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Anti-Arrhythmic Effect of Amiodarone Against Salbutamol and Aminophylline

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Abstract

Tachycardia refers to an abnormally fast resting heart rate. The higher-than-normal heartbeat means there is an increase in demand for oxygen by the myocardium (heart muscle) - if this persists it can lead to myocardial infarction. There are many causes to tachycardia, and one of them is the using of ant- asthmatic drugs like salbutamol and aminophylline which are well defined to cause tachycardia. This study Used the amiodaron to overcome tachycardia that associated with use of salbutamol and aminophylline. A group of 18 New Zealand rabbits were subdivided into 3 groups; first group (G1) was control, second group (G2) was salbutamol group, and the third group (G3) was aminophylline group. G2 and G3 received salbutamol and aminophylline respectively for one day, and then administered salbutamol plus amiodaron and aminophylline plus amiodaron respectively at another day, all the drugs were administered intravenously at dose (1mg\kg). The parameters are heart rate, respiratory rate and arterial oxygen tension which were measured in each group and after 15,30,60,90,120 minutes of administration. The results shows that when salbutamol and aminophylline used alone they caused increasing in heart rate and there was a highly significant difference ($P<0.01$) than normal. While the mixing of amiodarone with them, the heart rate was near to normal and there was non significant difference ($P>0.05$).

Keywords: Tachycardia; Salbutamol; Aminophylline; and Amiodarone.

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1. Introduction

The arrhythmia especially tachycardia considered a dangerous seriously when it be continuous. Tachycardia refers to an abnormally fast resting heart rate [1]. Tachycardia can be dangerous; depending on how hard the heart has to work. When the heart beats too rapidly, it pumps less efficiently and blood flow to the rest of the body, including the heart itself is reduced. The higher-than-normal heartbeat means there is an increase in demand for oxygen by the myocardium (heart muscle) - if this persists it can lead to myocardial infarction (heart attack), caused by the dying off of oxygen-starved myocardial cells [1,2]. In addition to that the most important consideration of tachycardia it is associated or followed with tachypnea, and because of the less efficiently blood flow to the rest of the body resulted by tachycardia, and because of the tachypnea; the arterial oxygen tension (PaO₂) will be lower than the normal [1,2,3].

The experiments have demonstrated that beta agonists (like salbutamol) cause the tachycardia and causes a decreasing of arterial oxygen tension (PaO₂) after administration if ventilation/perfusion ratios in the lung worsen due to the tachycardia [4,5,6,7,8].

The methylxanthines (like aminophylline) have direct positive chronotropic and inotropic effects on the heart, which results in tachycardia, which is in turn, caused increase in demand for oxygen by the myocardium and when it persists it can lead to myocardial infarction (heart attack) [5,6,7,9]. So, serious problems are results from the using of these agents especially when used for persistently [8,9].

Amiodarone is considered a widest anti arrhythmic agent and the most powerful antiarrhythmic drug available for the treatment and prevention of both atrial and ventricular arrhythmias. Amiodarone selected to overcome and protect against the unwanted effects of salbutamol and aminophylline [10,11,12].

1.1 Aim of the study

To investigate the counteracting effect of amiodarone when used in combination with salbutamol and aminophylline, and control the tachycardia.

Use of these drugs from the same source and at the same dose and same route of administration is to evaluate the most action on the same target. To control the tachypnea and decreasing of arterial oxygen tension (PaO₂) that associated with the use of salbutamol and aminophylline.

2. Materials and methods

A group of eighteen New Zealand rabbits were subdivided into 3 equal groups; first group (G1) was considered as control, second group (G2) was salbutamol group, and the third group (G3) was aminophylline group.

G1 was received the distilled water.

G2 and G3 were received distilled water firstly, and then treated with salbutamol (Bayer Co.-Germany) and aminophylline (Bayer Co.-Germany) (1mg/kg) respectively, at the next day and after ensuring that the animals regain normal, they were treated with a combination of salbutamol plus amiodaron (Bayer Co.-Germany), and aminophylline plus amiodarone respectively, the drugs were be administered intravenous by the marginal ear vine (1mg/kg) [13].

2.1 Experimental measurements

The respiratory rate (RR) was measured by visually counting the chest flank movements for one minute using a stopwatch, when the animal was sitting quietly. The heart rate (HR) was obtained by counting the heartbeats for one minute using a stethoscope. The arterial oxygen tension (PaO₂) was obtained by oximeter [14].

