Physiologic and biochemical effects of subarachnoidally administered xylazine and medetomidine in goats

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Abstract

Clinicophysiological, haematological and biochemical effects of xylazine (0.05 mg kg\(^{-1}\)) and medetomidine (0.01 mg kg\(^{-1}\)) were studied in nine adult goats after lumbosacral subarachnoid administration. The onset of analgesia by xylazine and medetomidine was observed in 9.11±1.07 and 8.66±2.37 min (mean±S.E.), respectively. Both \(\alpha_2\)-agonists produced moderate analgesia of hind quarter, perineum and flank, mild ataxia and sedation. The duration of analgesia after xylazine administration was 134.44±8.87 min and that after medetomidine was 158.33±9.96 min (mean±S.E.). Xylazine and medetomidine induced significant \((p<0.05)\) decrease in heart rate, respiratory rate and hypothermia. Haemoglobin (Hb), packed cell volume (PCV) and total leukocyte count (TLC) decreased significantly. Changes in the physiological and haematological parameters were transient in nature. Xylazine and medetomidine produced a significant \((p<0.05)\) increase in creatinine and glucose levels. However, these parameters fluctuated within normal range and started to recover within 120 min. However, serum urea nitrogen (SUN), serum chloride, sodium and potassium did not show any significant change. The effects produced by xylazine and medetomidine were however, comparable at these dose levels. The study indicates that xylazine at 0.05 mg kg\(^{-1}\) and medetomidine at 0.01 mg kg\(^{-1}\) did not induce any serious alteration in the physiological, haematological and biochemical parameters and can be safely used in inducing hind quarter, flank and perineal analgesia in goats. © 2000 Elsevier Science B.V. All rights reserved.

Keywords: Spinal anaesthesia; Goats; Xylazine; Medetomidine

1. Introduction

Xylazine and medetomidine are two, \(\alpha_2\)-adrenergic receptor agonists. The \(\alpha_2/\alpha_1\)-receptor binding selectivity indicates that medetomidine is more selective and specific \(\alpha_2\)-adrenergic receptor agonist than xylazine (Virtanen, 1989). Among all domestic animals ruminants are the most sensitive to xylazine. In recent years xylazine has been used epidurally in many species of animals. Although 2% lidocaine hydrochloride is the most commonly used drug for this purpose, studies have indicated that xylazine induces analgesia of the perineum when administered epidurally in horses (LeBlanc et al., 1988); ponies (Fikes et al., 1989) and cattle (Jean et al., 1990). Those studies indicate that xylazine provided analgesia that was longer in onset and duration than did the more conventional epidural administration of lidocaine. In goats very little information about the analgesic, cardiovascular and respiratory effects of subarachnoidally or epidurally administered xylazine is available. Previous studies (Aithal et al., 1996) indicated
that xylazine at 0.05 mg kg⁻¹ administered into the lumbosacral epidural space induced safe hind quarter analgesia in goats. Medetomidine being a more selective α₂-adrenoceptor agonist than xylazine has been used epidurally in cats (Duke et al., 1994a). To the authors’ knowledge, the safety of subarachnoid administration of medetomidine in goats has not been reported. In addition, reports of comparative effects of lumbosacral subarachnoidally administered xylazine and medetomidine on analgesic, cardiovascular and respiratory systems, head ptosis, position of pelvic limbs and sedation are lacking. In the present study, we determined and compared the analgesic, physiologic, haematologic and biochemical effects in response to xylazine at 0.05 mg kg⁻¹ and medetomidine at 0.01 mg kg⁻¹ each diluted to a total volume of 2 ml with 0.9% normal saline and administered into the lumbosacral subarachnoid space in healthy goats.

