

Effect Of Theophylline On Blood Pressure Of Normotensive Cats Pre-Administered With Adrenaline.

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Abstract: The effect of various volumes of theophylline (Aminophylline) (4mg/kg) on the blood pressure of normotensive cats pre-administered with adrenaline was determined. The results obtained revealed that theophylline showed a potentiating effect ($p < 0.05$) on catecholamines (adrenaline (10 μ g/ml) in elevating the systolic, diastolic and mean arterial blood pressure of the normotensive cats. Although, theophylline alone caused an increase ($p < 0.05$) in the diastolic and mean arterial blood pressure which may be due to the increase sympathetic discharge by theophylline. The antagonistic test carried out reveals the attenuating effect ($p < 0.05$) of the calcium channel blocker (nifedipine 2mg/ml) on the combination (adrenaline and theophylline). Theophylline possesses a potentiating effect on catecholamine in determining its effect on blood pressure of normotensive cats and it was inhibited by L-type calcium channel blocker (nifedipine).

Key words: Theophylline, accentuation, adrenaline, nifedipine, blood pressure.

I. Introduction

The arterial blood pressure is the lateral pressure exerted by the column of blood on the arterial wall [1]. The normal arterial blood pressure in the brachial artery for young adults at rest, in the sitting or lying position is approximately 120/80mmHg. Above this level (at about 140/90) is regarded as hypertension, while below the average level (at about 90/60) is regarded as hypotension. The actual blood pressure of an individual can be concluded by measuring it at three consecutive days. It is appreciably lower at night and is lower in women than in men [2].

Sympathetic stimulation increases both propulsion by the heart and resistance to flow (by increasing the peripheral resistance), which usually causes the pressure to increase greatly [3]. Circulating adrenaline and noradrenaline have almost the same effects on the different organs as those caused by direct sympathetic stimulation [4]. Hypertension also known as high blood pressure has been a condition of chronically elevated systemic blood pressure. However, the World Health Organization (WHO) recommended considering cases as hypertension if the systolic pressure is higher than 160mmHg or the diastolic pressure is higher than 95mmHg in adult. Cases with systolic pressure between 140-160mmHg and diastolic pressure between 90-95mmHg are considered as borderline cases [1]. Theophylline is a methylxanthine from xanthine-containing herbs such as Camellia Sinensis (Tea), Coffea Arabica (coffee beans), Cola Nitada (kola), Ilex Paraguariensis (mat), Paulina Capana (guarana) [5]. Other methylxanthines include caffeine and theobromine. Theophylline (a non-selective phosphodiesterase inhibitor) has much application commercially in Nigeria. It is used medically for the management of chronic obstructive pulmonary disease (COPD), asthma, infant apnea and as diuretic. The xanthines are infrequently used by herbalists as mild stimulants [6]. Also in combination with other beta adrenergic receptor sympathomimetics, Theophylline has been widely used in the management of respiratory diseases such as asthma and chronic obstructive pulmonary disease, this is due to the sympathomimetic effect of theophylline on the bronchial smooth muscle [7]. Theophylline has been used for the management of obstructive respiratory disorders such as Asthma and Obstructive pulmonary disease. But its cardiovascular unfavourable side effect reduces its therapeutic usage [8].

The present study was designed to test the potentiating effect of theophylline on adrenaline in the blood pressure of normotensive cats.

II. Materials And Methods

2.1 Chemicals Used

All chemicals and drugs were obtained commercially and were of analytic grade. They are; Theophylline (in different volumes), Acetylcholine (2 μ g/ml), Adrenaline (10 μ g/ml), Nifedipine (4mg/ml), Heparin solution, Normal saline solution, Thiopental sodium.

