

TAURINE CONTENT OF CARDIAC TISSUE IN SPONTANEOUSLY HYPERTENSIVE RATS

Celestine CHAU, Pat HEU, Shao-Chia CHOU*, J T MIYAHARA, S RAMANATHAN
(Dept of Pharmacology, School of Medicine, University of Hawaii, Honolulu, HI 96822, USA)

ABSTRACT The taurine content of cardiac tissue was determined in normotensive rats (NWR) and spontaneously hypertensive rats (SHR) at different ages from 2 to 24 wks. Taurine content increased with age in both NWR and SHR. At 4 wks taurine content of the NWR heart was higher than SHR. But the tissue taurine of SHR increased significantly higher than NWR by 6 wks and remained high throughout the age period studied.

KEY WORDS taurine; SHR; heart; age

Taurine (2-aminoethanosulfonic acid) is a simple, stable amino acid that is found in varying concentrations in many animal tissues; however, in spite of its ubiquitous distribution, its physiological or pathological function still remains obscure. In the heart, taurine accounts for over 60% of the total amino acid pool and it has been implicated in a broad variety of cardiac phenomena such as potentiating the inotropic action of strophanthin K in guinea pig atria⁽¹⁾, preventing the epinephrine-induced premature ventricular contractions in dog⁽²⁾ and delaying the appearance of cardiac lesions in the genetically myopathic hamsters⁽³⁾. Moreover in rat, dog, and man, myocardial taurine content is markedly elevated in congestive heart failure^(4,5). Elevated level of taurine in blood has been reported in myocardial infarction⁽⁶⁾.

This study was undertaken to examine whether similar changes in tissue taurine occur in the heart during the development of spontaneous hypertension. These ex-

periments were made possible by the recent acquisition of a small population of a strain of spontaneously hypertensive Wistar rats (SHR), first developed by Okamoto and Aoki as a model of essential hypertension⁽⁷⁾. Several studies on this model have already revealed alterations in the properties and responses of cardiac tissue, particularly to various pharmacological agents. Only a few have demonstrated any biochemical changes. Therefore, this study was undertaken to examine whether similar changes in tissue taurine occur in hearts of SHR during the development of hypertension.

MATERIALS AND METHODS

Male and female normotensive rats (NWR) and SHR of different ages were used. These rats were bred in our laboratories so that a constant supply of age and sex matched rats was assured. The original stock of SHR was obtained from the National Institutes of Health animal center.

The rats were anesthetized with ether. Hearts were quickly excised, freed from connective tissues and blood, and weighed. The hearts were stored at -20°C until ready for processing.

The hearts from age and sex matched NWR and SHR were homogenized in 2 volumes of ice-cold 10% trichloroacetic acid (TCA). The homogenate was centrifuged at 3000 ×g for 20 min. The supernatant was extracted with water saturated ether

Received 1982 Jul 15 Revised 1982 Oct 20

* Author for all correspondence

(5 vol) to remove the TCA. This process was repeated 6 times.

Taurine was separated by ion exchange chromatography by the method of Anzano, Naewbanij and Lamb⁽⁸⁾. Briefly, the method consisted of passing an aliquot (1 ml) of the TCA extract through a column of cation exchange resin (AG50 W-X8, 0.9 × 10 cm) and eluting with sodium citrate buffer (0.2 mol/l, pH 2.2). Taurine and other acidic compounds were eluted in the void volume. This eluate was then passed through an anion-exchange resin (AG 2-X8, 0.9 × 8 cm) and taurine was preferentially eluted with acetic acid (1 mol/l). Both the cation exchange and anion exchange columns were calibrated with standard taurine for the elution volume and recovery.

Taurine that was eluted from the columns, was estimated by the ninhydrin method for primary amino acids, as described by Moore⁽⁹⁾.

RESULTS

Taurine content in the hearts of NWR and SHR rats at 2, 4, 5, 10, 12, 14, 16, and 24 wks was determined and the results are included in Table 1. The amount of taurine in the hearts of both NWR and SHR increased with age. At 4 wks, taurine in NWR heart is greater than in 4 wks old SHR; however, the taurine content of SHR

Table 1. Taurine content of NWR and SHR at various ages. $\bar{x} \pm SD$

Age (wks)	Rats	NWR (mg/g heart tissue wet weight)	SHR
2	1	0.173	0.124
4	3	0.504 ± 0.099	0.219 ± 0.016***
6	1	0.556	0.797
10	2	0.759 ± 0.115	1.455 ± 0.246
12	1	1.201	1.536
14	2	1.230 ± 0.167	1.832 ± 0.211
16	2	1.828 ± 0.025	2.612 ± 0.139
24	2	2.452 ± 0.392	4.030 ± 0.120