2. Materials and methods

Nine non-descript adult goats of either sex weighing 15–25 kg were used in this study. The animals were apparently healthy and dewormed 1 month before the start of the experiment. The animals were stall fed and had free access to feed and water. The animals were kept off feed for 24 h and water was withheld for 12 h prior to the start of the experiment. During the course of trials the ambient temperature fluctuated between 38 and 39°C. The animals were assigned randomly in two groups. Nine trials each of the two treatments (forming two groups) were carried out in these nine animals keeping a gap of 1 week between each trial using one animal twice only. Freshly prepared solutions of xylazine at 0.05 mg kg⁻¹ or medetomidine at 0.01 mg kg⁻¹ were diluted to 2 ml using 0.9% physiologic saline solution. The dose rates of xylazine and medetomidine were determined after conducting pilot trials in a few goats. In these trials it was observed that after increasing the dose rates of both α₂-agonists, from the one used in this study, the depth of analgesia remained the same in all the dose rates tested, while sedation increased. Therefore, the dose rates of xylazine (0.05 mg kg⁻¹) and medetomidine (0.01 mg kg⁻¹) were selected. The animals were restrained in standing position. The lumbosacral region was clipped, shaved and painted with povidone iodine solution. A 20 gauge, 2.5 cm long hypodermic needle was placed into the subarachnoid space at the lumbosacral intervertebral space. The needle was directed to a 60 to 75° angle to the spinal cord along the median plane and was slowly advanced until the lumbosacral subarachnoid space was reached after penetrating the interarcuate ligament and dura mater. Correct position of needle was ascertained by free flow of CSF from the needle hub. The drug was then injected.

The base line values (time=0) for physiological and clinical parameters were made before injection of drug. Blood samples were also collected at time zero before drug administration. The two treatments were evaluated and compared on the basis of clinical, physiologic, haematologic and biochemical parameters. The investigator for the subjective determination of scores for analgesia, sedation and hind limb ataxia was not blinded but was the same person during each trial throughout the period of study. Onset of analgesia was recorded at perineal region using pin prick method. Depth of analgesia was recorded from the response shown by the animal at a particular region by pin pricks. Pin pricks were made at tail, perineum, udder/scrotum, thigh, digits, flank and thorax at 5, 10, 15, 20, 30, 45, 60, 75, 90, 105 and 120 min post-injection and graded in a scale of 0–3, where 0 represents no analgesia — strong reaction to pin pricks, 1, mild analgesia — weak response to pin pricks, 2, moderate analgesia — occasional response to pin pricks, 3, strong/complete analgesia — no response to pin pricks.

Hind limb ataxia was recorded at the same intervals and was graded in a scale of 0–4, where 0 stands walking without staggering, 1, able to stand but walk with some incoordination, 2, able to stand but walks with extreme incoordination, 3, unable to stand and assumes sternal recumbency, 4, unable to stand and assumes lateral recumbency. While grading sedation the animals were observed for their ability to sit with or without support along with the position of head and eyelids. Sedation was recorded and graded in a scale of 0–3 where 0 represents standing alert, keeping the head high or normal, position of eyelids normal; 1, standing but appears tired, dropping of head and eyelids; 2, able to sit without support, dropping of head and eyelids; 3, unable to sit without support, dropping of head and eyelids. For recording the
duration of analgesia (time from loss to return of
sensation) perineal region was considered as the area
where pin prick response was recorded till zero score/return of sensation was achieved up to 120 min or even
beyond that. Physiological parameters such as heart
rate (HR), respiratory rate (RR) and rectal temperature
(RT) were also recorded at the same time intervals
after injection of the drug. Blood samples were col-
lected in clean, dry vials containing EDTA before and
at 30, 60, 120 min and 24 h after injection of drug for
estimation of haemoglobin (Hb), packed cell volume
(PCV) and total leukocyte count (TLC). Blood sam-
plees were also collected in clean, dry test tubes at the
same intervals for separation of serum to estimate
serum urea nitrogen (SUN), creatinine, glucose, chlor-
ide, sodium and potassium. Data were subjected to
paired ’t’ test for comparison of means and students ’t’
test for comparison of means of two treatments (Sne-
decor and Cochran, 1967).