2.2 Animals

The animals chosen and used for this study were two male cats. The cats, each weighing 1.6kg and 1.3kg respectively, were brought to the laboratory from a domestic home with the consent of the owner (coupled

with the diplomatic agreement of what the cats will be used for) and were of good health. The animals were housed in standard environmental condition of temperature ($21\pm 2^{\circ}$) till the day the experiment was carried out. Mercy killing was given to the used cats at the end of the experiment.

2.3 Experimental Design

In the experiment, the same procedure was carried out on both cats. Normal saline was used for the control reading. Different volumes of adrenaline were administered prior to the administration of different volumes of theophylline intravenously. In the antagonistic study, both drugs were administered prior to the administration of nifedipine intravenously. All these were done after the animals have been anaesthetized, while heparin was used to flush each drug.

2.4 Determination of Blood Pressure Levels

The blood pressure values of the cat for normal saline (normal basal rhythm or control), and the administered with standard drugs (adrenaline) and acting agent (Theophylline) as well as results from the antagonistic studies as obtained from the microdynamometer are tabulated below. 1cm of the standard ruler was used in measuring the systolic and diastolic blood pressure which corresponds to 10mmHg of pressure change in the mercury in glass sphygmomanometer. To determine the diastolic pressure on the tracing, the value from the baseline to the lowest border of the tracing was read while the systolic pressure was read from the baseline to upper convex curve of the tracing.

2.5 Statistical Analysis

Blood pressure tracing results were analyzed using SPSS (Statistical Package for Social Sciences) and represented as Mean, Standard Error of Mean \pm (SEM) and percentage changes. The data collected were also analyzed using ANOVA while $p < 0.05$ were considered as significant [9].

III. Results

The blood pressure level of the normotensive cats after the intravenous infusion of theophylline (4mg/kg) only is shown in table 3,4 and 5. In relation to the blood pressure level caused by normal saline (control), theophylline caused a significant increase ($p < 0.05$) in the diastolic and mean arterial blood pressure.

3.1 Tables and Figures of Result

Table 1: Showing the systolic blood pressure, mean, standard error of mean and P-value of the cats for normal saline, acetylcholine and adrenaline. (All values in mmHg)

Volume(ml)	Basal blood pressure (normal saline 0.9%)	Acetylcholine (2 μ g/ml)	Adrenaline (10 μ g/ml)
0.1	63	42	63
0.2	66	40	74
0.4	67	32	85
0.8	69	27	87
1.0	66	28	84
Mean\pmSEM	66.20 \pm 0.77	33.80 \pm 3.07	78.60 \pm 4.56
P-Value		(a)	(a)

$P < 0.05$ = significant (a)

Table 2: Showing the diastolic blood pressure, mean, standard error of mean and P-value of the cat for normal saline, acetylcholine and adrenaline. (All values in mmHg)

Volume(ml)	Basal blood pressure (normal saline 0.9%)	Acetylcholine 2 μ g/ml	Adrenaline (10 μ g/ml)
0.1	40	23	43
0.2	43	20	48
0.4	44	14	46
0.8	44	11	51
1.0	43	12	47
Mean\pmSEM	42.80 \pm 0.73	16.00 \pm 2.34	47.00 \pm 1.30
P-Value		(a)	(a)

$P < 0.05$ = significant (a)

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Table3: Showing the systolic blood pressure, mean, standard error of mean and P-values of the cat for normal saline (control) and theophylline (acting agent). (All values in mmHg)

Volume(ml)	Basal blood pressure (normal saline 0.9%)	Theophylline 4mg/kg
0.1	63	65
0.2	66	71
0.4	67	72
0.8	69	68
1.0	66	68
Mean±SEM	66.20±0.97	68.80±1.24
P-Value		(ns)

ns=not significant (p>0.05)

Table4: Showing the diastolic blood pressure, mean, standard error of mean and P-value of the cat for normal saline (control) and Theophylline (acting agent). (All values in mmHg).

