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### **Cardiopulmonary Effects of Detomidine at Different Dose Levels In Cattle**

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#### **ABSTRACT:**

The study was carried out to evaluate the dose dependent action of detomidine on cardiovascular and pulmonary parameters in cattle. The dosage of detomidine given to cattle in this study were 10, 20 and 30  $\mu\text{g}/\text{kg}$  body weight intravenously. 18 cattle were randomly divided into 3 groups of 6 animals each. The parameters studied were heart rate, mean arterial pressure, central venous pressure, electrocardiogram, respiratory rate, the blood gas parameters like  $\text{PaO}_2$ ,  $\text{PaCO}_2$ ,  $\text{HCO}_3^-$  and pH values. The cardiovascular functions and pulmonary functions were studied before sedation, at peak sedation, after recovery and after taking feed and water. Heart rate reduced significantly and mean arterial pressure and central venous pressure showed increasing trend after detomidine administration. The electro cardiographic studies revealed no significant changes in P wave amplitude and duration, PR interval and nature of ST segment. The QT interval at peak sedation increased significantly revealing reduced heart rate. Respiratory rate increased after detomidine administration. Blood gas study revealed significant decrease in  $\text{PaO}_2$  and a non significant increase in  $\text{PaCO}_2$  and  $\text{HCO}_3^-$  levels after detomidine administration. All the cardiovascular and pulmonary parameters showed dose dependent variation in the values throughout the study. All the parameters returned to the base values after recovery. The dose rate of 20 and 30  $\mu\text{g}/\text{kg}$  body weight produced adequate sedation. But the 30  $\mu\text{g}/\text{kg}$  body weight, produced more depression of cardiopulmonary functions compared with 20  $\mu\text{g}/\text{kg}$  body weight. So, detomidine at the rate of 20  $\mu\text{g}/\text{kg}$  body weight can be used as an ideal dose of detomidine for sedation in cattle.

**KEY WORDS:** Detomidine, Cardiopulmonary effects, Cattle.

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## INTRODUCTION:

Primarily, local or regional analgesia is used in cattle for minor surgical procedures. Still sedation in cattle is often required for certain diagnostic procedures like endoscopy, laparoscopy, radiography etc., minor surgical procedures like opening an abscess in a vicious bullock, etc. Xylazine, the most common  $\alpha_2$  - adrenergic agonist used in cattle as a sedative analgesic<sup>1</sup>. Xylazine as a sedative at the dose rate of 0.1 mg - 0.5 mg/kg body weight was reported by several authors to induce AV block (transient hypertension) and regurgitation due to the relaxation of gastro-oesophageal sphincter, ruminal tympany<sup>2</sup> due to its  $\alpha_2$  - adrenergic agonistic action and abortion due to the oxytocic effect<sup>3</sup>.

Detomidine, an  $\alpha_2$  - adrenergic agonist produces dose dependent sedation with a wide margin of safety (5 to 300  $\mu\text{g}/\text{kg}$  body weight)<sup>4</sup>. It does not cause abortion and regurgitation even in unfasted animals<sup>5</sup>. Xylazine produced cardiopulmonary depression<sup>6,7,8,9</sup> whereas detomidine produced bradycardia, increase in mean arterial pressure and respiratory rate immediately after administration<sup>10,11,12</sup>.

Since the present study was carried out to evaluate different dose rates of detomidine for its cardiopulmonary effects and to find out the ideal sedative dose rate with minimal cardiopulmonary depression.