3. Results

The body weight of animals were 19±3.2 kg
(mean±S.E.). Absence of response to pin pricks at
perineal region provided satisfactory indication for the
onset of analgesia. The onset of analgesia by xylazine
and medetomidine was observed in 9.11±1.07 and
8.66±2.37 min (mean±S.E.), respectively (Fig. 1).
Response to pin pricks also provided satisfactory

Fig. 1. Onset of analgesia (mean±S.E.) after subarachnoid administration of xylazine and medetomidine in goats.
Fig. 2. Hindquarter analgesia (mean±S.E.) after subarachnoid administration of xylazine and medetomidine in goats.

Fig. 3. Perineal analgesia (mean±S.E.) after subarachnoid administration of xylazine and medetomidine in goats.

Fig. 4. Flank analgesia (mean±S.E.) after subarachnoid administration of xylazine and medetomidine in goats.
Fig. 5. Ataxia (mean±S.E.) after subarachnoid administration of xylazine and medetomidine in goats.

Fig. 6. Sedation (mean±S.E.) after subarachnoid administration of xylazine and medetomidine in goats.

Fig. 7. Duration of perineal analgesia (mean±S.E.) after subarachnoid administration of xylazine and medetomidine in goats.
alert and had normal gait with absence of analgesia in the perineal region, it was considered to have recovered from the effects of the drug. Recovery time was similar to that of duration of analgesia.

Both $\alpha_2$-agonists, caused a significant ($p<0.05$) decrease in HR 5 min after subarachnoid injection of the drug. It persisted significantly ($p<0.05$) lower in subsequent intervals and the values at 75 min in xylazine group and 90 min in medetomidine group were the lowest (Fig. 8). Even at the end of observation period the values remained significantly ($p<0.05$) lower than the base values. The difference was non-significant ($p>0.05$) between the two treatment groups at any interval. Xylazine caused a significant ($p<0.05$) decrease in RR 5 min after subarachnoid administration, whereas medetomidine caused a non-significant ($p>0.05$) decrease 10 min after subarachnoid injection, in subsequent intervals. Further significant ($p<0.01$) decrease in RR was recorded in both groups and the lowest values with xylazine were recorded at 60 min and with medetomidine at 105 min (Fig. 9). Thereafter, slight improvement in RR was seen but the
values remained significantly ($p<0.01$) lower than the base values. A non-significant ($p>0.05$) decrease in RT was observed at 5 and 20 min after injection of xylazine and medetomidine, respectively. In subsequent intervals a significant ($p<0.05$) decrease was recorded with xylazine, however, a non-significant ($p>0.05$) decrease persisted with medetomidine throughout the period of observation (Fig. 10).

A non-significant ($p>0.05$) decrease in Hb values was recorded at 30 min after xylazine and medetomidine administration. Significant ($p<0.05$) decrease was recorded in subsequent intervals in both groups (Table 1). Similarly, significant ($p<0.01$) decrease in PCV was recorded in the post-injection period with both $\alpha_2$-agonists. However, at 24 h the values returned to the preadministration level in both groups. TLC also

![Fig. 10. Mean±S.E. of rectal temperature (°F) after subarachnoid administration of xylazine and medetomidine in goats. *Significantly different from the base value ($p<0.05$).](image)

