Research Article

Combined Physico-chemical and Analgesic Effects of Electroacupuncture Plus Clonidine in Goats

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Abstract | The present study was aimed to investigate the combined physico-chemical and analgesic effects of electroacupuncture (EA) plus clonidine in goats. Thirty-six female goats were randomly allocated equally in six equal groups. The control group received 0.9% normal saline, 2nd, 3rd and 4th groups were treated with 10, 15, and 20µg/kg of clonidine respectively, while 5th and 6th groups were treated with EA and EA plus 10µg/kg of clonidine, respectively. Pain threshold, cardio-respiratory effects, rectal temperature, hematological and biochemical variables were assessed in all groups. Clonidine at the dosage of 20µg/kg increased the pain threshold, and decreased cardio-respiratory rates and rectal temperature in goats. EA plus 10µg/kg of clonidine resulted higher pain threshold for 45-60 min than those goats treated with clonidine at 10 and 15µg/kg or EA alone but showed similar pain threshold with goats treated with 20µg/kg of clonidine. Goats treated with EA plus 10µg/kg clonidine showed moderately higher mean arterial blood pressure, heart rate and respiratory rate up to 10-60min than those groups treated of clonidine. Moreover, a significantly lower serum glucose concentration was noted in EA plus 10µg/kg of clonidine treated goats at 15-60 min than those treated with clonidine alone. Creatinine, blood urea nitrogen, alanine/aspartate aminotransferase activities, and hematological variables for differently treated groups were insignificant. In conclusion, EA combined with a low dose of 10µg/kg of clonidine provided better analgesia in experimental animals.

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Introduction

Clonidine is an alpha$_2$-adrenergic agonist that binds to alpha-2A, B, and C subtypes (Neil, 2011). It decreases peripheral vascular resistance, cardiac output, and blood pressure through receptors activation. It may also reduce plasma renin activity and norepinephrine excretion. It possesses imidazoline II agonistic activity resulting in antihypertensive action (Reis and Piletz, 1997). The most common and dose dependent adverse effects of clonidine include dizziness, drowsiness, hypotension, bradycardia, and decreased motility of gastrointestinal tract (Naguy, 2016). The use of alpha$_2$-agonists in combination with ketamine in ruminants has been in practice leading to reduced risk of aspiration and regurgitation (Eze *et al.*, 2004). However, these combinations shows notable side effects like suppressed cardiovascular

functions, higher respiratory rate, and lowered body temperature in ruminants (Rings and Muir, 1982; Afshar *et al*., 2005).

Electroacupuncture (EA) causes electrical stimulation with fine needles and has been used successfully in human and animals to control pain provoked during surgical procedures (Chen, 1984; Wang and Jin, 1989). Earlier studies demonstrated that combination of EA and analgesic decrease the required dose of anesthetics by 45-55%, and >75%, in human and goat respectively (Qin *et al*., 1996; Liu *et al*., 2009).

Presently, studies on multimodal analgesia utilizing acupuncture-analgesia drug are the research interest to rationalize the therapeutic process to obtain better efficacies. EA in combination of sedative or analgesic drugs like fentanyl, pethidine etc show synergistic effects, but antagonistic effects with other analgesic including diazepam and ketamine (Klide and Kung, 1982; Xu *et al*., 1889). So far there is no report that investigated the analgesic effects of EA and clonidine combination in goats. The Present study aimed to investigate the analgesic and physio-chemical effects of EA plus various doses of clonidine in goats.

Materials and Methods

Animal preparation

Thirty-six healthy and dry (non-lactating) female cross-bred goats 1-2 year-old and weight 18.61±2.87 kg was purchased from the local market and randomly divided equally into 6 groups. Goats were fed with grasses and commercially available concentrate ration, and availed fresh drinking water adlibitum. All goats were dewormed and adapted for 10 days on working environment. Goats were kept fasted for 12 hrs before the start of experiment. The experiment was conducted according to the protocol approved by the Ethical Committee of the Faculty of Animal Husbandry and Veterinary Sciences, The University of Agriculture Peshawar, Pakistan.

