Evaluation of IV administration of romifidine (α2- agonist) butrophanol (Opiod receptors agonist antagonist) combination on sedation, analgesia and haemato-biochemical effects in Horse

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Abstract

The present investigation aimed to evaluate and compare sedative, analgesic, hematological and biochemical effects of i/v injection of three different doses of romifidine and butrophanol combination. Twelve clinically healthy horses were used and classified into 3 groups. Each group (n=4 horses). Onset, duration, signs and degree of sedation were determined depending on the behavioral changes. Onset and duration of analgesia were determined according to response to standard painful stimulus by pin pricking of skin and muscle. The degree of ataxia was recorded. Pulse and respiratory rates and rectal temperature were determined 5 minutes before injection and at 15, 30, 60, 90 and 120 minutes following injection. Blood samples were collected from jugular vein for estimation of RBCs, WBCs, differential leukocytic counts, Hemoglobin % and PCV %. Serum was used for determination of AST, ALT, Triglycerides, Glucose, Creatinine, Total protein, Albumin, Globulin, Albumin/Globulin ratio, Cholesterol, Urea and blood urea nitrogen. Rapid onset and longest duration of both sedation and analgesia appeared in the 3rd group. The depth of sedation induced by combination of (romifidine, 80 ug/ Kg bwt and butrophanol, 40 ug/Kg bwt) was greater than that induced by in 1st group (romifidine 40 ug/Kg bwt and butrophanol 20 ug/Kg bwt) or in group2nd (romifidine 60 ug/Kg bwt and butrophanol 30 ug/Kg bwt). No significant differences were observed in the onset of analgesia among the three groups. Little ataxia appeared in 1st group. Mild to moderate ataxia were observed in 2nd and 3rd groups. Pulse and respiratory rates showed significant decrease. Changes in rectal temperature were not significant. RBCs, WBCs counts, PCV% and Hb% showed significant decreases. Both ALT and AST activities were decreased significantly. A significant increase in total protein, albumin and globulin values were observed and then gradually decreased till nearly reached to its baseline at 120 minutes post injection. A significant increase of glucose values were observed in all group of combinations. Cholesterol and triglycerides values showed significant increases. A significant to non significant changes in both creatinine and urea values were observed, on the other hand blood urea nitrogen showed significant increase.

Key words: Sedative, Analgesic, Haemato-biochemical effects, I/V injection, Romifidine Butrophanol Combination, Horse.

Introduction

Alpha-2adrenoceptor agonists are used to produce sedation, analgesia and muscle relaxation in horses. Romifidine (2-bromo-6-fluro-2-imidazolidene-

benzaminemonohydrochloride) is a potent and selective alpha-2adrenoceptor agonist that produces pharmacological effects typical for this group of drugs and characterized by sedation, muscle rexation, reluctance to move, reduced responsiveness to environmental stimuli, bradycardia, decreased cardiac output and reduced respiratory rate (England, Clarke and Goossens, 1992, Hamm, Turchi and Jochle, 1995, Yamashita et al., 2000 and Freeman and Bowen, 2002). Alpha-2 agonists have gained wide acceptance as sedative analgesics in horse. Due to insufficient stability of sedation in current equine practice, alpha-2adrenoceptor agonists are often used in combination with morphine or other opioids to improve sedation and analgesia (Short, 1992 and Schatzman et al., 2001). Butrophanol is a synthetic, centrally acting narcotic analgesic indicated for the relief of pain associated with colic and minor surgery in horse and exhibits partial agonist and antagonist activity at the U opiod receptor(Forney etal., 2007) and agonist activity at the K-opiod receptor(Caulkett et al.,2003). Combination of romifidine with butrophanol have application in clinical practice due to decreases the time of onset of sedation, reduce the response to imposed stimuli and increase the duration of action when compared with romifidine alone (Clarke, etal,. 1991 and England and Watts, 1997). The addition of butorphanol didn't influence the cardiovascular system more than romifidine alone, but may some increase in respiratory depression (Clarke et al. 1991). The combination was used to sedate horses for a variety of surgical, therapeutic and diagnostic procedures (Browning and collins, 1994).The combination of romifidine and butrophanol is a safe and effective neuroleptanalgesic and the horses were insensible to aural or tactile stimulation. Alpha-2 agonists produce analgesia by stimulation of alpha-2 adrenoceptors in the substantia gelatinosa of the dorsal horn of spinal cord, thereby, inhibiting the release of neurotransmitter norepinephrine and substance P (LeBlanc and Caron, 1990). Sedation with alpha-2 agonists resulted from decreased activity of ascending neural projections to cerebral cortex and limbic system (Benson, 1999). Analgesia with alpha-2 agonists appeared to be a result of both cerebral and spinal effect. Possibly in part mediated by serotonin and the descending endogenous analgesic system (Benson, 1999). Administration of alpha-2 agonists and opiod agonist combination caused decrease in hematological parameters including; RBCs, WBCs counts, PCV% and Hb% and increased glucose, cholesterol, blood urea nitrogen, creatinine and ALT while decreased total protein and albumin. The changes in haematological and haematobiochemical parameters were transient and caused no marked systemic effects (Wasak, 1983 and Benson et al., 1984). The present study aimed to evaluate and compare sedative, analgesic, hematological and biochemical effects of intravenous injection of three different doses of romifidine and butorphanol combination in horses.

