ISSN: 0975-3583,0976-2833 VOL14, ISSUE 07, 2023

ORIGINAL RESEARCH ARTICLE

Effect of Tannic Acid on Myocardial Contractility, Lipid Profile and Cardiovascular Parameters in L- NNA induced Hypertensive Wistar Rats

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Article History: **Received:** 29.06.2023 **Revised:**03.07.2023 **Accepted:** 16.07.2023

Abstract

Objective: The influence of Tannic acid on various cardiovascular parameters in experimentally induced hypertension in rats to make an animal model of hypertension by the administration of nitric oxide syn thase inhibitor N (omega)-nitro-L-arginine and in which Tannic acid was injected in Wistar rats.

Methods: A case control experimental study was done in the department of Physiology of KGMU, Luc know among 18 Wistar rats weighing 250-300g. The rats were allowed to acclimatize for 10 days before administration of L-NNA & Tannic Acid. After acclimatization, the animals were randomly assigned into three groups, comprising six rats each. General conditions, Card iovascular parameters, Lipid levels, Mycardial contractility were the parameters that were observed during the experiment.

Results: Mean PR (BPM) in the first week was 275.50, 274.33 and 277.17 in group 1, 2 and 3 respectively with statistically insignificant difference as $p>0.05$. Mean ±SD for total cholesterol (mg/dL) was 93.39±12.11 and 83.60±17.53 in control and group 3 respectively with statistically insignificant difference as $p>0.05$.

Conclusion: Summarizing, there were no statistically significant differences in most of the cardiovascular parameters before and after the administration of tannic acid in hypertensive rats induced by administration of L-NNA.

Keywords: Cardiovascular activity**,** Lipid Profile, Pulse Rate, Tannic acid

Introduction

Hypertension (HTN) is a frequent and extreme disorder which leads to approximately 40 percent incidence of coronary vascular disorders and deaths due to stroke[1] and ranks second for final stage renal disease[2]. Based on consensus recommendations in 2017 American College of Cardiology and American Heart Association (ACC / AHA), HTN has of late been redesignated as ≥130/80 mmHg blood pressure (BP) (from the older range of 140 upon 80 mmHg)[3].

HTN incidence intensifies with age and is greater in black population than Caucasians, Latinos, and Hispanic Americans who are grouped by age and sex. The variability in the incidence of HTN might be due in part to the increases in nation-wide obesity as well as to the growing portion of the senile population[3]. In addition, with a gradually increasing prevalence, hypertension (HT) is a significant health issue. It was also estimated to have impacted 972 million people worldwide, with a prevalence of 26.4% in 2000. It is expected that by 2025 it will have an incidence of 29.2% and impact 1 billion 56 million individuals[4].

A prominent risk variable for stroke, M I, heart and renal dysfunction is hypertension (HT). It is projected that HT would result in 7.1 million deaths, in early years worldwide. As per the statistics collected in 2000 by the World Health Organization and H T stands first in the world's preventable deaths[5]. Significant development has progressed in the overall understanding, diagnosis, and management of H T

N over the past several decades. However, there is still an increased chance of adverse events of cardiovascular disease (CVD) amongst cases with HTN compared to those without HTN. There are also consistent and characteristic issues to controlling HTN of race and gender related disparities. To combat side events related to the condition, it is therefore important to achieve greater regulation of HTN from a public health point of view[6].Most of the studies proved that different lifestyles; exercise and foods such as fruits, vegetables, and herbal medicines have the ability to lower blood pressure. Natural products are the thriving source for the finding of new drugs due to its chemical constituents which have long been used in Indian history also. Polyphenol-rich fruits and vegetables, as well as beverages like tea and wine, act as inhibitor agents and protect against differing cancers in human host and cardiovascular pathologies (Gulcin et al. 2010)[7]. Tannin-containing polyphenols possess biological functions such as anti - tumor, anti - viral, anti - HIV, reduction of lipid peroxidation, and plasmine production (Cosan et al. 2010)[8]. Tannic acid has significant biological functions such as anti - carcinogenic, anti - oxidant, anti - mutagenic, antimicrobial, antiallergic, anti-inflammatory and cessation of bleeding[9]. Based on cell type used and its grading, tannic acid can also be used as an antioxidant or prooxidant. The antihypertensive effect of polyphenols is also known (Rodrigo et al. 2012)[10].Therefore, in the present study in-vivo and ex-vivo model, was planned to understand the influence of Tannic acid on various cardiovascular parameters in experimentally induced hypertension in rats to make an animal model of hypertension by the administration of nitric oxide synthase inhibitor N (omega)-nitro-L-arginine and in which Tannic acid was injected in Wistar rats. In which we have further evaluated the possible mechanism for the antihypertensive effect of tannic acid.