*** P < 0.01 as compared to NWR,

Table 2. Systolic blood pressure measured by a Narco Bio-Systems Model PE-300 sphygmomanometer on tail, 15 rats/group, $\bar{x} \pm SD$

Age (wks)	NWR (mm Hg)	SHR
4-5	107 ± 47	110 ± 27*
10-11	136 ± 16	185 ± 39**
16	136 ± 16	203 ± 27**
32	137 ± 12	202 ± 23**

* P > 0.05, ** P < 0.05

commences to exceed NWR by 6 wks, and is significantly higher in SHR than in NWR by the 10th wk. This higher level is maintained in SHR throughout the age period studied.

The pattern of change of taurine content in NWR and SHR seems to follow the changes in blood pressure. Table 2 incorporates the changes in blood pressure of NWR and SHR from age 4 wks to 32 wks.

DISCUSSION

Earlier reports in the literature on taurine content in SHR and NWR hearts are contradictory. Nara *et al*⁽¹⁰⁾ reported no difference at 12 wks, while Huxtable and Bressler⁽⁵⁾ reported higher taurine content in SHR.

The data presented here indicate that the taurine content in the hearts of both NWR and SHR increases with age. However, the rate of increase in SHR is greater by 4th wk and 10th wk taurine content in SHR is significantly higher than NWR. This higher level is maintained up to 24 wks.

Although the concentration of taurine is significantly higher in SHR, it is difficult to explain the reason for this increase. The level of taurine can be regulated by 3 mechanisms; 1) catabolism of taurine, 2) endogenous biosynthesis or 3) uptake of taurine from circulation. Chubb and Huxtable⁽¹¹⁾ have reported an increase in

taurine content in isoproterenol-induced cardiac hypertrophy and have shown that this elevated taurine level is due to an increased influx of taurine. In formulating a possible mechanism for the regulation of taurine influx, they suggest a β -adrenergically activated cyclic AMP-mediated mechanism controlling isoproterenol induced taurine influx. Whether or not the taurine level in SHR is regulated by a β -adrenergic-cyclic AMP mechanism, cannot be answered at the moment. Since our earlier results have shown decreased cyclic AMP content in the hearts of SHR commencing at 8 wks, it is possible that taurine level in SHR is not under the strict control of β -adrenergic-cyclic AMP system.

It is interesting to note that taurine content in SHR is higher than NWR and the rate of increase parallels the increase in blood pressure. In order to understand the effect of taurine on blood pressure, Nara *et al*⁽¹⁰⁾ have supplemented taurine in the diet. They have observed that taurine supplement had no effect on blood pressure in normal rats, while it reduced the blood pressure of stroke prone-SHR to the level of SHR. The stroke-prone SHR normally have significantly higher blood pressure than the SHR, and taurine appeared to equalize blood pressure in these two

strains. However, the effect of taurine on the blood pressure of SHR was only marginal. Our results presented here seem to suggest that increased taurine content in SHR has probably no effect on the blood pressure. Further work is necessary to define the possible role of taurine in regulating blood pressure or in the development of spontaneous hypertension.

ACKNOWLEDGMENT We wish to thank the Hawaii Heart Association, Inc. for a research grant to support this project.

REFERENCES

- 1 Chazov EI, Malchikova LS, Lipina NV, Asafov GB, Smirnov VN. *Circ Res* 1974 Sep; 34-35 (Suppl 3):11
- 2 Read WO, Welty JD. *J Pharmacol Exp Ther* 1963 Mar; 139 (3):283
- 3 McBroom MJ, Welty JD. *J Mol Cell Cardiol* 1977 Oct; 9 (10):853
- 4 Huxtable R, Chubb J. *Science* 1977 Oct 28; 198 (4315):409
- 5 Huxtable R, Bressler R. *Ibid* 1974 Jun 14; 184 (4142):1187
- 6 Lombardini JB, Cooper MW. *J Lab Clin Med* 1981 Dec; 98 (6):849
- 7 Okamoto K, Aoki K. *Jpn Circ J* 1963 Mar; 27 (3):282
- 8 Anzano MA, Naewbanij JO, Lamb AJ. *Clin Chem* 1978 Feb; 24 (2):321
- 9 Moore S. *J Biol Chem* 1968 Dec 10; 243 (23):6281
- 10 Nara Y, Yamori Y, Lovenberg W. *Biochem Pharmacol* 1978; 27 (23):2689
- 11 Chubb J, Huxtable R. *Eur J Pharmacol* 1978 Apr 1; 48 (3):357