Materials and Method

The present study was performed on twelve adult clinically healthy horses of both sexes, aging 4 to 7 years and weighing 350 to 400 kg. Physical examination was carried out 24 hours before sedation. Food, but not water, was withheld for 12 hours before. The area over the jugular vein was clipped and surgically prepared for aseptic placement of each trial needles. Horses were classified into three main groups each of 4 horses in each group injected

intravenously with three different doses of romifidine* and butorphanol** mixed in the same syringe. The dose of the two used drugs in the combination were 40 ug/Kg bwt romifidine and 20 ug/Kg bwt butrophanol , 60 ug/Kg bwt romifidine and 30 ug/Kg bwt butrophanol and 80 ug/Kg bwt romifidine and 40 ug/Kg bwt butrophanol for the 1st, 2nd and 3rd group respectively. The onset, duration, signs and degree of sedation were estimated depending on the behavioral changes. Grades of sedation were scored as follow:

0= no sedation (normal frequency and velocity of movement, ear and neck carriage, eye alertness, lip separation).

1= mild sedation (slightly decreased frequency and velocity of movement, lower ear and neck carriage, reduced eye alertness, appearance of lip separation, slightly relaxed postural tone and wide stance).

2= moderate sedation (moderate decreased frequency and velocity of movement, obvious ear tip separation , appearance of crossed leg, buckled knee and / or fetlocks, more relaxed postural tone).

3= deep sedation (markedly decreased frequency and velocity of movement, increased occurrence and severity of crossed leg, dropping (ptosis) of the head, more lower lip and/or eye- lid, buckled knee and/or fetlocks, pronounced loss postural tone, protrusion of the penis and frequent urination).

The onset and duration of analgesia were determined according to response to a standard painful stimulus by pin pricking of skin and muscle. Degree of ataxia was recorded by walking the horse for a certain distance. Pulse and respiratory rates and rectal temperature were determined and recorded 5 minutes before i/v administration (baseline) and at 15, 30, 60, 90 and 120 minutes post administration.

Blood analysis

Blood samples were collected from jugular vein at 5 minutes before i/v injection and at 15, 30, 60, 90 and 120 minutes post injection with and without anticoagulant for estimation of RBCs and WBCs (Maxine and Benjamine, 1985), hemoglobin (Hbg%) (Zijlstra, 1961), heamatocrite (PCV %) (Maxine and Benjamine, 1985) and differential leukocytic count (DLC %) (Dacia and Lewis, 1975). Serum biochemical analysis were included AST and ALT activities (Reitman and Frankel, 1957), Creatinine (Faulkner and King, 1976), total protein (Doumas, 1975), Albumin Doumas et al., 1971, Glucose and Triglycerides Tinder, 1969, Cholesterol (Katterman etal., 1984), Urea and blood urea nitrogen (Davidson and Henary, 1969).

Statistical analysis

The determined results were analyzed using analysis of variance procedure of the statistical analysis system computer package (SAS, 1987).