Materials and Methodology

A case control experimental study was done in the department of Physiology of KGMU, Lucknow after taking ethical clearance. Eighteen Wistar rats weighing 250-300g were recruited for the study. The animals were procured from Indian Institute of toxicological research (IITR) Lucknow. The study was approved by the animal ethics committee of "King George's Medical University, Lucknow. Standard rat pellets (from authorized suppliers) were given to each animal for nourishment and tap water was provided as drinking water. All precautions were taken to avoid animal sufferings.
L-NNA and Tannic acid was purchased from Finar chemicals (India). All the other chemicals likely to be used in the Ex- vivo model were obtained from standard suppliers and were of analytical grade quality.
The rats were allowed to acclimatize for 10 days before administration of L-NNA & Tannic Acid. After acclimatization, the animals were randomly assigned into three groups, comprising six rats each.

1. Group I: (n= 6) Control (rats received only standard rat feed similar to other animals for the whole study period).
2. Group II: (n= 6) L-NNA in dose of 0.5g/l (added to drinking water) and Tannic acid in dose of 50 mg/kg was given for 15 days.
3. Group III: (n= 6) first L-NNA in dose of 0.5g/l was given for 15 days (added to drinking water) and then Tannic acid in dose of 50 mg/kg was given intra peritoneally for next 15 days (in-vivo model)General conditions, Card iovascular parameters, Lipid levels, Myocar dial contractility were the parameters that were observed during the experiment. These parameters (except lipid levels & myocardial contractility) of each animal were recorded at the start, 1st week, 2nd week, 3rd week and at the end of study (4th week).Myocardial contractility and lipid levels were recorded in the 4th week.Data so collected was tabulated in an excel sheet. The means and standard deviations of the measurements per group were used for statistical analysis (SPSS 22.00 for windows; SPSS inc, Chicago, USA). For each assessment point, data were statistically analyzed using one way ANOVA. Difference between two groups was determined using student t-test and the level of significance was set at $p < 0.05$.

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 07, 2023

Results

Table 1: Comparison of Pulse Rate (BPM) among the groups at different intervals

PR (BPM)	N	Minimum	Maximum	Mean	Std. Deviation	p value
Week 1						
Group 1	6	272	279	275.50	2.665	0.41
Group 2	6	260	280	274.33	7.339	
Group 3	6	272	280	277.17	2.994	
Week 2						
Group 1	6	248	280	270.33	11.553	0.02*
Group 2	6	288	380	334.67	29.358	
Group 3	6	283	321	296.50	13.019	
Week 3						
Group 1	6	250	280	270.50	10.654	<0.01*
Group 2	6	434	453	445.33	7.090	
Group 3	6	330	393	344.50	24.189	
Week 4						
Group 1	6	260	290	278.67	10.930	<0.01*
Group 2	6	290	374	314.00	31.629	
Group 3	6	424	453	441.17	10.572	

*: statistically significant

Mean PR (BPM) in the first week was 275.50, 274.33 and 277.17 in group 1, 2 and 3 respectively with statistically insignificant difference as $p>0.05$. Mean PR (BPM) at second and third week remained approximately the same in group 1, while it was increased to 334.67, 445.33 and 296.50, 344.50 in group2 and 3 respectively with statistically significant difference as $p<0.05$. After the 4th week, mean PR(BPM) was 278.67, 314 and 441.17 in group 1, 2 and 3 respectively with statistically significant difference as $p<0.05$ (table 1).

Table 2: Comparison of lipid profile between group 3 and control

Parameters	Control Group		Group 3		t test	p value
	Mean	SD	Mean	SD		
TC (mg/d L)	93.39	12.11	83.60	17.53	0.94	0.39
HDL (mg/d L)	49.04	4.92	50.91	4.53	0.77	0.48
TG (mg/d L)	62.01	1.22	59.51	2.63	1.73	0.15

Table 2, shows the comparison of lipid profile between group 3 and control. Mean± SD for total cholesterol (mg/d L) was 93.39±12.11 and 83.60±17.53 in control and group 3 respectively with statistically insignificant difference as $p>0.05$. Mean HDL (mg/ dL) was 49.04 in control group and 50.91 in group 3. Mean TG (mg/d L) was 62.01 in the control group and 59.51 in group 3. When mean HDL (mg/d L) and TG (mg/d L) was compared statistically among the control and group 3, it was found to be statistically insignificant.

Table 3: Comparison of Perf usate Pressure (mmHg), LVDP (Left Ventricular Developed Pressure) (mmHg) and Per fus ate flow between group 3 and control

Parameters	Control Group		Group 3		t test	p value
	Mean	SD	Mean	SD		
Perfu sate Pressure	128.95	2.74	75.12	0.28	51.48	<0.01*
LVDP	46.44	1.49	88.60	0.44	0.73	<0.01*
Per fusate Flow	10.19	-	10.38	-	-	-

*: statistically significant

Mean±SD for perfusate pressure was 128.95±2.74 and 75.12±0.28 in control and group 3 respectively with significant difference as $p<0.05$. Mean LVDP was 46.44 in the control group and 88.60 in group 3. When mean LVDP was compared statistically among the control and group 3, it was found to be statistically significant. Mean perfusate flow was 10.19 in control group and 10.38 in group 3.

