

Raja Bandung Banana (*Musa paradisiaca* L. cv Raja Bandung) Prevents Increased Systolic Blood Pressure in Rats Given Acute Stress Test

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ABSTRACT

The relationships between stress and hypertension have been evaluated. Heightened blood pressure (BP) reactions to acute stress have been implicated in cardiovascular disease's development. Consumption of fruit or vegetables lowering BP. This study aimed to evaluate the effect of Raja Bandung Banana (*Musa paradisiaca* L. cv Raja Bandung) on blood pressure after acute restraint stress and forced swim test. Twenty male *Sprague dawley* rats were divided into 4 groups (A,B,C,D) and adapted for 3 days. At 4th day, groups were administered 2 g/200gBw AIN-93M, then exposed to acute restraint (1hour), except group A. After restraint, A&B received water, C received diazepam 0.5mg/kgBW, and D received banana 2.52 g/200gBW. One hour later, the forced swim test was carried out (45 minutes). Blood pressure was measured 1 hour after swim. Result showed, mean of blood pressure significantly increased after treatment ($p < 0.01$) all groups. But, the increasing of blood pressure in C and D group was lower than unrestraint (A) and control (B) group. There was significant difference of blood pressure between control (A&B) and intervention group (C&D), but no significant difference between C and D. This result indicates that Raja Bandung Banana can prevent increased blood pressure on acute stress condition as effective as diazepam.

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1. INTRODUCTION

Health is not merely the absence of disease or infirmity but a positive state of complete physical, mental and social well-being [1]. In the fact, living in today's world is nearly impossible without encountering stress. Stress can be self-controlled. The presence of certain amount of stress is necessary for everyone to perform their best, but when its levels push to the limit, however, stress become distress and people will no longer function effectively [2].

People have been exposed many various pressures that can be developed to stress. More than two-thirds of college students experience some type of stress, 38% of female college students and 27% of males reported that their stress level were so high [3]. The employees get pressure at workplace. Working under pressure has become the rule rather than exception, as the result, stress has become one of the most common problems. The number of cases of work-related stress, depression, and anxiety in UK in 2013/14 were 39% [4]. In Indonesia, the prevalence of psychological distress was 6% in 2013 [5]. Current estimates indicate that

the annual cost of stress and stress-related disease exceeds \$100 billion in US and 617 Euro in Europe in 2013 as a direct result of health care cost, lost productivity, absenteeism, and social welfare costs [2],[6]. Stress not only affects the economical aspect, but would be developed as serious and continued health disorder if not handled properly, such as coronary heart disease, hypertension, eating disorder, ulcer diabetes, depression, migraine headache, sleep disorder, and chronic fatigue.

The regular physical activity or exercise is good for our health. Their benefits are significantly reduce risk for developing or dying from heart disease, stroke, type 2 diabetes, colon and breast cancers, high blood pressure, and osteoporotic fracture [7]. It also seems to reduce symptoms of depression, anxiety, and improve mood [2]. But, people often do exercise with wrong way such as not in good condition or too high intensity and duration, so they don't get the benefits.

Nowadays, there are some sudden death cases in athlete. Since 1966 until 2004, there were 1.101 cases of sudden death on young athlete that have been reported, 40% cases were happened on young athlete under 18 years old and 33% on under 16 years old athlete. The 90% case caused by cardiovascular, 50% of them have cardiomyopathy and congenital heart disease, and 10% have atherosclerosis at their coronary artery [8]. It has been identified that an excessive elevation of SBP during exercise testing had been a stronger predictor of mortality due to CVD than SBP at rest in some previous studies [9]-[11]. Heightened blood pressure (BP) reactions to acute stress have been implicated in cardiovascular disease's development. Study showed that hypertension was occurred and developed on people who are exposed to stress, either physical, social, or psychological stress [12]-[14].