*Sedivet, Boehringer ingelheim Vet medica, Inc., Saint Jseph, Mo, USA, 2-bromo-6-floro-2-midazolinnhylidene-Benzamine monohydrochloride.

**Torbugesic, Fort Dodge laboratories, Inc., Fort Dodge, Lowa, 50501, I-N-cyclobutyl methyl-3, 14- dihydroxy morphinan.

Result

Sedative and analgesic effects:-

Data presented in table (1) showed significant differences in the mean values of onset and duration of sedation among the three groups of romifidine and butrophanol combinations. The rapid onset of sedation (2.25±0.14 minute) and the longest duration (95.75±2.17 minute) appeared with the 3rd group of romifidine, 80 ug/Kg bwt and butrophanol, 40 ug/Kg bwt. The onset and duration of sedation were (3.75±0.10 and 58.25±1.65 minutes) and (2.83±0.12

and 79.00±1.68 minutes) in both 1st and 2nd groups of combination respectively (Fig., 1). There were no significant differences in the mean values of onset of analgesia among the three groups with significantly difference in the duration period. The 3rd group showed rapid onset (3.85±0.22 minute) and longest duration period of analgesia (88.00±1.08 minute).The lowest analgesic period (50.50±2.10 minute) appeared in the 1st group. Degree of sedation was dose dependant and increased by increasing the dose. The response to audiovisual stimuli decreased post administration of the combinations. Deep and better sedation was observed in the 3rd group of romifidine and butrophanol combination and characterized by markedly decreased in the frequency and velocity of movement, increased occurrence and severity of crossed leg, dropping of the head, more lower lip and /or eye lid, buckled knee and/or fetlocks, pronounced loss of postural tone, protrusion of the penis with frequent urination. The depth of sedation induced by combination of romifidine, 80 ug/ Kg bwt and butrophanol, 40 ug/Kg bwt (score 3) was greater than that induced by either romifidine 40 ug/Kg bwt and butrophanol 20 ug/Kg bwt (score1) or romifidine 60 ug/Kg bwt and butrophanol 30 ug/Kg bwt (score2). Degrees of ataxia were recorded as; no to little ataxia was observed in 1st group of combination in which horses were able to walk and handler able to pick up leg easily. Mild to moderate ataxia were found among the 2nd and 3rd group of combination where horses showed a minimal swaying, crossed leg and unstable. The periods of analgesia were shorter than the periods of sedation (table 1& Fig., 1).

Clinical effects:-

Pulse rate decreased significantly for along time extended from 15 to 120 minutes after i/v administration in the three groups of romifidine and butrophanol combinations except after 90 and 120 minutes in the 1st group the pulse rate increased. The lowest rate was recorded in the 3rdgroup of romifidine- butrophanol combination from (40.00±0.41 beats/ minute) to (26.25±0.48 beats/ minute) post 15 minutes from i/v administration of romifidine and butrophanol combinations (table, 2). Changes in temperature were not statistically significantly different and nearly returned to the baseline value in all groups of combinations. However, respiratory rates showed a significant decrease from baseline value in all groups of romifidine and butrophanol combinations (table, 2). Frequent urination observed all over periods of clinical examination post administration of romifidine-butrophanol combination.

Haematological and Biochemical effect: RBCs count (Million/mm3) showed no significant decrease, while WBCs count (Thousands /mm3) showed significant changes from 15 to 120 minutes post i/v administration in the three groups of romifidine and butrophanol combinations (table, 3). PCV% showed significant decrease with lowest values recorded at 60 minutes post i/v injection (34.75±0.63, 33.75±0.85, 36.00±0.41 in 1st, 2nd and 3rd group of romifidine and butrophanol combination respectively). Hb% value significantly decreased all over periods of experiment among the 1st and the 2nd group of combination, however Hb% value showed insignificant decrease from 15 to 120 minutes post i/v administration in the 3rd group of combination (table, 3). Neutrophils% showed significant increase in all periods of experiment and

