentiated cells, which are present in the bone marrow similar to all the cells of the immunological system. Monocytes not only produce intense phagocytic activity, but also secrete enzymes, plasma proteins, prostaglandins, cytokines and reactive oxygen species (superoxide and hypochlorite acid) and reactive nitrogen species (Nitric oxide - NO).⁽²⁴⁾

Reduced NO levels were observed in this work in the ATCo \geq 10 group. NO is a reactive nitrogen species, which is important in defense against microbial pathogens and tumor cells.^(25,26) Some pathogens are extremely sensitive to NO produced by monocytes.⁽²³⁾

There are studies^(6,27) that demonstrate that the antimicrobial and antitumor functions of macrophages/monocytes related to NO diminish due to stress.⁽⁶⁾ This decrease has been associated to a larger incidence of infections and the spread of tumors in animals subjected to extended stress conditions.⁽²⁸⁾

A significant reduction in hemoglobin levels and MCHC in the ATCo \geq 10 group was also observed in this work. Hemoglobin is a protein that makes up about 35% of the weight of red blood cells and is responsible for the transportation of oxygen from the lungs to tissues throughout the body. Besides the transportation of oxygen, hemoglobin participates in the nutrient transport process. In this process, the blood exchanges nutrients for waste products secreted by the cells. The blood needs to transport sufficient oxygen and this depends on the iron levels in the organism.⁽²⁹⁾

Although this study highlighted reductions in NO and hemoglobin in the ATCo \geq 10 group there seems to be a need for further investigations including, for example, eating habits, as the nutritional aspect is extremely important to homeostasis. The ingestion of antioxidant substances for example, constituted by long-chain polyunsaturated fatty acids, vitamins E and C, beta-carotene, zinc, copper and selenium, help to remove reactive oxygen species and reactive nitrogen species avoiding oxidative stress which also affects the immune system. With reduced antioxidant substances, oxidants inhibit the release of pro-inflammatory cytokines.⁽³⁰⁾ Moreover hemoglobin levels change with exogenous factors, such as with the ingestion of insufficient iron.

This work observed significantly lower total leukocyte counts in the ATCo \geq 10 group. Leukocytes are primarily involved in immune defense. There are five different types of leukocytes: basophils, eosinophils, neutrophils, lymphocytes and monocytes.⁽³¹⁾

Several endogenous and exogenous factors influence the total leukocyte count in animals and humans: including variations in temperature, stress and physical exercise; electric shocks or even a cold bath can cause changes.⁽³²⁾ There are some studies⁽⁵⁾ in animals and humans that demonstrate that stress reduces the total leukocyte count, thus corroborating our results.

Basophils possibly participate in allergic processes as they have some substances in their granulations such as: histamine, heparin, chondroitin sulfate, kallikrein, trypsin and chymotrypsin. The basophil response is translated into two complementary processes: degranulation and release of histamine; synthesis and release of acid derivatives (leukotrienes, thromboxanes and prostaglandins).⁽³³⁾

In asthma, anaphylaxis and urticaria, basophils release histamine, a chemotactic factor to attract eosinophils to sites of inflammation.^(34,35) The significantly lower basophil count found in the ATCo \geq 10 group seems to indicate a lower potential defense against allergic processes. If a flight controller drinks excessive alcohol, this process may be further impaired, as alcohol may reduce the action of histamine as it has metabolism enzymes in common. Increased acetaldehyde in the blood resulting from abnormalities in the alcohol dehydrogenase gene in Asiatic populations can cause the release of histamine from mast cells and basophils, which in turn induces hypersensitivity

reactions (flushing). These reactions may be blocked by antihistamine drugs. H₂-receptor antagonists influence the ethanol metabolism by inhibiting the activity of alcohol metabolizing enzymes in the stomach and liver. A reduction in the activity of stomach alcohol dehydrogenase results in an increase in blood ethanol concentrations, which may impair psychomotor skills.⁽³⁶⁾

There is evidence that ethanol affects the brain histamine levels by changes in the activity of enzymes involved in the synthesis and metabolism of histamine.⁽³⁶⁾ Alterations in these values may help to diagnose some diseases. The number of basophils will be increased (basophilia) when a patient has ulcerative colitis, chronic sinusitis, nephrosis, hemolytic anemia, and Hodgkin's disease or after splenectomy. However basopenia occurs in cases of hyperthyroidism, in pregnancy, acute infection, Cushing's syndrome and during periods of stress.⁽³³⁾

The platelet count was significantly lower in the ATCo \geq 10 group, but this was not characterized as thrombocytopenia. This result may be due to the stressful activity or perhaps, eating habits such as dietary deficiencies in iron, folic acid and vitamin B12 or even excessive use of sleeping tablets. One explanation for the drop in platelets related to stress may be based on a reduction in NO, as several works have demonstrated that NO synthesis depends on L-arginine in platelets and endothelial cells.⁽³⁷⁾

Psychological stress appears due to different conditions, such as the demands of work, family tension, financial concerns, among other factors, including the personal capacity of handling these challenges. These varied conditions, when associated to emotional instability, depression, lack of concentration, judgment difficulties and an impaired immune system may negatively affect the lives of these people, who operate the air traffic control systems in Brazil.⁽¹¹⁾

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