## MATERIALS AND METHODS:

18 cattle were randomly divided into 3 groups of 6 animals each. The dosage of detomidine given to cattle in this study were intravenous injection of 10, 20 and 30  $\mu\text{g}/\text{kg}$  body weight in group I, II and III respectively. The parameters studied were heart rate, mean arterial pressure, central venous pressure, electrocardiogram, respiratory rate, the blood gas parameters like  $\text{PaO}_2$ ,  $\text{PaCO}_2$ ,  $\text{HCO}_3^-$  and pH values. Heart rates were recorded by direct auscultation, mean arterial pressure by cannulation of carotid artery and the pressure changes were recorded using vital signs monitor, central venous pressure in cm of  $\text{H}_2\text{O}$  by percutaneous jugular vein puncturing technique using an indwelling catheter and the pressure changes were recorded using vital signs monitor and the electrocardiographic recordings were taken with lead II. The parameters were studied before sedation, at peak sedation, after recovery and after taking feed and water.

## RESULTS AND DISCUSSION:

The results of the cardiovascular and pulmonary function studies were give in table 1 and table 2 respectively. The mean heart rate decreased significantly following detomidine administration in a dose dependent manner in all the groups. The decrease in heart rate due to the administration of  $\alpha_2$  - adrenergic agonists was attributed to the effect of drug on carotid sinus baroreceptor reflex<sup>13</sup>, withdrawal of sympathetic tone<sup>11</sup>, increase in parasympathetic tone<sup>11</sup>, direct

depressive action on cardiac pace maker and conduction tissue and reduction in myocardial inotropic effect<sup>14</sup>. More persistent duration of bradycardia with detomidine particularly at high doses<sup>15</sup>. The dose dependent bradycardia of detomidine to the direct negative chronotropic effect on the heart<sup>16</sup>. After recovery, the heart rate still remained less than the base value and the mean values after taking feed and water were comparable with base values. The findings concurred with<sup>8,12,17,18,19,20</sup>.

Increased mean arterial pressure following detomidine sedation seen, as compared to the popularly used xylazine - an  $\alpha_2$  adrenergic agonist and other sedative tranquillizers like phenothiazine derivatives<sup>21</sup>. Xylazine as an  $\alpha_2$  -adrenergic agonist decreased the mean arterial pressure due to decreased myocardial contractility and cardiac output<sup>22</sup>, sympatholytic action, inhibition of catecholamine release and blocking of central and peripheral  $\alpha$  – adrenoreceptors<sup>23</sup>. The phenothiazine derivatives induced hypotensive effect as a result of peripheral  $\alpha$  receptor adrenergic blockade and inhibition of centrally mediated reflexes<sup>24</sup> and reduction in vascular resistance<sup>25</sup>.

**Table 1. Mean  $\pm$  SE values of Heart rate, Mean arterial pressure and Central venous pressure**

Parameters	Group	Before sedation	At peak sedation	After total recovery	After taking feed and water
Heart rate / min	I	60.17 <sup>b</sup> $\pm$ 1.65	50.25 <sup>a</sup> $\pm$ 1.43	58.49 <sup>b</sup> $\pm$ 1.83	60.82 <sup>b</sup> $\pm$ 1.32
	II	56.55 <sup>b</sup> $\pm$ 1.28	44.61 <sup>a</sup> $\pm$ 1.12	54.03 <sup>b</sup> $\pm$ 1.86	54.95 <sup>b</sup> $\pm$ 1.46
	III	62.74 <sup>b</sup> $\pm$ 2.25	48.65 <sup>a</sup> $\pm$ 1.28	60.29 <sup>b</sup> $\pm$ 1.32	64.85 <sup>b</sup> $\pm$ 1.16
Mean arterial pressure (mm of Hg)	I	108.23 <sup>a</sup> $\pm$ 2.46	116.69 <sup>b</sup> $\pm$ 1.73	112.07 <sup>b</sup> $\pm$ 3.25	110.47 <sup>a</sup> $\pm$ 3.18
	II	106.47 <sup>a</sup> $\pm$ 2.16	115.92 <sup>b</sup> $\pm$ 2.91	110.38 <sup>a</sup> $\pm$ 1.36	108.01 <sup>a</sup> $\pm$ 2.60
	III	99.80 <sup>a</sup> $\pm$ 2.91	114.37 <sup>b</sup> $\pm$ 3.20	112.60 <sup>b</sup> $\pm$ 1.36	100.84 <sup>a</sup> $\pm$ 4.31
Central venous pressure (cm of H <sub>2</sub> O)	I	5.10 <sup>a</sup> $\pm$ 0.73	8.50 <sup>c</sup> $\pm$ 0.21	6.20 <sup>a</sup> $\pm$ 0.36	5.30 <sup>a</sup> $\pm$ 0.32
	II	6.50 <sup>a</sup> $\pm$ 0.27	8.30 <sup>b</sup> $\pm$ 0.20	7.40 <sup>b</sup> $\pm$ 0.36	7.00 <sup>b</sup> $\pm$ 0.29
	III	7.20 <sup>b</sup> $\pm$ 0.31	10.50 <sup>d</sup> $\pm$ 0.51	8.80 <sup>c</sup> $\pm$ 0.34	7.60 <sup>b</sup> $\pm$ 0.36

