Effects of Simulated Heat Wave on Senile Mice

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I. Introduction

- In our experiment, we investigated the effects of simulated heat wave on senile mice by using a meteorological environment simulation chamber.
- We took eighteen senile mice in the experiment. We randomly divided them into three groups, namely, the control group (n = 6), heat wave group (n = 6), and heat wave BH4 group (n = 6).
- Mice in heat wave and heat wave BH4 groups were placed in the simulation chamber and exposed to simulated heat waves according to the heat wave data recorded during July 2001 in Nanjing, China.
- Mice in heat wave BH4 group were treated with gavage with BH4 in prior to heat wave exposure.
- Weights and rectal temperatures were recorded daily. Levels of soluble intercellular adhesion molecule (sICAM-1), endothefin (ET-1) and nitric oxide (NO) in plasma were measured at the end of the experiment as biomarkers of cardiac function.
- We analyzed their changes to preliminarily determine the mechanism of the effects of heat waves on cardiovascular functions in senile mice.

II. Results and Analysis

1. Heat Wave Curve

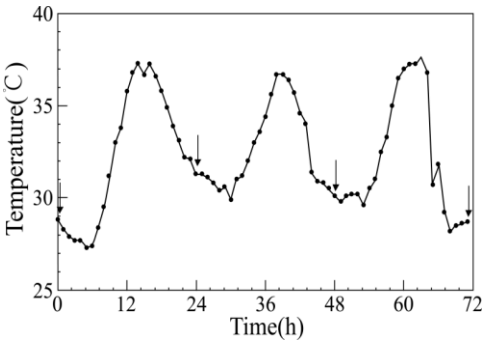

Figure 1. Temperature curve of the simulated heat wave. The *arrows* denote sampling time points when the body temperatures and weights of experimental mice were measured in the three experimental groups.

- Figure 1 shows the temperature simulation curve in our experiment.
- We developed a heat wave model which was based on a heat wave that occurred in July 2001 in Nanjing, China.
- The average daily maximum temperature was 36.6 ℃.
- The experiment period started from 0 o'clock on 9 July 2001 and ended at 24 o'clock on 11 July.
- The temperature of the control group was set at 27 ℃, which was the average summer temperature in Nanjing from 2001 to 2010.

2. Body Weight and Rectal Temperature

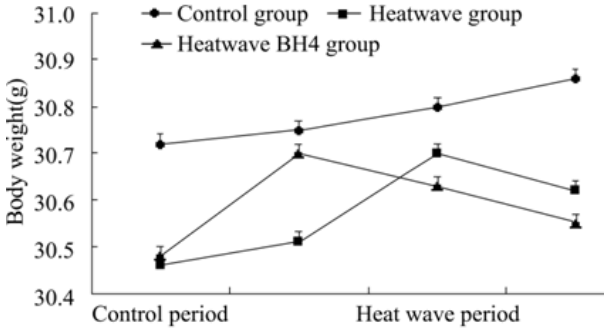

Figure 2. Body weights of senile mice in the control, heat wave, and heat wave BH4 groups.

- Figure 2 shows that the body weights in all three groups slightly increased by the end of the experiment ($p > 0.05$).

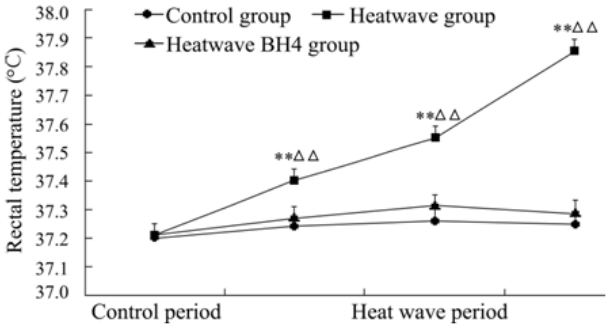

Figure 3. Rectal temperatures of senile mice in the control, heat wave, and heat wave BH4 groups. Heat wave exposure for 3 d. ** $p < 0.01$ vs. control group; ΔΔ $p < 0.01$ vs. heat wave BH4 group at the same time of measurement.

- Figure 3 shows that the mice in each group showed increased rectal temperature with the progression of the heat process between the start and the end of the experiment.
- Rectal temperature significantly increased by 0.65 ℃ in the heat wave group, whereas that of the heat wave BH4 and control groups slightly increased by 0.07 ℃ and 0.05 ℃, respectively.
- Rectal temperature increases in the heat wave group were significantly higher than those in the control group ($p < 0.01$), but the rectal temperature differences between the heat wave BH4 and control groups were not statistically significant ($p > 0.05$).

3. Analysis of sICAM-1

Table 1. The sICAM-1 levels in senile mice at the end of the experiments.