One of the medications to manage stress is diazepam drug. High consumption of benzodiazepines (BDZ) occurs in populations exposed to stress. In Serbia and Montenegro, the total consumption of psychiatric drugs significantly increased in 2000-2004 [15]. Diazepam reaching the first place on the list of the most frequently prescribed drugs associated with hypertension [16].

The more natural medication is needed to prevent high blood pressure on stress condition. Food is a good choice for stress and hypertension management. Potassium can modulate the vasodilatation, and influence the mechanism of renin-angiotensin system – inhibition of renin secretion and increase the sodium excretion-, so that it can decrease the blood pressure. Consumption of Kepok Banana can lower the normal blood pressure significantly, from 114.9//68.7 mmHg to 103.2//62.8 mmHg [17]. In addition, diet influences brain neuronal activity by modifying the rate of synthesis and release of specific neurotransmitters [18].

Cerebral dysfunction of serotonin (5 HT) has been associated with stress response and with affective disorders. Study investigated that cerebral dysfunction of serotonin achieved through a low tryptophan diet, increase the sensitivity of rats to stressful stimuli [19]. Tryptophan is serotonin precursor that important to stress, mood, sleep regulation, and sensory transmission control. Other neurotransmitter that benefits for stress and depression is dopamine. It is formed from amino acid Tyrosine. Banana has both of the amino acids although they are in small amounts [20]-[21].

From the facts above, this study aimed to evaluate banana especially the Indonesian local banana because Indonesia is one of the biggest banana producing countries. Raja Bandung Banana is local banana that readily available in Indonesia in large quantities. In markets, it has very low price compared with other banana. Because some of this banana has seed inside, it makes this banana less public attractive and desirable. People are more frequent use this banana to feed the bird than for their own consumption.

2. RESEARCH METHOD

2.1. Animals

The study was pre-posttest control group design experimental that conducted at the Pusat Studi Pangan dan Gizi (PSPG), Pusat Antar Universitas, Universitas Gadjah Mada (UGM), Indonesia and approved by the Ethics Committee of Medical Faculty, UGM. Twenty male Sprague dawley rats, 2-3 months old, weighing about 150-200 g were obtained from the Laboratory Animal of PSPG UGM. The animals were housed in group (n=5) in home cages, maintained under a standard dark-light cycle at room temperature. The rats had free access to food and water (*ad libitum*).

2.2. Treatment

Rats were randomized into four groups: (A) un-restraint + water + swim, (B) restraint + water + swim, (C) restraint + diazepam drug 0.5 mg/kgBW + swim, (D) restraint + Raja Bandung Banana 2.52 g/200gBW + swim. First, rats were adapted for 3 days and received standard diet AIN-93M. At the 4th day, all groups were administered 2 g AIN-93M. After that, groups were exposed to 1 hour restraint stress, except group A. After restraint stress, A & B group received water, C received diazepam 0.5mg/kgBW, and D received banana 2.52 g/200gBW. One hour later, the forced swim test was carried out (45 minutes). The blood pressure level was measured 1 hour after the end of forced swim test.

2.3. Materials

Raja Bandung Banana was supplied by Plasma Nutfah Pisang Yogyakarta, Indonesia. The medium size Raja Bandung Banana has weight average ± 70 -100 g. In this study, 140 g banana was used (assumption on human consumption of 2 medium bananas). For intervention on rats, the weight of banana was multiplied with 0.018 (conversion factor). Banana has been homogenized with homogenizer tool (Armfield model L4R) before it given. Other treatment group used diazepam drug. The administered of diazepam 0.2 mg/kgBW reduced the 63.5% cortisol on rats that given electric current [22]. Another study showed, only low (0.5mg/kg) and medium-dose (1mg/kg) diazepam blocked the detrimental effects of chronic stress [23], so the 0.5 mg/kg dose was used in this study.