Experimental Design

The control group was administered with normal saline (0.9% NaCl solution) intramuscular (IM), 2nd, 3rd, and 4th groups were administered with 10, 15 and 20µg/kg of clonidine, IM, respectively. The 5th group received only EA stimulation and the 6th group received EA stimulation combined with 10µg/kg of clonidine, IM.

Electroacupuncture stimulation

A set of acupoints i.e., Bai Hui, San Tai, Erh Gen and San Yanluo were used for EA stimulation. The area of the aforementioned acupoints were shaved, painted with 10% povidone-iodine, and sterile needles were inserted for EA stimulation. The needles of the Bai Hui and San Tai points were connected to one of the output ports of a pulse generator (Multifunctional electrical pulse generator (G6805-3), Hua Yi Medical Instrument Factory, Shanghai, China), whereas needles of the Erh gen and Sanyanluo points were connected to another output port of the same pulse generator (Shah *et al*., 2016). Electro acupuncture frequency was adjusted at 60 Hz and a constant intensity of 3.2V electrical current was maintained during the course of EA stimulation.

Measurement of physiological variables

Experimental goats were controlled in sternal recumbancy and acclimatized to their surroundings for 30 min before the start of experiment. Physiologic variables (arterial blood pressure, heart rate, respiratory rate, and rectal temperature) were recorded through a 5-lead ECG digital monitor at 0, 5, 10, 15, 20, 30, 45, 60, 90, and 1,440 min. Atipamizole ($\alpha_2$adrenoceptor antagonist as reversal agent was injected intravenously after 60 min in clonidine in treated goats.

The pain threshold was measured on the center of the left flank at 0, 15, 30, 45, 60- and 1,440 min. The site was scrubbed three times with soap water and finally with 75% ethanol. Briefly, 2 electrodes soaked with saturated potassium chloride were placed 1-2 cm apart on the skin of left flank. A Galvano faradism apparatus (DL-ZII, Shantou Medical Equipment Factory Co Ltd, Shantou, China) was used to deliver the pulsed direct current to the electrodes, which forced potassium ions into the subcutaneous tissues. Voltage was increased gradually. The pain threshold voltage was recorded at the moment, when there obvious contractions of the local skin and muscles, head turned toward the abdomen, hunched back, and evasive body movements of goats. The recording of pain threshold was repeated for 3 times. Percentage change was calculated with formula = $([V^n - V^0]/V^0) \times 100\%$

Where V^n is the mean voltage for the pain threshold during the experiment and V^0 is the mean voltage for the pain threshold before the experiment (time 0).

Hematological and biochemical variables

A vacutanier was used to collect 10ml of blood from the jugular vein puncture for determining the hematological (WBCs count, RBCs count, hemoglobin level, HCT, MCV, MCH and biochemical parameters (serum glucose concentrations, creatinine level, blood urea nitrogen (BUN) level, alanine/aspartate aminotransferase (AST, ALP and ALT) activities at 0, 30, 60, 90 and 1,440 min following the early described procedure (Shah *et al*., 2016). Hematological variables were analyzed with an automatic hemoanalyzer (PocH-100iV, Sysmex Corp, Kobe, Japan), and biochemical variables were determined through a serum biochemistry analyzer (Ameda Labordiagnotik GmbH, Krenngasse 128010 Graz/Austria).

Statistical analysis

Data are presented as mean ±SD. Dada were analyzed through analysis of variance (ANOVA) technique using SPSS, version 16. The significant difference among means of different parameters was determined through Bonferroni test at $P<0.05$.