Table 1

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Drug $^a$</th>
<th>Baseline</th>
<th>30 min</th>
<th>60 min</th>
<th>120 min</th>
<th>24 h</th>
</tr>
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<tbody>
<tr>
<td>Haemoglobin (Hb) (g l$^{-1}$)</td>
<td>X</td>
<td>110.00±4.49</td>
<td>107.78±4.65</td>
<td>107.33±4.00</td>
<td>107.78±3.64</td>
<td>108.89±3.61</td>
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<tr>
<td></td>
<td>M</td>
<td>109.44±3.86</td>
<td>105.00±3.33</td>
<td>101.67±3.73$^*$</td>
<td>99.44±3.27$^*$</td>
<td>106.11±3.41</td>
</tr>
<tr>
<td>Packed cell volume (PCV) (LL$^{-1}$)</td>
<td>X</td>
<td>0.29±0.01</td>
<td>0.27±0.01$^{**}$</td>
<td>0.26±0.01$^{**}$</td>
<td>0.26±0.01$^{**}$</td>
<td>0.28±0.01</td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>0.29±0.00</td>
<td>0.28±0.00$^{**}$</td>
<td>0.26±0.01$^{**}$</td>
<td>0.27±0.01$^{**}$</td>
<td>0.29±0.01</td>
</tr>
<tr>
<td>Total Leukocyte count (TLC) ($\times 10^9$ l$^{-1}$)</td>
<td>X</td>
<td>9.92±0.72</td>
<td>8.66±0.67</td>
<td>7.46±0.67$^{**}$</td>
<td>7.38±0.95$^{*}$</td>
<td>9.14±0.83</td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>10.98±0.41</td>
<td>8.54±0.43$^{**}$</td>
<td>6.73±0.56$^{**}$</td>
<td>7.21±0.79$^{**}$</td>
<td>9.11±0.73$^*$</td>
</tr>
<tr>
<td>Serum urea nitrogen (mmol l$^{-1}$)</td>
<td>X</td>
<td>7.48±0.87</td>
<td>7.68±1.27</td>
<td>7.71±1.51</td>
<td>7.46±0.68</td>
<td>7.11±1.24</td>
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<td></td>
<td>M</td>
<td>7.27±0.29</td>
<td>6.44±0.65</td>
<td>7.82±0.80</td>
<td>7.47±0.89</td>
<td>6.41±0.50</td>
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<td>Creatinine (mmol l$^{-1}$)</td>
<td>X</td>
<td>93.14±1.97</td>
<td>112.50±3.35$^{**}$</td>
<td>112.38±3.01$^{**}$</td>
<td>121.24±2.76$^{**}$</td>
<td>91.21±1.87</td>
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<tr>
<td></td>
<td>M</td>
<td>93.59±1.30</td>
<td>108.90±1.29$^{**}$</td>
<td>112.60±3.63$^{**}$</td>
<td>112.80±3.83$^{**}$</td>
<td>93.71±1.78</td>
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<td>Glucose (mmol l$^{-1}$)</td>
<td>X</td>
<td>4.84±1.50</td>
<td>8.60±1.68$^{*}$</td>
<td>6.05±1.04</td>
<td>8.98±1.59</td>
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<tr>
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<td>M</td>
<td>3.33±0.81</td>
<td>4.14±0.70</td>
<td>4.25±0.86</td>
<td>7.07±1.26$^{**}$</td>
<td>3.94±0.97</td>
</tr>
<tr>
<td>Chloride (mmol l$^{-1}$)</td>
<td>X</td>
<td>102.55±3.82</td>
<td>103.78±3.66</td>
<td>102.90±3.85</td>
<td>102.33±3.31</td>
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<tr>
<td></td>
<td>M</td>
<td>98.96±1.99</td>
<td>100.38±4.38</td>
<td>102.08±3.91</td>
<td>100.23±5.41</td>
<td>100.19±4.50</td>
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<tr>
<td>Sodium (mmol l$^{-1}$)</td>
<td>X</td>
<td>148.22±1.13</td>
<td>149.22±1.12</td>
<td>143.78±3.28</td>
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<td>M</td>
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<td>145.56±1.99</td>
<td>144.11±2.77</td>
<td>147.78±2.68</td>
<td>147.11±2.31</td>
</tr>
<tr>
<td>Potassium (mmol l$^{-1}$)</td>
<td>X</td>
<td>5.46±0.42</td>
<td>5.81±0.35</td>
<td>4.81±0.50</td>
<td>5.63±0.56</td>
<td>5.32±0.41</td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>6.01±0.33</td>
<td>5.59±0.33</td>
<td>6.19±0.37</td>
<td>5.87±0.32</td>
<td>6.24±0.44</td>
</tr>
</tbody>
</table>

$^a$ X, xylazine; M, medetomidine.

* Significantly different from base value ($p<0.05$). **Significantly different from base value ($p<0.01$).
decreased significantly \((p<0.01)\) in both groups in the post-injection period. The values improved at 24 h but remained lower than the base values (Table 1).