then returned to its baseline values at 120 minutes in all romifidine and butrophanol combinations. Eosinophils%, Lymphocyte% and Monocyte% exhibited significant to insignificant increase and decrease throughout all periods of experiment in the 3rd group of combination (table, 3). IV administration of all doses of romifidine and butrophanol combinations revealed significant decreases in both ALT and AST activity and extended through out all periods of experiment. A significant increase in total protein, albumin and globulin values were observed in all periods of this study, and then gradually decreased till nearly reached to their baseline values at 120 minutes post injection (Table, 4). Significant increases of glucose level were observed post administration of romifidine and butrophanol combination groups.Cholesterol and triglycerides values were showed significant increases and continued till the end of all experiments (Table, 5). A significant increase in creatinine, urea and blood urea nitrogen values were observed following administration of romifidine and butrophanol combinations, and then showed significant decreases gradually (Table, 5).

Discussion

The experiment confirms the previous reports evaluating sedative, analgesic and haemato-biochemical effects of intravenous administration of romifidine and butrophanol combination in horses. α2-agonists are commonly considered as sedative and a potent analgesic agent, especially in horses. Butrophanol is a synthetic mixed agonist-antagonist opiods, has become particularly popular to induce safe and effective neuroleptanalgesia when used in combination with romifidine (Browning &Collins, 1994).

Our results revealed rapid onset of sedation and analgesia (2.25±0.14 & 3.85±0.22 minutes, respectively) with longest duration period (95.75±2.17 & 88.00±1.08 minutes, respectively) appeared in the 3rdgroup of romifidine, 80 ug/Kg bwt and butrophanol, 40 ug/Kg bw combination .This results were in agreement with Short (1992), Thurmon etal., (1996) and Abu-Ahmed (2007). In the present study degree and duration of both sedation and analgesia were considered a dose dependant of romifidine and butrophanol. The same results were observed by Figueiredo, Muir, Smith and Wolfrom (2005). Deep and better sedation was observed in the 3rd group of romifidine and butrophanol combination. The same results were found by Corletto, Raisis and Brearley (2005). The previous results could be attributed to the CNS suppression evoked by α2-agonistic action of romifidine and Kappa (K) agonistic action of butrophano, where stimulation of K opiod receptor in the CNS causes intracellular inhibition of adenylate cyclase closing the influx membrane calcium channels, hyperpolarization of the cell membrane potential causing suppressing of action potential transmission of ascending pain pathways. Whileα2- adrenoceptor agonists reduce norepinephrine outflow with the CNS, thus dampening the CNS sympathetic tone (Watling, 1998 and Forney etal., 2007). In regard to the degree of ataxia, our result revealed mild to moderate ataxia were observed among the 2nd and 3rd group of combination. The same results were demonstrated by Short (1992) who added that a higher dose was associated with high degree of ataxia. Also Clarke and paton (1988) and Taylor, et al. (1988) reported greater ataxia was observed post combination of α2-agonists with butrophanol while Browning and Collins (1994) concluded