Results and Discussion

Sedative and analgesic effects of clonidine

The goats treated with different doses of clonidine showed dose dependent side effects like salivation and sedation at 6.56±4.83 min. Muscle relaxation, snoring, tongue protrusion, and closing of eyelids occurred at 14±5 min after drug administration, while teeth grinding, excitement, and tympany were occasionally observed in few goats. The EA stimulated goats showed sedation at 11±3.22 min., while in the EA plus clonidine treated goats exhibited calmness at 5.85±2.71 min. The Muchly test of sphericity revealed significant (P= 0.004) differences in pain threshold values among the goats of different groups. Pain thresholds in goats injected with clonidine 10,15 and 20µg/kg of clonidine were increased significantly at 15-60 min than goats of control group. However, the goats of EA plus 10µg/kg of clonidine group showed higher pain threshold for 45-60 min than those goats received clonidine at 15µg/kg or EA alone, but not different with goats that were injected with 20µg/kg of clonidine intramuscularly (Table 1).

Effects of EA and clonidine administration on physiologic variables

Different doses of clonidine administration resulted in dose-dependent decrease in Mean Arterial Pressure (MAP), heart rate, respiratory rate, and rectal temperature at 5-45min, 10-60min, 10-45min, and 5-60min respectively. However higher values for MAP, heart rate, respiratory rate, and rectal temperature at 10-60min were recorded in goats treated with EA plus clonidine at 10µg/kg, than those treated with 15, 20 µg/kg of clonidine alone (Tables 2, 3, 4, 5).

Effect of EA and clonidine on hematology and biochemical values

The RBCs, WBCs, BUN, ALT, ALP, creatinine level of experimental goats remained in normal range after EA and clonidine administration (data not shown). Serum glucose level increased significantly after clonidine administration at 10, 15 and 20µg/kg at 15-60 min, while it was significantly lower in EA plus clonidine treated goats at 15-60 min (Table 6).

The selection of acupuncture points and specific frequencies for stimulation are the important factors that influence the EA-induced analgesia. EA stimulation at frequencies between 30-100 Hz has resulted in efficient analgesia during surgeries in cattle (Han, 2003; Wang and Jin, 1989). However, frequencies of 36 Hz and 60 Hz have been successfully used to activate acupoints (Bai hui, San tai, Erh gen, and San yan luo) for effective analgesia in goats (Liu *et al*., 2009; Cheng *et al*., 2012; Shah *et al*., 2016). In present study, profound analgesia was obtained with frequency of 60Hz for EA at showed that EA at Bai hui, San tai, Erh gen, and San yan luo acupoints. Earlier study showed that EA 60 Hz frequency is responsible for concurrent release of enkephalin, β-endorphin, and dynorphin in most of the analgesic-related nuclei in the CNS of goats (Cheng *et al*., 2012). Moreover, analgesia induced by EA is found to be further facilitated by adrenergic neurotransmitters like noradrenaline (Han, 2008). The method of pin pricking is used to asses the analgesia subjectively in animals (Shah *et al*., 2013; DeRossi *et al*., 2003). Likewise, algesimetry method has been used in sheep and goats to measure pain threshold, based on a leg-lifting response to a subcutaneous electrical stimulus. These methods may measure the learned cognitive behavior but not the involuntary reflexes (Ludbrook *et al*., 1995; Grant and Upton, 2001). However, potassium iontophoresis method seems more convenient and efficient for pain induction (Humphries *et al*., 1994). In this study, potassium iontophoresis was used as an effective method of pain induction in goats.

Table 1: *Effects of electroacupuncture and clonidine on changes in pain threshold (V) in healthy adult female goats (mean ±SD, n = 6 goats/group).*