2.4. Stress Test

The psychological stressor that used in this experimental was restraint stress. The animal was placed in a 12 cm x 5 cm plastic tube which is made from PVC pipe, enclosed, to immobilize the animal. There was a 1 cm hole at one end of tube for the tail and five smaller holes at the other end for breathing. The restraint had been carried out for 1 hour. After the restraint, the animal got vigorous exercise immediately after restraint end. It was forced swim test. The animals were placed in large boxes (40 cm width x 48 cm length x 41 cm depth) that were filled with water until the rats would not be able to touch the bottom of box during the swimming test. The height of box should be high enough to prevent the rats from escaping from the box. The swimming test had been carried out for 1 hour, in groups. After the swimming test, the rats were dried gently using towels and placed under the sun light before the blood pressure measured.

2.5. Blood Pressure Analysis

On the 4th day, the systolic blood pressure was measured twice, at the early morning before any treatment and 1 hour after the end of forced swim test. The blood pressure measurement used Sphygmomanometer S-2, Versi 6.90 from HSE (Hugo Sachs Elektronik) D-7806 March/Freiburg, with tail-cuff method.

2.6. Statistical Analysis

Data were expressed as mean \pm standard deviation and analyzed using SPSS version 14.0. The normal distribution of variable was tested and confirmed by SaphiroWilk test. The data with normal distribution were analyzed using parametric test. The change in blood pressure between pretest and posttest were compared by paired-sample t test in each group. The mean difference between groups were compared by one way ANOVA, if the result showed significant different, the test was continued with multiple comparison used post hoc bonferroni test to see the most effective group. The significance level was set at $P < 0.01$ (99% CI) for all statistical comparison.

3. RESULTS AND DISCUSSION

The effects of treatment on blood pressure are shown in Table 1. In the beginning, before the stress administration, the rats's blood pressure show not significantly different ($P > 0.05$). That can be concluded, all rats in all groups are in the same condition.

Table 1. Mean \pm SD of the Systolic Blood Pressure

Group	Pre-test (mmHg)	Post-test (mmHg)	<i>P</i> *
A (un-restraint + water + swim)	89.40 \pm 4,67	130.20 \pm 1,92 ^a	0.000
B (restraint + water + swim)	84.20 \pm 4,38	134.20 \pm 4,43 ^a	0.000
C (restraint + Diazepam + swim)	83.80 \pm 4,14	106.60 \pm 4,50 ^b	0.002
D (restraint + Banana + swim)	87.00 \pm 5,09	107.20 \pm 2,77 ^b	0.000
<i>P</i> **	0.222	0.000	

*) paired sample *t* test, significant different if $p < 0.01$ (99% CI)

***) one way ANOVA test, significant different if $p < 0.01$ (99% CI). The result of multiple comparisons (Post hoc bonferroni test) was shown by superscript. Same superscript means no significant difference between groups.

After the treatment, the blood pressure increase significantly in all groups ($P < 0.01$). Groups that only got oral intervention with water (Group A and B) show the higher elevation of blood pressure in posttest. Compared between that two groups, the blood pressure after swimming test increases higher in

group that got restraint than unrestraint one, although the difference is not significant statistically (shown with same superscript).

This study shows that acute stress administration can increase the blood pressure significantly. The previous study showed the increases in SBP and DBP to the mental stress task were substantial and significant (57.61mmHg and 38.31mmHg; $p < 0.001$) [24]. A meta analysis of cohort studies showed that individuals who had stronger responses to stressor tasks were 21% more likely to develop blood pressure increase when compared to those with less strong responses in adult aged between 18 and 64 years [25]. Administration of stress with air pressure 5 times a week, each 30 minutes, could increase the SBP 13 mmHg [26] with light exposure 3 times a week each 30 minutes increases SBP significantly [27], and with restraint a week increase 49.5 mmHg [28].

The body responds to stress by activating the fight-or-flight mechanism, which prepares a person to take action by stimulating the vital defense systems. This stimulation originates in the hypothalamus and pituitary glands in the brain. The hypothalamus activates the release of catecholamines from adrenal glands. These hormonal changes increase hearth rate, blood pressure, and blood flow, blood glucose, and oxygen uptake [2].