that combination of romifidine with butrophanol induced little significant ataxia. Our result was in agreement with Taylor, (1985), Taylor etal., (1988) and Thurmon et al., (1996) who reported that the response to audiovisual stimuli decreased post combination with butrophanol. Pulse rate showed a significant decrease post i/v romifidine and butrophanol combinations and the lowest rate was appeared at 15 minutes ((26.25±0.48 beats/ minute) in the 3rd group of combination. The same results were reported by (Gasthuys et al., 1996, Amarpal et al., 2002, Selmi et al., 2002 and Kinjavdeker et al., 2006). Bradycardia is thought to be result of increased vagal tone in response to depression and reflex barorreceptor stimulation in the carotid sinus in response to initial hypertension caused by administration of an alpha-2 agonist (Naylor etal., 1997). Changes in temperature were not statistically significant and returned to the baseline value in all groups of combinations. The slight decrease in rectal temperature regarded to be secondary to CNS depression and reduction in muscular activity (MacDonald etal., 1988). Freeman and England (2000) and Freeman, Bowen, Bettschart-Wolfensberger, Alibhai and England (2002), reported that higher doses of romifidine caused decrease in respiratory rate than lower doses. In this study we observed a significant decrease in respiratory rates. This was also observed by Clarke etal., (1991) and Selmi etal., (2001). The reduction in respiratory rate might be secondary to the CNS depression caused by Alpha-2 adrenergic agonist and kappa opiod receptor agonist (Watling, 1998, Jeffery etal., 1999, Figueiredo etal., 2005 and Forney etal., 2007). Frequent urination and increase in urine production after administration of alpha-2 adrenoceptor agonists may be due to hyperglycemia and inhibition of antiduretic hormone (ADH) release (Hall et al., 2001). In the present study RBCs count showed insignificant decreased, while PCV% and Hb% values exhibit significant decrease in the 3rd group of combination. The decrease was transient and returned to the baseline values by the end of the experiment. The same result was reported by (Wasak, 1983, Wagner etal., 1991 and Nouh and Abdel-Wahed, 2000). WBCs in the 1st group of combination exhibit a significant increase at all time intervals of the study except at 30 minutes post i/v administration of romifidine-butrophanol combination where the count was near the baseline values. In the 2nd and 3rd groups of combination, WBCs count showed significant decrease throughout the investigation periods except at 15 minutes in the 2nd group where the value was near the baseline. The decrease in WBCs count was agreed with the finding reported by (Wasak, 1983). The decrease in RBCs &WBCs counts PCV and Hb values might be explained on the basis of increased blood cells storage in the spleenic capsule relaxation (Kumar and Singh, 1978). The relaxation of the spleenic capsule coul;d be a consequence of decreased sympathetic tone and reducing norepinephrine and epinephrine caused by the alpha2 adrenoceptor action of romifidine (MacDonald et al., 1988 and Virtanin 1989)., and Kappa agonistic action of butrophanol(Watling, 1998 and Forney etal., 2007). In all groups of combination differential leukocytic count exhibited slight fluctuation throughout time intervals of this study, interestingly there was a significant increase in neutrophil % in all groups and at all time intervals, which might be caused by histamine released from the hypothalamic neurons, where there are new evidence suggesting a role of histamine in chemotaxis of neutrophils (Leist etal., 1995 & Marieb, 2001). Eosinophils were decreased significantly in

both 1st and 2nd romifidine and butrophanol combinations and in 3rd group varied between increased to significant decreased, and then gradually returned to normal value. The same results were reported with Abu-Ahmed (2007). Lymphocyte and Monocyte values were increased and decreased varied between significant to non significant difference. Concerning serum analysis our results revealed significant decreases in both ALT and AST activities. The same results were reported by (Nakamuta etal., 1997 and Masaki et al., 2004) on the other hand Short (1987) reported a significant change in ALT and AST activity following i/v injection of romifidine in donkeys. The decrease in enzyme activities might be induced by histamine through a preventive mechanism of liver injury by affecting the rate of hepatic damage via inhibition of production and/or release of some inflammatory cytokines (Nakamuta etal., 1997 and Masaki et al., 2004).A significant increase in total protein, albumin and globulin levels were reported in all groups of combination. The increased was transient and turned to near the baseline values by the end of the experiment. This result was in agreement with the findings reported by (Amer and Misk, 1980 and Abu-Ahmed, 2007). On the other hand serum triglycerides and cholesterol showed significant increase in all experimental groups, this might be exerted through the release of hypothalamic neuronal histamine by the alpha2 adrenoceptor action and Kappa opiod receptor agonist. Hypothalamic neuronal histamine reduces fat deposition in the adipose tissue by increasing lipolysis where histamine neurons contribute to maintenance of energy homeostasis (Tsuda, 2002), a concept which is more confirmed by the observation that, H1Komice (histamine receptor knockout mice) exhibits a substantial hypertrophy of a dipocytes and obesity (Mollet etal., 2001 and Masaki etal., 2004). Creatinine, urea and blood urea nitrogen showed a significant increased in all groups of combination and in all periods of experiment. This result agreed with that obtained by (Abu-Ahmed, 2007) and disagreed with the findings of (Kinjavadekar etal., 2001). The previous findings might be a result of some alteration in renal function followed the vasodilatation exerted by the released histamine and the reduced adrenergic tone, resulted in decreased cardiac output which would cause apparent changes in renal function (Fengyun et al., 2002). Glucose level showed a significant increased following administration of romifidine and butrophanol combination. This result was agreed with Abu-Ahmed (2007) who reported a significant increase in glucose following i/v injection of romifidine and butrophanol combination in donkeys and disagreed with the findings obtained by (Benson etal., 1984, and Strubbe, 1989). It is therefore concluded that, i/v administration of combinations between romifidine-butrophanol considered a potent neuroleptanalgesic, provide better, safe and effective sedative analgesic agents in horses and produced dose-dependant sedation and analgesia with mild transient alteration in clinicophysiological, haematological and biochemical parameters, recommending usage of this combination in clinical practice due to the rapid onset of sedation, reduced the response to imposed stimuli and increased the duration of action.