Groups	15 minutes	30 minutes	45 minutes	60 minutes	1440 minutes
Control	3.22±0.38^{c}	3.11±0.19^{c}	3.22±0.38^{c}	3.11±0.19^{c}	3.33±0.57
Clonidine 10µg/kg	47.74±1.60^{b}	57.56±1.40^{b}	62.31±0.4^{b}	31.4±1.07^{b}	5.2±0.44
Clonidine 15µg/kg	74.54±2.07^{a}	95.72±0.73^{a}	65.45±0.80^{b}	29.09±0.23^{b}	6.22±0.88
Clonidine 20µg/kg	86.79±2.00^{a}	144.33±4.30^{a}	134.66±2.76^{a}	98.13±0.65^{a}	5.22±0.44
EA	74.16±2.93^{a}	83.00±3.54^{a}	87.16±2.58^{b}	43.83±2.14^{b}	4.44±0.65
EA plus clonidine 10µg/kg	76.08±0.57^{a}	115.21±1.34^{a}	121.73±1.15^{a}	89.13±2.11^{a}	4.28±0.38

*Values are represented as mean ± SD. Start of administration of electroacupuncture or injection of clonidine was designated as time 0. *Control mean normal saline (0.9% NaCl) solution injection intramuscular, EA mean electroacupuncture stimulation.$^{a-c}$ Within a column values with different superscript letters show significant (P<0.05) difference.*

Table 2: *Effect of electroacupuncture and clonidine on changes in mean arterial pressure (mm Hg) in healthy adult female goats (mean±SD, n=6 goats/group).*

Groups	0 min	5 min	10 min	15 min	20 min	30 min	45 min	60 min	1440 min
Control	110.33±0.50	110.33±0.50^{b}	112±1.00^{c}	110.3±0.50^{c}	110.3±0.50^{c}	111.33±1.5^{c}	112±1.73^{c}	111.33±1.52^{c}	110.33±0.5
Clonidine 10µg/kg	110.00±1.00	105.33±2.13^{b}	100±2.00^{b}	95.0±1.00^{a}	91.0±1.00^{a}	92.00±1.70^{b}	102.66±1.1^{b}	110.33±5.00^{b}	109.66±5.0
Clonidine 15µg/kg	108.66±4.60	100.66±0.50^{a}	98.33±1.50^{a}	96.0±1.00^{a}	90.33±5.50^{a}	85.33±7.50^{a}	90.66±7.0^{a}	97±3.60^{a}	108±1.00
Clonidine 20µg/kg	107.00±2.60	92.33±6.60^{a}	88.66±5.50^{a}	87±4.30^{a}	82.33±6.60^{a}	80.00±4.30^{a}	92.66±2.5^{a}	99±1.00^{a}	107.33±3.20
EA	110.33±1.10	108.66±1.50^{b}	108.66±3.70^{c}	108.66±2.0^{c}	109.0±1.00^{c}	107.33±1.50^{c}	108.33±1.5^{c}	109±1.00^{c}	109.66±2.0
EA plus clonidine 10µ g/kg	105.33±3.0	102±2.00^{b}	100.66±1.50^{b}	99±1.00^{b}	97.33±0.50^{b}	96.33±1.50^{b}	101±2.60^{b}	110.33±1.50^{c}	104.6±3.20

See Table 1 for remainder of key.

Table 3: *Effect of electroacupuncture and clonidine on changes in the heart rate (beat/min) in healthy adult female goats (mean±SD, n=6 goats/group).*