In recent study, the level of blood pressure after exercise on restraint group is higher. The systolic blood pressure also increase after the vigorous exercise, 15.6 mmHg after high intensity treadmill [29] and 19.2 mmHg after 1 hour swim test [28]. But, combination of psychological and physical stress administration can increase the catecholamine higher than alone [30].

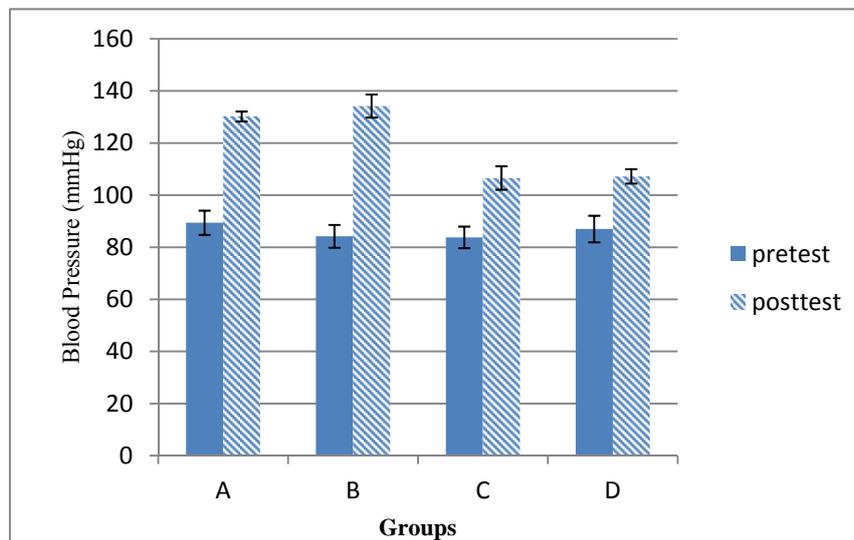


Figure 1. Mean of Pretest and Posttest Blood Pressure \pm SD. Group A: unrestraint+water+swim; B: restraint+water+swim; C: restraint+diazepam+swim; D: restraint+Raja Bandung banana+swim

The level blood pressure on posttest are significant different between groups ($P < 0.01$). Group that got water after restraint test has the highest level of blood pressure (134.2 mmHg) than which got banana or diazepam. The multiple comparisons show that the mean difference of posttest blood pressure between B group and C group is significant, also between B group and D group ($P < 0.01$).

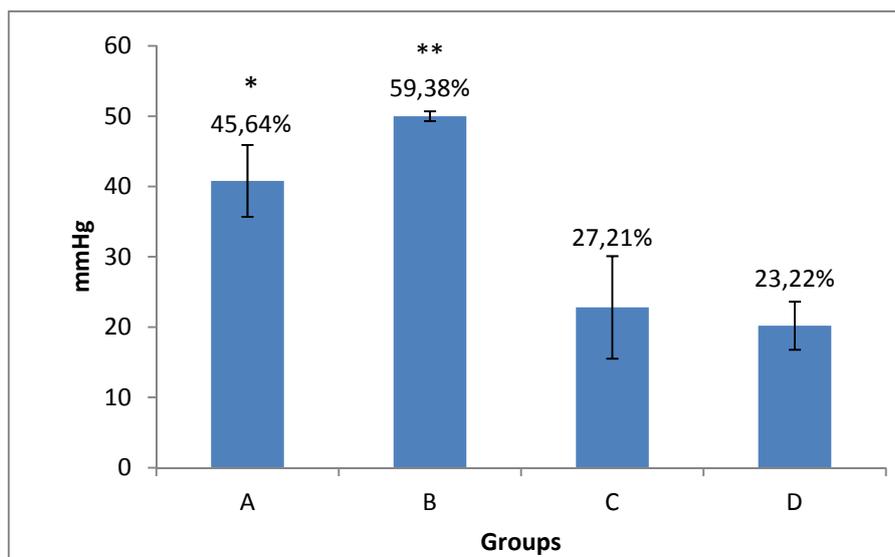


Figure 2. The Elevation of Blood Pressure After The Restraint and Oral Treatment. Group (A) unrestraint+water+swim; (B) restraint+water+swim; (C) restraint+diazepam+swim; (D) restraint+Raja Bandung banana+swim. * $p < 0.05$ = group A compared with group B, and $p < 0.01$ compared with C, and D. ** $p < 0.01$ = group B compared with C and D.