Means bearing different superscripts in a parameter differ significantly (P<0.01)

Among the two  $\alpha_2$  adrenergic agonists namely xylazine and detomidine, xylazine caused significant reduction in cardiac output and it persisted longer, when compared with detomidine. Hence the increase in the mean arterial pressure following detomidine administration could be attributed to the increased systemic vascular resistance<sup>21,26</sup>, maintenance of cardiac output<sup>15</sup> due to its effect on cardiac afterload<sup>27</sup>. The findings was in concurrence with<sup>20, 28</sup>.

The mean central venous pressure increased significantly at the dose rates of 10,20 and 30  $\mu$ g/kg body weight of detomidine at the peak sedation. Detomidine as an  $\alpha_2$  adrenergic agonist increased the peripheral vascular resistance<sup>21</sup> with reduction in heart rate<sup>16,29</sup> and produced no change in the cardiac output due to its effect on afterload<sup>27</sup>. The findings was in concurrence with<sup>17</sup>.

Table 2. Mean  $\pm$  SE values of Respiratory rate and Blood gas parameters

Parameters	Group	Before sedation	At peak sedation	After total recovery	After taking feed and water
Respiratory rate / min	I	17.56 <sup>a</sup> $\pm$ 0.63	19.24 <sup>c</sup> $\pm$ 0.48	18.43 <sup>b</sup> $\pm$ 0.57	17.74 <sup>a</sup> $\pm$ 0.55
	II	18.35 <sup>b</sup> $\pm$ 0.37	21.14 <sup>de</sup> $\pm$ 0.61	20.26 <sup>d</sup> $\pm$ 0.59	18.51 <sup>b</sup> $\pm$ 0.76
	III	20.63 <sup>d</sup> $\pm$ 0.39	23.91 <sup>f</sup> $\pm$ 0.66	21.79 <sup>e</sup> $\pm$ 0.61	20.36 <sup>d</sup> $\pm$ 0.43
PaO <sub>2</sub> (mm of Hg)	I	90.26 <sup>b</sup> $\pm$ 2.42	80.72 <sup>a</sup> $\pm$ 3.17	89.94 <sup>b</sup> $\pm$ 2.55	90.27 <sup>b</sup> $\pm$ 2.45
	II	93.15 <sup>b</sup> $\pm$ 2.78	81.26 <sup>a</sup> $\pm$ 3.73	90.61 <sup>b</sup> $\pm$ 2.61	92.73 <sup>b</sup> $\pm$ 1.88
	III	91.72 <sup>b</sup> $\pm$ 2.72	78.84 <sup>a</sup> $\pm$ 1.07	90.25 <sup>b</sup> $\pm$ 2.39	91.68 <sup>b</sup> $\pm$ 1.85
PaCO <sub>2</sub> (mm of Hg)	I	32.38 $\pm$ 4.85	33.16 $\pm$ 4.67	32.65 $\pm$ 4.67	32.23 $\pm$ 5.02
	II	34.12 $\pm$ 4.71	35.27 $\pm$ 4.96	34.51 $\pm$ 4.72	34.22 $\pm$ 4.71
	III	32.86 $\pm$ 5.03	40.84 $\pm$ 5.34	35.19 $\pm$ 5.09	32.67 $\pm$ 4.68
HCO <sub>3</sub> <sup>-</sup> (mEq/L)	I	22.54 $\pm$ 1.37	23.01 $\pm$ 0.97	22.98 $\pm$ 1.44	22.55 $\pm$ 1.63
	II	23.28 $\pm$ 1.36	23.81 $\pm$ 1.26	23.73 $\pm$ 1.40	23.59 $\pm$ 1.30
	III	24.07 $\pm$ 1.35	24.86 $\pm$ 1.51	24.62 $\pm$ 1.73	24.28 $\pm$ 1.39
pH	I	7.390 $\pm$ 0.03	7.360 $\pm$ 0.05	7.380 $\pm$ 0.05	7.396 $\pm$ 0.06
	II	7.378 $\pm$ 0.04	7.343 $\pm$ 0.05	7.362 $\pm$ 0.05	7.375 $\pm$ 0.05
	III	7.362 $\pm$ 0.05	7.303 $\pm$ 0.04	7.350 $\pm$ 0.05	7.369 $\pm$ 0.05