The SUN values did not show any significant change (Table 1). Xylazine and medetomidine produced a significant \((p<0.01)\) increase in creatinine values post-injection up to 120 min. The values, however, returned to the preadministration level at 24 h. Similarly, significant \((p<0.05)\) increase in serum glucose was recorded during the post-injection period. The values however, remained above the base line at 24 h (Table 1). Serum chloride, sodium and potassium values did not show a definite trend throughout the observation period (Table 1).

4. Discussion

The pin prick response method gave a satisfactory indication for ascertaining the onset and depth of analgesia. In comparison to local anaesthetics, xylazine or medetomidine produced a delayed response to onset of analgesia. A delayed onset of analgesia by xylazine in comparison to lignocaine has been reported in various animal species (Fikes et al., 1989; Grubb et al., 1992; Aithal et al., 1996). This has been attributed to the fact that the analgesia induced by xylazine is spinal cord mediated, whereas it is spinal nerve mediated in lignocaine (LeBlanc et al., 1988). Further, the onset of analgesia by xylazine and medetomidine as reported by earlier workers may be related to either species difference, level of injection (subarachnoid or epidural injection), site of injection (lumbosacral or sacrococcygeal), dose rate or a combination of these factors (LeBlanc et al., 1988; Fikes et al., 1989; Skarda and Muir, 1996). Xylazine, medetomidine in animals (Livingston et al., 1992) and dexmedetomidine in human beings (Cullen, 1996) have been reported to produce good spinal analgesia. In the present study, these agents also produced spinal analgesia of longer duration than lignocaine hydrochloride. It was probably due to the fact that \(\alpha_2\)-adrenoceptor agonists provide a local depot of the drug and are released slowly over a longer period of time (Nolan et al., 1987). Similar results were obtained by Grubb et al. (1992). The mechanism by which xylazine and medetomidine induce spinal analgesia was not investigated in this study.

Analgesia produced by xylazine was probably due to its local anaesthetic effects (Aziz and Martin, 1978), which inhibit impulse conduction in primary afferent nerve fibres or of stimulation of \(\alpha_1\)- and \(\alpha_2\)-adrenoceptors in the spinal cord and CNS (Aziz and Martin, 1978), through inhibition of the release of neurotransmitters (Kuraishi et al., 1985) and decreased neuronal activity (Vainio, 1983). The primary site of antinoceptive action of \(\alpha_2\)-agonists after intrathecal administration is at \(\alpha_2\)-adrenergic receptors in the substantia gelatinosa of the dorsal horn of spinal cord (Yaksh, 1985), where they inhibit the release of substance P, which is involved in pain sensation (Grubb et al., 1993). This is probably the area which modulates the response to noxious or mechanical cutaneous stimulation in various species (Fleetwood-Walker et al., 1985). By contrast analgesia induced by medetomidine might have been the result of its binding to \(\alpha_2\)-adrenoceptors in the spinal cord (Vainio, 1983). These drugs have been reported to inhibit nociceptive responses when injected into the first lumbar epidural space of sheep (Eisenach, 1992), lumbosacral epidural space in goats (Aithal et al., 1996) and first intercoccyygeal epidural space of horses (LeBlanc et al., 1988), ponies (Fikes et al., 1989) and cattle (Jean et al., 1990).

Depending on the drug, dose rate, volume and site of injection, a wide range of segmental analgesic zones were observed in animals after epidural or subarachnoid administration of \(\alpha_2\)-agonists (Fikes et al., 1989; Skarda and Muir, 1994). In the present study, xylazine and medetomidine produced qualitatively equal degree of analgesia of hind quarter, flank and thorax. We speculate that both drugs were absorbed from the subarachnoid space, thereby inducing general inhibition of sympathetic nervous system activity and reflexes (Virtanen, 1986). Similar results were obtained by Muir et al. (1992) in horses, when they administered xylazine and detomidine epidurally. Comparatively longer duration of analgesia by medetomidine, though non-significant, as compared to xylazine is due to dose dependency and may probably be due to its being more potent than xylazine and the pharmacokinetic differences between the two drugs that determines the half life or clearance of a drug.