From Figure 2, the change of blood pressure after treatments is shown. Among the restraint groups (B, C, D), group D has the lowest increase (23.22%) of blood pressure, then followed by group C (27.21%). The Group B has the highest increase among them (59.38%). Statistically, the increasing of blood pressure on restraint groups is significant different between water treatment (B) and diazepam (C) or between water and Raja Bandung Banana (D). Diazepam and Raja Bandung Banana administration can suppressed the elevation of SBP, but the mean difference is not significant ($P > 0.05$).

Benzodiazepines (BZDs), particularly diazepam, have been among the most frequently prescribed drugs, especially in developed country. This drug is used as anxiolytic, hypnotic, sedative, amnesic, antiepileptic, and muscle relaxant properties [31]. Diazepam reaching the first place on the list of the most frequently prescribed drugs associated with hypertension in Serbia [16]. In this recent study, the dosage treatment is 0.5mg/kgBW, so the average rats with weighing 200 g will get 0.1 mg/day. This dosage is same with 5.5 mg/day in human. Previous study has evaluated that BZDs (Clonazepam) 1-2 mg/d can stabilize blood pressure fluctuations in 82% patients with unstable hypertension significantly [32]. The recommended doses of diazepam in the treatment of anxiety are 4–40 mg/day divided in two doses at least [33].

Besides that, the administration of Raja Bandung Banana can lower the increases blood pressure after vigorous exercise more than that diazepam did. Raja Bandung Banana weighing 100 g consists of 28.64 g carbohydrates; 0.5 g fat; 1.2 g protein; 2.47 g fiber; 105.24 mg phenol. The previous study on subject who was frustration, angry, or depression under pressure showed that high carbohydrates consumption can decrease and help them manage these responses [34]. In addition, banana has dopamine, one of the neurotransmitter. Dopamine is formed by Amino acid Tyrosine, a natural compound that can be found in animal product, oat, banana, and grains. Based on the research, *Musa cavendishii* banana flesh had 2.5-10 mg dopamine [20], other study showed 0,42 mg/100 g dopamine on fleshed banana [21]. Another amino acid is tryptophan, the serotonin precursor. The administration of tryptophan increases the brain serotonin synthesis. Serotonin has some psychological function and behavior such as mood and sleep regulator. Abnormalities of brain serotonin have been related to depression, anxiety, and aggression (Tanke, 2008). The increases of both neurotransmitter may give relax sensation and decrease stress, so the elevation of blood pressure after exercise does not high.

Beside the compound which has psychological effect, banana is one of the fruits that rich in potassium. Regular 100 g banana contains 358 mg potassium and 8.7 mg vitamin C [35]. Consumption of Kepok Banana (another local banana in Indonesia) can lower the normal blood pressure significantly, from 114.9/68.7 mmHg to 103.2/62.8 mmHg [17]. Decreased of blood pressure can be explanation because potassium can modulate the vessel vasodilatation, and influence the mechanism of renin-angiotensin system with inhibition of renin secretion and increase the sodium excretion, so that it can decrease the blood pressure [36].

4. CONCLUSION

The acute stress test could increase the systolic blood pressure significantly but the administration of Raja Bandung Banana has been demonstrated to prevent it and has the similar effect compared with diazepam. From this result, consumption of two medium sizes of Raja Bandung Bananas gives the better condition for stress or under pressure person who will take vigorous exercise.

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