Volume(ml)	Basal blood pressure (normal saline 0.9%)	Theophylline (4mg/kg)
0.1	40	40
0.2	43	44
0.4	44	46
0.8	44	46
1.0	43	46
Mean±SEM	42.80±0.73	44.40±1.16
P-Value		(a)

Table5: Showing the mean arterial blood, mean, standard error of mean and drug interaction of the cat for theophylline and adrenaline. (All values in mmHg).

Volume (ml)	Basal blood pressure (normal saline 0.9%)	Adrenaline (10µg/ml)	Theophylline (4mg/kg)	Adrenaline(10µg/ml) + Theophylline(4mg/kg)
0.1	47	50	52	56
0.2	51	56	55	56
0.4	51	59	57	62
0.8	52	63	56	63
1.0	51	59	55	62
Mean+SEM	50.40±0.87	57.40±2.16	55.00±0.84	59.80±1.56
		(a)	(a)	(a)

Table6: Showing the drug interaction and percentage changes. (All values in mmHg)

Drugs + Acting agent	Adrenaline 0.4ml (10µg/ml) + Theophylline 0.4ml (4mg/kg)			Adrenaline 0.4ml (10µg/ml) + Theophylline 0.4ml (4mg/kg) + Nifedipine 0.2ml (4mg/kg)	
	Blood pressure parameter	Basal blood pressure	Adrenaline + Theophylline	Percentage Change (%)	Adrenaline + Theophylline + Nifedipine
SBP	67	78	14.1	57	26.92
DBP	44	54	18.51	36	33.33
PP	23	24	4.16	11	54.16
MABP	52	62	16.13	43	30.64

Fig. 1 showing the systolic and diastolic blood pressure produced after administration of normal saline, adrenaline and theophylline

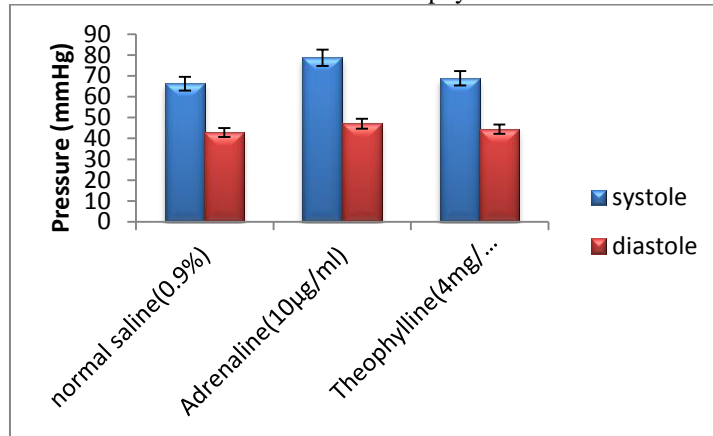


Fig. 2 showing the mean arterial blood pressure and pulse pressure produced after administration of normal saline, adrenaline and theophylline

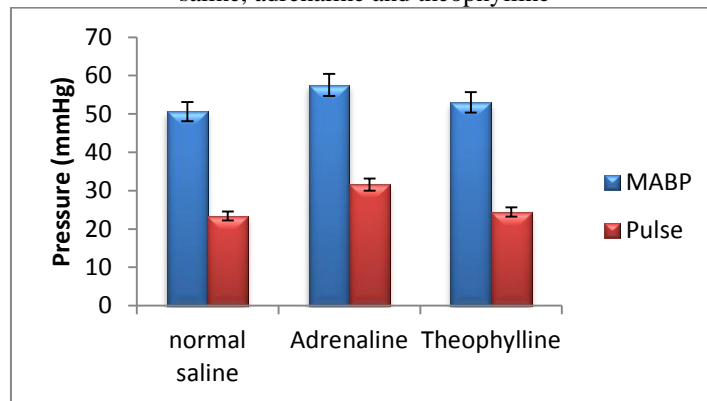


Fig. 3 showing the systolic blood pressure, diastolic blood pressure, pulse pressure and mabp produced by the administration of theophylline and theophylline + adrenaline