Groups	0 min	5 min	10 min	15 min	20 min	30 min	45 min	60 min	1440 min
Control	89.33±1.15^{a}	89.66±0.57^{a}	89.0±1.00^{a}	89.33±0.57^{a}	89.00±1.00^{a}	90.66±1.15^{a}	90.66±1.15^{a}	90.00±1.00^{a}	88.66±2.3
Clonidine 10µg/kg	89.66±2.08^{a}	78.66±10.0^{a}	78.66±12.2^{a}	74.66±6.11^{b}	73.33±8.32^{b}	74.33±8.14^{b}	77.33±8.32^{a}	85.33±14.04^{a}	89.66±2.08
Clonidine 15µg/kg	88.66±10.0^{a}	80.00±9.0^{a}	77.66±6.00^{b}	74.66±5.70^{b}	67.0±3.05^{b}	67.66±4.93^{b}	68.33±6.00^{b}	76.00±5.03^{b}	88.66±10
Clonidine 20µg/kg	90.00±3.05^{a}	76.0±4.00^{a}	76.00±3.2^{b}	71.33±4.16^{b}	70.66±1.73^{b}	65.66±1.00^{b}	62.00±1.52^{b}	64.66±8.32^{b}	90.00±3.05
EA	90.33±1.52^{a}	90.66±7.50^{a}	91.66±7.5^{a}	90.66±8.08^{a}	92.00±6.92^{a}	91.33±5.7^{a}	92.0±6.920^{a}	93.33±5.77^{a}	90.33±1.5
EA plus clonidine 10µg/kg	88.0±1.00^{a}	84.6±0.577^{a}	85.33±4.16^{a}	83.66±3.78^{a}	83.66±5.13^{a}	81.0±5.56^{a}	84.00±5.56^{a}	85.33±3.51^{a}	88.0±1.00

See Table 1 for key.

Table 4: *Effect of electroacupuncture and clonidine on changes in respiration rate (breaths/min) in healthy adult female goats (mean±SD, n=2 goats/group).*

Groups	0 min	5 min	10 min	15 min	20 min	30 min	45 min	60 min	1440 min
Control	23.66±1.52	22.66±2.51	22.00±2.00^{a}	23.66±2.51^{a}	23.33±3.05^{a}	22.66±4.61^{a}	23.00±4.35^{a}	24.00±3.35	23.33±1.15
Clonidine 10µg/kg	23.33±0.57	22.0±1.00	21.66±0.57^{a}	21.33±1.52^{a}	19.66±0.50^{a}	19.66±0.57^{b}	21.33±1.52^{b}	21.33±1.15	23.0±0.00
Clonidine 15µg/kg	24.00±1.00	22.33±1.15	21.33±1.15^{a}	21.00±1.00^{a}	20.33±0.57^{a}	20.00±1.73^{b}	20.63±1.52^{b}	23.00±1.00	23.66±0.57
Clonidine 20µg/kg	24.00±2.64	22.33±4.04	20.00±6.00^{b}	20.66±5.29^{b}	19.33±6.42^{b}	19.00±6.24^{b}	20.66±3.51^{b}	21.33±3.78	24.00±0.00
EA	23.33±0.570	23.00±0.00	22.00±0.00^{a}	22.33±1.15^{a}	22.33±0.57^{a}	22.33±1.15^{a}	22.33±0.57^{a}	23.33±0.57	23.66±0.57
EA plus clonidine 10µg/kg	23.00±0.00	22.66±2.5	21.00±1.00^{a}	21.00±2.64^{a}	21.33±4.50^{a}	21.33±2.51^{a}	22.00±1.73^{a}	23.00±0.00	23.00±0.00

See Table 1 for key.

Table 5: *Effect of electroacupuncture and clonidine on changes in temperature (F) in healthy adult female goats (mean±SD, n=6 goats/group).*

Groups	0 min	5 min	10 min	15 min	20 min	30 min	45 min	60 min	1440 min
Control	102.2±0.34	101.93±0.11[a]	102.2±0.40[a]	102.06±0.28	102.1±0.17[a]	102.1±0.40[a]	102.23±0.40[a]	102.1±0.17[a]	102.1±0.23
Clonidine 10µg/kg	101.42±0.71	101.35±0.82[a]	101.06±0.27[a]	101.04±0.40[a]	101±0.43[a]	101.06±0.63[a]	101.06±0.70[a]	102.01±0.18[a]	102.01±0.18
Clonidine 15µg/kg	102±00.00	100.63±0.32[b]	100.3±0.32[b]	100.33±0.30[b]	100.2±0.34[b]	100.00±0.00[b]	100.14±0.12[b]	101.9±0.0[a]	1001.9±0.73
Clonidine 20µg/kg	101.7±0.36	100.36±0.15[b]	100.00±0.0[b]	99.66±0.57[b]	98.66±0.57[b]	98.66±0.57[b]	98.66±0.57[b]	99.33±0.57[a]	102.18±0.32
EA	102.4±0.34	102.6±0.51[a]	102.6±0.51[a]	102.3±0.28[a]	102.2±0.17[a]	102±0.00[a]	102±0.00[a]	102±0.00[a]	102.5±0.46
EA plus clon 10µg/kg	102.04±0.95	102.1±1.38[a]	102.03±1.50[a]	101.7±1.32[a]	101.5±1.27[a]	101.36±1.09[a]	101.32±0.48[a]	101.4±0.80[a]	102.05±1.28