Further, increasing the volume of the anaesthetic solution has been reported to produce more cranial/cephalad migration of analgesics (Johnson et al.,
seen that motor neurons (Skarda and Muir, 1994). It has been due to its possible local action in the hind limb (Grubb et al., 1992). Hind limb ataxia in medetomidine group might be due to its postulated local anaesthetic action on hind limb motor neurons (Skarda and Muir, 1992). This may be attributed to blockade of autonomic and motor nerves as also reported by Skarda and Muir (1992) and Aithal et al. (1996).

Mild ataxia was apparent in the animals of both groups while walking throughout the period of observation. $\alpha_2$-Agonists result in a selective blockade of sensory fibres so that analgesia is achieved without hind limb dysfunction (Grubb et al., 1992). The ataxia produced by xylazine in the present study may be related to its postulated local anaesthetic action on hind limb motor neurons (LeBlanc et al., 1996) probably due to structural similarity with lignocaine (Antonacci et al., 1973). Xylazine has been shown to have a local anaesthetic effect on frog sciatic nerve trunk preparations similar to that of 0.5% procaine hydrochloride (Aziz and Martin, 1978). However, prevalence of hind quarter ataxia was less in this study as compared to that produced by lignocaine (Grubb et al., 1992). Hind limb ataxia in medetomidine group might be due to its possible local action in the hind limb motor neurons (Skarda and Muir, 1994). It has been seen that $\alpha_2$-adrenergic antagonists effectively reversed sedation, but did not completely abolish analgesia and ataxia induced by epidurally/subarachnoidally administered $\alpha_2$-agonist in horses (Skarda and Muir, 1994) further indicating at least a possible partial local analgesic spinal effect of $\alpha_2$-agonists. Since the dose of xylazine and medetomidine used in this study was much less as than in previous studies, only mild ataxia was noticed. However, a local anaesthetic action of xylazine has been cited as the reason for ataxia when its dose exceeded 0.24 mg/kg (LeBlanc et al., 1988).

Frequent urination was noticed in most of the animals after administration of xylazine or medetomidine. This may be due to inhibition of production and release of ADH. In another study, increased urine production was attributed to the osmotic diuretic effect of increased glucose by $\alpha_2$-agonists (Duke et al., 1994a). Heart rate decreased following the administration of xylazine or medetomidine. Several mechanisms contribute to the $\alpha_2$-agonist induced bradycardia which include decreased sympathetic outflow from the CNS, inhibition of norepinephrine release from sympathetic nerve terminals, direct depression of cardiac pacemaker and conduction tissue, increased vagal tone and a direct increase in the release of acetyl choline from parasympathetic nerves in heart (MacDonald and Virtanen, 1992).
LeBlanc and Eberhart (1990) found no measurable change in cardiovascular parameters after caudal epidural administration of xylazine in horses. Respiratory rate also decreased in both groups of \( \alpha_2 \)-agonists and was comparable. Decrease in respiratory rate may be due to the direct depression of the respiratory centres (Kumar and Thurmon, 1979; Rings and Muir, 1982). Significant decrease in respiratory rates was also observed after the administration of xylazine in cattle (Jean et al., 1990; Skarda and Muir, 1992); goats (Aithal et al., 1996); sheep (Waterman et al., 1987) and medetomidine in dogs (Vesal et al., 1996) and cats (Duke et al., 1994b). Significant decrease in body temperature by xylazine might be due to a fall in the ambient temperature during the course of the trial. However, decrease in rectal temperature by xylazine or medetomidine may also be due to generalized sedation, decrease in metabolic rate, muscle relaxation and CNS depression. \( \alpha_2 \)-Agonists have been reported to induce prolonged depression of thermoregulation (Ponder and Clarke, 1980). These agents also have been found to depress the hypothalamic nor-adrenergic \( \alpha_2 \)-receptors to cause hypothermia (MacDonald et al., 1988). Reduced basal metabolic rate and muscle activity on the one hand and depression of thermoregulation on the other hand may result in hypothermia (MacDonald et al., 1988). Further, the decrease in rectal temperature by \( \alpha_2 \)-agonists is not only related to central \( \alpha_2 \)-adrenergic mechanisms (Livingston et al., 1984) but probably also related to other depressing CNS mechanisms, because hypothermia could not be prevented by prior administration of yohimbine (Virtanen, 1986).