The measurement of these parameters have been done before treatment for all experimental groups to record the normal values (zero time), and after treatment, each; 15, 30, 60, 90, 120 minutes after injection of the drugs.

2.2 Statistical analysis

The obtained data of the present study were tested with paired and unpaired t-tests, were used accordingly for assessing the effectiveness of employed therapy in the same group, and between any tow groups. The differences were accepted as significant if the calculated value for (t) was equal or greater than its tabulated value at (0.05) level of (P) (i.e. $0.01 < P \leq 0.05$) and highly significant if ($P \leq 0.01$) [15].

3. Results

Effect on the heart rate: Amiodarone prevented the heart rate to increase in G2 when combined with salbutamol, and caused non significant increase ($P > 0.05$) in heart rate when compared to the control one , and the heart rate was 224 ± 0.04 beat\min, and the normal heart rate was 218 ± 0.01 beat\min, of the same group.

While the treatment with salbutamol only caused a highly significant increased ($P < 0.01$) the heart rate (293 ± 0.03) beat\min, comparing to the heart rate of control group, figure (1).

Amiodarone was also prevented the heart rate to increase in G3 when combined with aminophylline, and caused non significant increase ($P > 0.05$) in heart rate when compared with the heart rate of control group, and the heart rate was 223 ± 0.03 beat\min after treatment with combination of salbutamol plus amiodarone, while the heart rate of control group was 218 ± 0.05 beat\min.

While the treatment with aminophylline only the heart rate was 285 ± 0.05 beat\min, and there was a highly significant increase ($P < 0.01$) comparing to the heart rate of control group, figure (2).

The respiratory rate (RR.) and arterial oxygen tension (PO₂), were differed from the corresponding normal values when salbutamol and aminophylline administered only, and there was a highly significant ($P < 0.01$)

increase in RR., and a highly significant ($P < 0.01$) decrease in (PO₂), in each of salbutamol and aminophylline groups (G2 and G3), table (1) and table (2).

While the combination of amiodarone with salbutamol and with aminophylline; there was non significant ($P > 0.05$) increase in RR., and non significant decrease (PO₂), when compared to the corresponding values in the control group, table (1) and table (2).

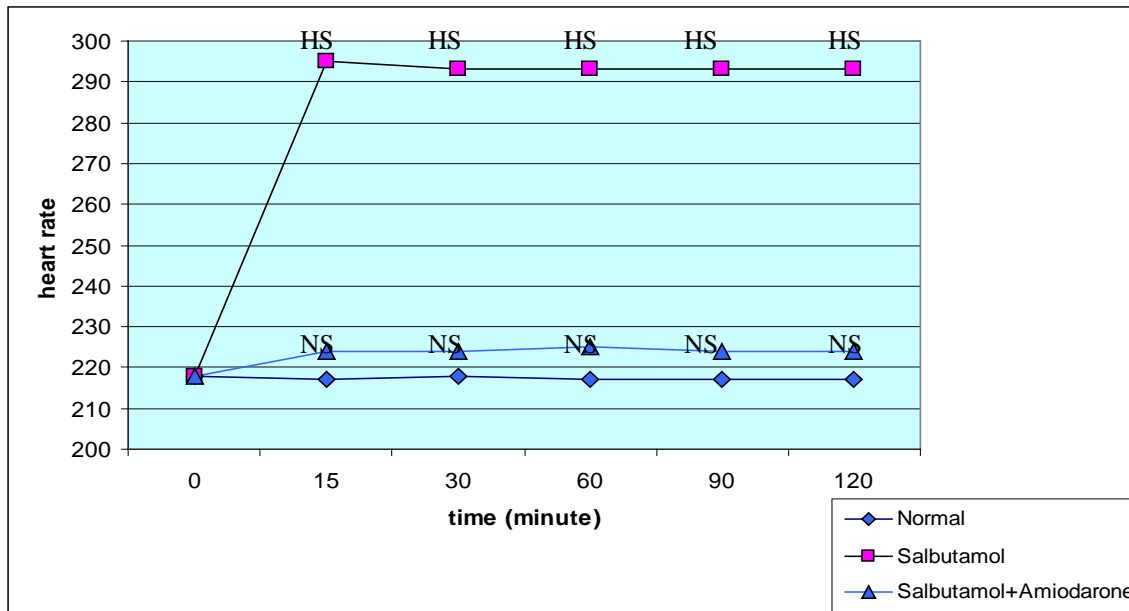


Figure (1). Counteracting effect of amiodarone (IV, 1mg/kg) on tachycardia caused by salbutamol (IV, 1mg/kg). HS=highly significant difference comparing to the normal group ($P < 0.01$). NS=non significant difference comparing to the normal group ($P > 0.05$).