See Table 1 *for key.*

Table 6: *Effects of electro-acupuncture and clonidine on changes in glucose concentration in healthy adult female goats (mean±SD, n= 6 goats/group).*

Groups	0 minutes	15 minutes	30 minutes	45 minutes	60 minutes	1440 minutes
Control	84 ± 4.5	84 ± 5.2[b]	83 ± 5.5[b]	83 ± 6.2[b]	84 ± 5.2[b]	84 ± 5.5
Clonidine 10µg/kg	83 ± 3.0	95 ± 4.5[a]	100 ± 3.4[a]	93 ± 1.0[a]	87 ± 1.7[a]	83 ± 3.6
Clonidine 15µg/kg	84 ± 2.0	100 ± 6.2[a]	116 ± 5.2[a]	104 ± 3.6[a]	102 ± 3.6[a]	83 ± 3.0
Clonidine 20µg/kg	90 ± 3.0	130 ± 8.1[a]	171 ± 8.2[a]	136 ± 5.5[a]	104 ± 5.5[a]	85 ± 4.5
EA	84 ± 5.2	85 ± 6.2[b]	85 ± 7.0[b]	84 ± 6.2[b]	84 ± 6.1[b]	84 ± 5.2
EA plus clonidine 10µg/kg	86 ± 1.7	85 ± 6.0[b]	86 ± 4.5[b]	85 ± 2.6[b]	91 ± 3.6[b]	86 ± 1.7

See Table 1 *for key.*

Electroacupuncture induced analgesia is not strong enough to be used as a sole analgesia in individuals undergoing major surgical procedures (Han, 2008). Therefore, acupuncture-drug balanced analgesia is the area of interest for researchers (Dong and Wang, 2006; Han, 2008). To estimate the EA induced analgesia quantitatively, studies have utilized an analgesic drug alone and lower dose of analgesic drug in combination with EA for getting complete analgesia (Liu *et al.*, 2009). It has been reported, that the analgesic effects achieved by EA at 100 Hz for 30 min and morphine at a dose rate of 4mg/kg are equivalent in rats (Tang *et al.*, 1997). However, 10mg/kg dose of morphine is needed for strong analgesic effect, therefore EA induced analgesia is approximately half of that resulting from 10mg/kg dose of morphine (Gades *et al.*, 2000; Tang *et al.*, 1997). Therefore, some researchers investigated the combined use of EA and xylazine in goats for induction of analgesia without adverse effects like bloat, aspiration saliva, decrease in heart and respiratory rates, and rectal temperature, and prolong recumbancy (Liu *et al.*, 2009). A study of Cui *et al.* (2017) compared the analgesic effects of lidocaine at dose of 4.4mg/kg epidurally with epidural injection of lidocaine at 2.2mg/kg plus EA, and reported that EA results in superior analgesia. In our earlier study, EA plus 5µg/kg of dexmedetomidne and 20µg/kg dexmedetomidine alone showed the similar level of analgesia in goats (Shah *et al.*, 2016). In the present study, the pain threshold was significantly higher in goats that received EA plus 10µg/kg of clonidine than EA or clonidine (10µg/kg) alone. It is clearly indicates that there is synergism between EA and clonidine. This synergism is possible due to the coactivation of alpha$_2$-adrenergic receptors or opioidergic-noradrenergic alterations (Shankar, 1996; Kabalak, 2013). However, the further study is imperative to probe the precise mechanism of synergism. Alpha$_2$-agonists like xylazine induce a significant decrease in blood pressure and heart rate in goats (Kinjavdekar *et al.*, 2000; Afshar *et al.*, 2005; Liu *et al.*, 2009). In current study, clonidine at 15 or 20µg/kg resulted in significant decrease in the heart rate, which is in agreement with earlier findings in sheep and goats administered with others alpha$_2$-agonists (Lawrence *et al.*, 1997; Kutter *et al.*, 2006; Shah *et al.*, 2016).