Means bearing different superscripts in a parameter differ significantly (P<0.01)

The electro cardio graphic studies revealed no significant changes in P wave amplitude and duration, PR interval and nature of ST segment. The QT interval at peak sedation increased significantly revealing reduced heart rate. The QT interval was inversely related to the heart rate<sup>18,30</sup>. Decrease in heart rate during detomidine sedation was directly proportional to the increasing dose<sup>15</sup> due to the temporal relationship that supported the involvement of bar receptor reflex<sup>16</sup> as evidenced by increasing PaCO<sub>2</sub> tension in the present study.

Following administration of detomidine, the mean respiratory rate increased in all the groups. The results were in line with<sup>4,10</sup>. Elevated respiratory rate during high doses of detomidine<sup>21</sup> which could be attributed to the stimulation of chemoreceptor's due to elevated carbondioxide tension<sup>11,12</sup>.

The blood gas studies revealed decreased PaO<sub>2</sub> level during sedation. The mean PaCO<sub>2</sub> level did not show any significant increase apart from a slight elevation during sedation. The mean HCO<sub>3</sub><sup>-</sup> level also remained unaltered statistically.

Xylazine an  $\alpha_2$  - adrenergic agonist induced elevated PaCO<sub>2</sub> level with corresponding decrease in PaO<sub>2</sub> level and compensatory bicarbonate level due to the reduced cardiac output<sup>22</sup> and hypotension<sup>14,31</sup>. The compensatory HCO<sub>3</sub><sup>-</sup> level during xylazine was attributed to the increased absorption of HCO<sub>3</sub><sup>-</sup> from the intestine because, xylazine reduced gastro intestinal motility. Detomidine maintained the PaCO<sub>2</sub> level without significant alterations in the HCO<sub>3</sub><sup>-</sup> level due to the maintenance of cardiac output<sup>11,15,21</sup> and maintenance of arterial blood pressure due to increase in the systemic vascular resistance<sup>21,26</sup>.

## CONCLUSIONS:

All the cardiovascular and pulmonary parameters showed dose dependent variation in the values throughout the study. All the parameters returned to the before sedation levels after recovery. The dose rate of 20 and 30 µg/kg body weight produced adequate sedation. But the 30 µg/kg body weight, produced more depression of cardiopulmonary functions compared with 20 µg/kg body weight. So, detomidine at the rate of 20 µg/kg body weight can be used as an ideal dose of detomidine for sedation in cattle with respect to cardiovascular and pulmonary parameters.

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