Discussion

Tannic acid has numerous pharmacological applications. It is known that most plant-derived polyphenolic antioxidants also act as pro-oxidants under certain conditions. Tannins are widely distributed throughout the plant kingdom and tannic acid, or penta-m-digalloyl glucose, is one of the principal tannins. The term tannin is ordinarily used as a synonym for tannic acid. It is used as an additive in medicinal products for humans, including those used for treatment of burns, diarrhea and chemical antidotes in poisoning and as a local astringent[11]. It is also used as a clarifying agent in the brewing and wine industries, and as a flavoring agent in baked foods, frozen dairy desserts, candy and meat products. Tannic acid is reported to be toxic to animals if injected into the bloodstream or consumed in large amounts. It is also a potent anti-oxidant and exhibits anti-mutagenic and anti-carcinogenic activities[12].

In this study, mean PR (BPM) in the first week was 275.50, 274.33 and 277.17 in group 1, 2 and 3 respectively with no statistical significance ($p>0.05$). Mean PR (BPM) at second and third week remained approximately the same in group 1, while it was increased to 334.67, 445.33 and 296.50, 344.50 in group 2 and 3 respectively with statistically significant difference ($p<0.05$). After the 4th week, mean PR (BPM) was 278.67, 314 and 441.17 in group 1, 2 and 3 respectively with statistically significant difference $p<0.05$.

In this study, mean±SD for total cholesterol was 93.39±12.11 and 83.60±17.53 in control and group 3 respectively with statistically insignificant difference as $p>0.05$. Mean HDL (mg/dL) was 49.04 in control group and 50.91 in group 3. Mean TG (mg/dL) was 62.01 in the control group and 59.51 in group 3. When mean HDL(mg/dL) and TG(mg/dL) were compared statistically among the control and group 3, it was found to be statistically insignificant. Yumiko Nakamuraet al[13] in their study revealed that Tannic acid had no effect on the concentrations of serum lipids or on the total hepatic cholesterol concentration.

Yugarani et al[14] in 1993 studied the effects of tannic acid on serum and liver lipids of genetically hyper-chole sterolemic (RICO) and normo -cholesterolemic (RAIF) male rats. RICO and RAIF rats had a lower level of serum lipid when fed a high-fat diet supplemented with tannic acid than the high-fat diet containing no tannic acid. The low-density lipoprotein cholesterol (LDLC)/ high density lipoprotein (HDLC) ratio is also lower in RAIF and RICO rats fed a high-fat diet with tannic acid than the high-fat control diet. The lower ratio is desirable because of the lower risk in developing atherosclerosis. Tannic acid was also reported to cause favorable decreases in serum lipid parameters in spontaneous hypertensive (SHR) and normotensive Wistar Kyoto (WKY) rats.

In this study, Mean ±SD for perfusate pressure was 128.95±2.74 and 75.12±0.28 in control and group 3 respectively with significant difference ($p<0.05$). Mean LVDP was 46.44 in the control group and 88.60 in group 3. When mean LVDP was compared statistically among the control and group 3, it was found to be statistically significant. Mean perfusate flow was 10.19 in control group and 10.38 in group 3. Hence tannic acid improves cardiovascular function to some extent in rats.

Xue- wu Zhou et al[15] (2009) in their study reported that tannic acid pretreatment significantly increased MAP at 60 minutes and 150 minutes, and left ventricular systolic pressure (LVSP) at 60 minutes, and the heart rate was obviously slowed at 120 minutes, and left ventricular end diastolic pressure (LVEDP) was lowered (all $P < 0.05$). The vascular reactivity was significantly improved at 120 minutes in tannic acid pretreatment +shock group compared with shock group ($P < 0.05$). In vitro experiment proved that tannic acid pretreatment significantly slowed heart rate at 90 minutes as well as increased +dp/ dtmax at 10 minutes and 20 minutes and -dp/dtmax at 10 minutes (all $P < 0.05$).

Comparing our results with previous studies, it was observed that the impact of tannic acid on ECG as well as lipid parameters has not been fully understood. Therefore, further studies are needed in which

tannic acid is administered in vivo at different concentrations and the toxicity of which is measured multi-directionally.

Conclusion

LVDP was significantly more in group 3 as compared to the control group. Our results showed increase in blood pressure after administration of L-NNA and no protective effect of tannic acid was seen .Since tannic acid could not prevent the cardiac derangements caused by L-NNA, hence, cannot be used as a cardioprotective agent. Further Studies are needed in which tannic acid is administered in vivo at different concentrations and the toxicity of which is measured multi-directionally. Summarizing, there were no statistically significant differences in most of the cardiovascular parameters before and after the administration of tannic acid in hypertensive rats induced by administration of L-NNA.

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