Moreover, EA alone did not cause significant decrease in MAP and heart rate of goats. In the present study, the combination of EA and clonidine resulted in moderately less decrease in MAP and heart rate in goats than the clonidine alone. This reduction in heart rate may be attributable to a decrease in sympathetic tone (Kastner *et al*., 2007; Peng *et al*., 1982).

Almost all alpha$_2$-agonists cause respiratory depression because of CNS effects (Young *et al*., 1990; Lammintausta, 1991). In ruminants, these drugs exhibit bronchospasm and increased pulmonary vascular resistance, resulting in edema of lungs, and there by improper gases exchange, leading to hypoxemia (Alex, 2010). The findings of the present study are in close agreement with the previous studies as clonidine administration at 15 or 20µg/kg to experimental goats resulted in significant respiratory depression (DeRossi *et al*., 2003). However, the combined use of EA and clonidine at 10µg/kg induced less respiratory depression than clonidine alone. Similarly, all alpha$_2$-agonists cause depression of hypothalamic alpha$_2$-adrenoceptors leading to subnormal body temperature (Ponder and Clarke, 1980; MacDonald *et al*., 1988). In present study, clonidine at 15 or 20µg/kg decreased rectal temperature in goats at 5-45 min after its administration. The reduction in rectal temperature might be due to muscles relaxation, decreased metabolic rate, and depression of thermoregulatory mechanisms (Ahmad *et al*., 2011; Shah *et al*., 2014). The clonidine treated goats showed by hyperglycemia. Earlier researchers also found that all alpha$_2$-agonist drugs resulted in hyperglycemia in goats, sheep, and water buffalos (Brockman, 1981; Singh *et al*., 2013; Shah *et al*., 2016). The hyperglycemia might be due to α2-adrenergic blockage of insulin release, and stimulation of glucagon release from α and β cells of the pancreas respectively, as well as glucose synthesis in hepatic cells. Moreover, muscular relaxation can impair the glucose absorption on tissue level, ultimately result in higher glucose concentration in blood (Brockman, 1981; Gasthuys *et al*., 1987; Singh *et al*., 2013).

Conclusions and Recommendations

Results of the current study showed that EA plus clonidine at 10µg/kg provided a similar analgesia to clonidine at 20µg/kg without significant effects on physiological and biochemical parameters.

The present study showed that EA plus clonidine at 10µg/kg provided a similar analgesia to clonidine at 20µg/kg without significant effects on physiological and biochemical parameters. Therefore, EA plus clonidine combination may be used for clinical examination, diagnostic procedures, biopsy, application of plaster casts and surface medication, and minor surgeries in goats. This experiment provides baseline data for the clinical application of EA in combination with clonidine in order to reduce the dose, cost, and side effects of the anesthetic agent.

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Novelty Statement

To the authors knowledge no research work has been done on acupuncture plus clonidine combination in goat, so it is a new era to reduce the dose, cost and side effects of the drugs.

Author's Contribution

ZS and SM designed research project, IU presented the basic idea, TS and HAU analyzed the data and wrote the manuscript, SN help in manuscript format design and FAK Help in hematological and biochemical analysis. MKS revised the manuscript. All authors read and approved the final submission.

Conflict of interest

The authors have declared no conflict of interest.

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