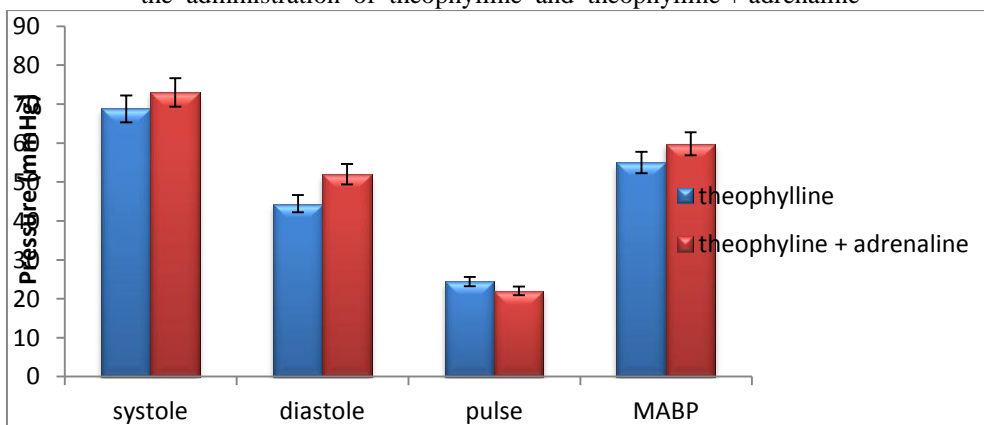
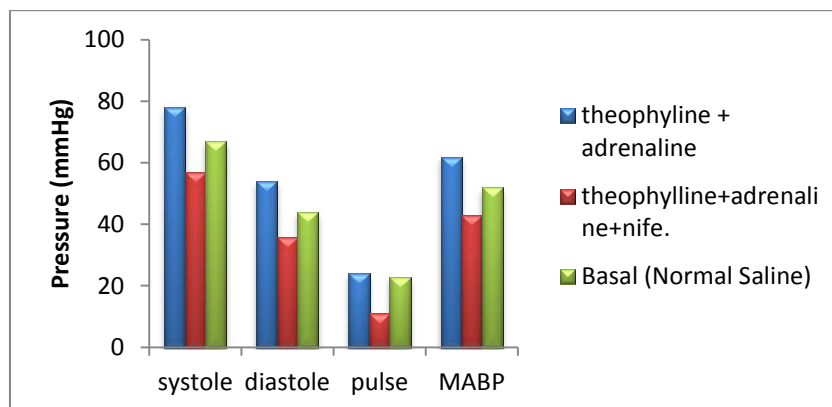


Fig. 4 showing drug antagonistic studies (theophylline and adrenaline + nifedipine)



IV. Discussion

The increased diastolic blood pressure may be due to increased muscle sympathetic nerve activity caused by theophylline which is in accordance with the findings of [3] and [10]. The increased diastolic blood pressure can no doubt alter the mean arterial blood pressure by causing an increase to it. Other studies postulated; Theophylline produced a 7% increase in mean arterial blood which was not attenuated by beta blocker (propranolol) [11]. Similarly, the observed significant increase in Mean arterial blood pressure of the normotensive cats, and the significant increase in systolic blood pressure might be due to the phosphodiesterase inhibitory effect of theophylline [12]. Also, the observation that nifedipine significantly reduced all the blood pressure parameters, such as; the systolic blood pressure (27%), diastolic blood pressure (33%) and mean arterial blood pressure (31%), is in line with the fact that Nifedipine (L-type calcium channel blocker) reduces the intracellular concentration of depolarizing calcium ion [13].

V. Conclusion

In conclusion, the present study suggests therefore, that theophylline should be co-administered with a L-type calcium channel blocker in order to attenuate its unfavourable cardiovascular side effect. However, further investigation and elucidation should be carried out on isolated perfused heart.

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