		Group(s)	sICAM-1 (pg/mL)
Mean ± SE		Control	121.19 ± 6.244
		Heat wave	189.42 ± 8.246
		Heat wave BH4	139.81 ± 2.651
p value	of ANOVA among	all three groups	0.000
	of *post hoc* test between	Control & heat wave	0.000
		Control & heat wave BH4	0.003
		Heat wave & heat wave BH4	0.000

- Table 1 shows the sICAM-1 levels in different groups of senile mice at the end of the experiments.
- Compared with the control group, the sICAM-1 levels of the heat wave group significantly increased by 68.23 pg/mL ($p < 0.01$).
- The sICAM-1 levels of the heat wave group increased by 49.61 pg/mL than those of the heat wave BH4 group, with a statistically significant difference between groups ($p < 0.01$).
- The sICAM-1 levels of the heat wave BH4 group increased by 18.62 pg/mL compared with those of the control group; the increase was minimal but significant ($p < 0.01$).
- These results show that heat waves significantly increased the secretion of sICAM-1 in senile mice. BH4 via gavage alleviated the effect of heat waves on the secretion of sICAM-1 in senile mice.

4. Levels of ET-1, NO, and ET-1/NO

Table 2. ET-1 levels, NO levels, and NO/ET-1 ratios in senile mice at the end of the experiments.

		Group(s)	ET-1 (ng/L)	NO (μmol/L)	NO/ET-1 (%)
Mean ± SE		Control	164.38 ± 10.53	47.39 ± 6.77	28.62 ± 2.21
		Heat wave	160.91 ± 7.39	62.06 ± 4.87	38.49 ± 1.84
		Heat wave BH4	164.19 ± 16.21	90.47 ± 9.15	55.19 ± 1.63
p value	of ANOVA among	all three groups	0.905	0.000	0.000
	of *post hoc* test between	Control & heat wave	0.321	0.025	0.001
		Control & heat wave BH4	0.486	0.000	0.000
		Heat wave & heat wave BH4	0.368	0.000	0.000

- Table 2 shows the ET-1 levels in senile mice of each group declined slightly during the experiment. Compared with the control group, the ET-1 level in the heat wave group decreased by 3.47 μmol/L, and that in the heat wave BH4 group decreased by 0.19 μmol/L with no significant difference ($p > 0.05$).
- The NO levels in the heat wave and heat wave BH4 groups were both significantly higher than that in the control group ($p < 0.01$). Compared with the control group, the NO level in the heat wave group increased by 14.67 μmol/L, and that in the heat wave BH4 group increased by 43.08 μmol/L. The NO level in the heat wave BH4 group was significantly higher than that in the heat wave group ($p < 0.05$).

- Trends in the NO/ET-1 ratios largely resembled those of NO levels. The NO/ET-1 ratios in both the heat wave and heat wave BH4 groups were significantly higher than that in the control group ($p < 0.01$). The NO/ET-1 ratio in the heat wave group raised by 9.87%, and that of the heat wave BH4 group raised by 26.57%. The NO/ET-1 ratio of the heat wave BH4 group increased by 16.7% compared with that of the heat wave group. Significant differences between the two groups were observed ($p < 0.01$).

III. Discussion and Conclusions

- The results show that the NO levels in the heat wave and heat wave BH4 groups significantly increased after heat exposure. The feeding of BH4 to senile mice resulted in a more pronounced increase in NO levels.
- A comparative analysis among the rectal temperature measurements in senile mice in each group showed that the rectal temperature of heat wave mice exhibited a more pronounced consecutive daily increase during 3 d of heat exposure, whereas smaller increases were observed in the control and heat wave BH4 groups.
- The NO contents in mice of each group were sorted from highest to lowest, its value in the heat wave BH4 group was 43.08 μmol/L higher than that of the control group, and 28.41 μmol/L higher than that of the heat wave group after heat exposure.
- The rectal temperature measurements of each group were compared with those of the control group. The results show that the increase in NO was significantly lower in the heat wave group than that in the control group.
- Moreover, rectal temperature was significantly higher in the heat wave group than that in the control group. By contrast, the increase in rectal temperature was smaller in the heat wave BH4 group, which had the highest NO content, than that in the control group.
- The effect of heat wave stimulation on the ET-1 levels in mice was very small, and the ET-1 levels only showed a minimal decline.
- Heat waves significantly increased the NO levels in senile mice, making the NO/ET-1 balance favor vasodilation, enhancing body heat dissipation, and promoting the decline in temperature. As the heat wave progressed, NO released by the senile mouse endothelium was insufficient to mitigate the effects of the heat wave. Thus, the mice body temperature notably increased as the heat wave progressed.
- BH4, as a NOS synthase, promoted NO release in senile mice *in vivo*, enhancing the cooling efficiency and reducing heat hazards to senile mice.