Table (1). The respiratory rate and arterial oxygen tension (PO₂), in salbutamol, salbutamol plus amiodarone 1mg/kg, IV treated group, compared to the corresponding normal values.

Time\min.	Normal (control)		Salbutamol		Salbutamol + Amiodarone	
	Resp. rate	Po ₂	Resp. rate	PO ₂	Resp. rate	PO ₂
15	112±0.02	95±0.03	126±0.04 S	87±0.01 HS	119±0.02 NS	93±0.01 NS
30	112±0.02	95±0.04	131±0.03 HS	80±0.02 HS	119±0.01 NS	93±0.04 NS
60	113±0.01	95±0.01	131±0.06 HS	80±0.06 HS	118±0.02 NS	93±0.04 NS
90	113±0.02	95±0.07	133±0.03 HS	82±0.04 HS	118±0.04 NS	94±0.02 NS
120	113±0.01	95±0.05	131±0.05 HS	82±0.02 HS	118±0.03 NS	93±0.05 NS

S= significant difference comparing to the normal group ($P < 0.05$).

HS= HS=highly significant difference comparing to the normal group ($P < 0.01$).

NS= non significant difference comparing to the normal group ($P > 0.05$).

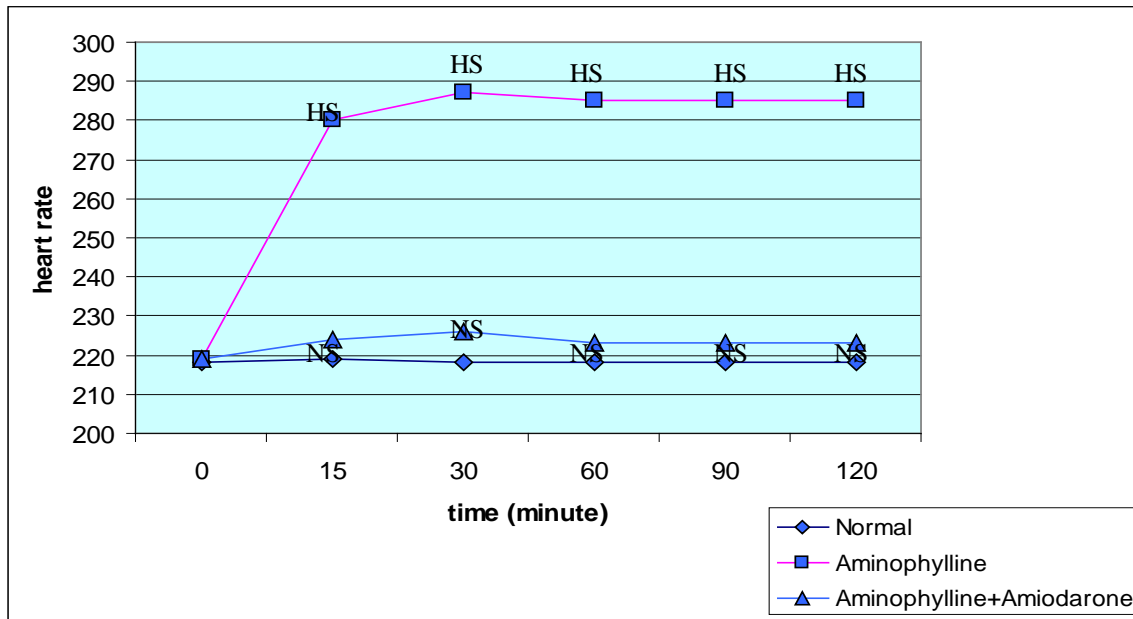


Figure (2). Counteracting effect of amiodarone (IV, 1mg/kg) on tachycardia caused by aminophylline (IV, 1mg/kg).