Hb, PCV and TLC decreased after xylazine and medetomidine administration. Pooling of the circulating blood cells in the spleen or other reservoirs secondary to decreased sympathetic activity may explain the decrease in Hb, PCV and TLC recorded in this study as also reported with other tranquilizers in dog (Solimon et al., 1965). The decrease in PCV and Hb during the period of anaesthesia or sedation may be due to shifting of fluid from extravascular compartment to intravascular compartment (Wagner et al., 1991) in order to maintain normal cardiac output in the animal. However, while experimenting with detomidine in horses, Gasthuys et al. (1987) observed an increase in PCV at 30 min of drug administration. This could be caused either by increased urine production due to activation of capillary fluid shift mechanism or by the release of the splenic red blood cells reservoir (Kumar and Thurmon, 1978).

The fluctuations in creatinine values may be attributed to a temporary inhibitory effect of the drug on renal blood flow, which in turn might have caused a rise in creatinine. However, it is difficult to ascribe this to possible renal damage, because all the reported values were within normal limits. Hyperglycaemic effects of \( \alpha_2 \)-agonists are well known. There have been many investigations into the hyperglycaemic effects of xylazine (Eichner et al., 1979; Hsu and Hummel, 1981) and medetomidine (Cullen, 1996). Hyperglycaemia observed in this study may be due to an \( \alpha_2 \)-adrenergic inhibition of insulin release by stimulation of \( \alpha_2 \)-receptors in the pancreatic \( \beta \)-cells (Angel and Langer, 1988) and to an increased glucose production in the liver (Hsu and Hummel, 1981). Though it is not clear from this study that the action of subarachnoid xylazine or medetomidine on liver and \( \beta \)-cells of pancreas is either direct or indirect. However, in the author’s view it may be an indirect action since these drugs were absorbed from the subarachnoid space and thereby stimulated the \( \alpha_2 \)-adrenoceptors in \( \beta \)-cells and liver. However, Mirakhur et al. (1984) opined that hyperglycaemia may be due to rise in adrenocortical hormones during stress. A rapid and longer increase of blood glucose in xylazine group than medetomidine group in the present study might be due to the predominant action of xylazine on \( \alpha_2 \)-adrenoceptors in \( \beta \)-cells of pancreatic islets along with \( \alpha_1 \)-adrenoceptor agonistic effects (Hsu and Hummel, 1981) as also seen in other ruminants (Brikas et al., 1987). However, we hypothesize that in medetomidine group a weak or nil \( \alpha_1 \)-adrenoceptor agonistic effect might have produced a slow and transient increase of blood glucose. Serum electrolytes remained unaltered throughout the period of the study. The overall observation on blood biochemical parameters suggested that the alteration seen in different parameters were the outcome of general stress produced during the study as the changes were transient.

5. Conclusions

The results of the study indicate that subarachnoid administration of xylazine (0.05 mg kg\(^{-1}\)) and mede-
tomidine (0.01 mg kg⁻¹) at lumbosacral space produce selective sensory blockade of nociceptive fibres lasting longer than 2 h, with minimal motor inhibition in conscious goats. Further experiments are needed to support the hypothesis that medetomidine also has a local analgesic action similar to that of xylazine. Both drugs caused mild sedation, ataxia, mild cardiopulmonary depression and renal diuresis. The haematological and biochemical alterations produced by these drugs were transient in nature and returned to normal levels as the effects of these drugs weaned off. The haematological changes were due to temporary shifting of fluid from extravascular compartment to the intravascular one. Similarly, alterations in biochemical indices were due to generalized stress produced by these drugs. The effects produced by xylazine and medetomidine were however, comparable at these dose levels. Therefore, both drugs can be safely used for inducing analgesia of hind quarter, flank and perineum.

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References