HS=highly significant difference comparing to the normal group ($P<0.01$).

NS=non significant difference comparing to the normal group ($P>0.05$).

Table (2). The respiratory rate and arterial oxygen tension (PO₂), in aminophylline aminophylline plus amiodarone 1mg/kg, IV treated group, compared to the corresponding normal values.

Time\min.	Normal (control)		Aminophylline		aminophylline +Amiodarone	
	Resp. rate	Po ₂	Resp. rate	PO ₂	Resp. rate	PO ₂
15	112±0.02	95±0.03	125±0.02 S	86±0.03 HS	115±0.01 NS	92±0.05 NS
30	112±0.02	95±0.04	125±0.02 S	83±0.01 HS	113±0.03 NS	92±0.04 NS
60	113±0.01	95±0.01	128±0.04 HS	80±0.03 HS	115±0.03 NS	93±0.04 NS
90	113±0.02	95±0.07	137±0.02 HS	80±0.05 HS	115±0.02 NS	95±0.03 NS
120	113±0.01	95±0.05	137±0.04 HS	80±0.05 HS	115±0.03 NS	95±0.04 NS

S= significant difference comparing to the normal group ($P<0.05$).

HS= HS=highly significant difference comparing to the normal group ($P<0.01$).

NS= non significant difference comparing to the normal group ($P>0.05$).

4. Discussion

All results of the present study were demonstrated that the combination of amiodarone plus salbutamol or aminophylline, its of an important preventing effect to avoid the increasing in the heart rate firstly, irregular respiration and decreasing of arterial oxygen tension secondly, from this point of review to remember that not the use of salbutamol or aminophylline to produce bronchodilation is enough, but must to realize the real irregularity in heart rate and respiration and how to control on them, considered the most important [2,7,8,9,16,17].

The reason of using the drugs in present study at the same dose and same route of administration is to detect the difference in the effect by the drug itself [7].

In salbutamol group and when salbutamol used alone at the second day; it caused a highly significant ($P < 0.01$) increase in the heart rate (a real tachycardia) and its persisted for many hours, and in the same time respiratory rate was increased and the PO₂ was decreased and there was a highly significant difference ($P < 0.01$) in comparing to the normal. While at the third day, and when amiodarone used with salbutamol, the heart rate and respiratory rate were not increased and the PO₂ not decreased and were near to normal and there was non significant difference ($P > 0.05$).

In aminophylline group, the same effect to amiodarone was observed when used at the third day to prevent the unwanted effects of aminophylline [16,17].

From the obtained results, its clear that used of amiodarone as ant arrhythmic agent was of protective effect to the heart from the accelerating rate caused by salbutamol and aminophylline which are the most known and most used drugs for asthma, and which are increase the chance of myocardial infarction especially when used repeatedly and for asthmatic patients, and also who are basically suffering from low PO₂, and irregular respiration [12,16,17,18].

The stimulation of B₂ receptor by salbutamol, results in activation of adenylyl cyclase and increased conversion of adenosine triphosphate (ATP) to cAMP. Activation of the cyclase enzyme is mediated by the stimulatory coupling protein G_s. cAMP is the major second messenger of β -receptor activation. In the heart, β -receptor activation increases the influx of calcium across the cell membrane and its sequestration inside the myocardial cell.[1,4].

While aminophylline administration, was associated with inhibition of phosphodiesterase by aminophylline (as methylxanthines) and increases in cAMP which result in increased influx of calcium, and this lead to tachycardia.[1,7].

Amiodarone markedly prolongs the action potential duration, amiodarone also significantly blocks inactivated sodium channels. Its action potential prolonging action reinforces this effect. Amiodarone also has adrenergic and calcium channel blocking actions. Consequences of these actions include slowing of the heart rate and atrioventricular node conduction. The broad spectrum of actions may account for its relatively high efficacy. So

the concomitant use of amiodarone with salbutamol, and with aminophylline made to overcome the arrhythmia that resulted from salbutamol, and aminophylline when they used alone [3,11,12].

5. Conclusions

The use of amiodarone was effective to prevent and control tachycardia and tachypnea and also prevent the arterial PO₂ to decrease due to salbutamol and aminophylline. It can be use the amiodarone at a small doses to overcome the unwanted effects of ant asthmatic drugs especially when decide to use them persistently.

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