Conclusion

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safe and effective sedative analgesic agents in horses and produced dose-dependant sedation and analgesia with mild transient alteration in clinicophysiological, haematological and biochemical parameters, recommending usage of this combination in clinical practice due to the rapid onset of sedation, reduced the response to imposed stimuli and increased the duration of action.

References

Abu-Ahmed, Howaida, M. (2007): Clinical importance of xylazine, detomidine and romifidine in domestic animals. Ph.D., Fac. Vet. Med .Alex. Univ.

Amarpal, Kinjavdekar, P., Aithsal, HP., Pawde, AM AND Pratap, K. (2002): Analgesic, sedative and hemodynamic effects of spinally a ministrated romifidine in female goats. J. Vet. Med. A Physiol Pathol Clin Med., 49(1):3-8.

Amer, A.A. and Misk, N.A.C. (1980): Rompun in goat with special reference to its effect on the cerebral spinal fluid (C.S.F.) Vet.Med. Rev., 2:168-174.

Benson, C.J. (1999): Physiological effects of pharmacological agent. Vet. Clinical Services, Anaethesia and Analgesia (Internet).

Benson, G.J., Thurmon, J.C., Neff-Davis, C.A., Corbin, J.E., Davis, L.E., Wilknson, B., Tranquilli, W.J. (1984): Effect of Xylazine Hcl upon plasma glucose concentrations in adult pointer dogs. J Am. Anita. Hosp. Assoc., 20: 791-794.

Browning A.P. and Collins J.A. (1994): Sedation of horses with romifidine and butrophenol. The Veterinary Record, v.22 p. 90 91.

Caulkett, N., Read, M., Fowler, D. and Waldner, C. (2003): Acomparasion of the analgesic effects of butrophanol with those of meloxicam after elective ovariohystrectomy in dogs. Can.Vet.J. July, 44 (7):565-570

Clarke, K.W. and Paton, B.S. (1988): Combined use of detomidine with opiates in the horse. Eq. Vet. J. 20, 331- 334.

Clarke, K.W.; England, G.C.W. and Gossens, L. (1991): Sedative and cardiovascular effects of romifidine, alone and in combination with butorphanol, in the horse. J. Vet. Anaesth. 18, 25-30.

Corletto, F., Raisis, A.A. and Brearley, J.C. (2005): Combination of morphine and butrophanol as preanasthetic agents in combination with romifidine for field castration in ponies. Vet. Anaeth. Analg. 32(1):16-22.

Dacia, J.V. and Lewis, S.M. (1975): Practical Haematology. 5thEd. The English Language Book Society and Churchill livingstone, pp.21-42.

Davidson, I. and Henary, J.B. (1969): Clinical Diagnosis by Laboratory Methods, Saunders Co., Piladelphia, Pennsylvania

Doumas, B.T. (1975): Colorimetric determination of total protein .Clin. Chem. Acta, 35:89.

Doumas, B.T., Walson, W.A. and Biggs, H.G. (1971): Albumin standards and the measurements of serum albumin with bromochresol green. Clin.Chem.Acta.31:87.

England, G, C, W Watts, N. (1997): Effects of romifidine and romifidine- butrophenol for sedation in dogs, Journal of Small Animal Practice. V.38, p. 561-564.

England, G.C.W.; Clarke, K.W. and Gossens, L. (1992): A comparison of sedative effects of three alpha-2 adrenoceptor agonists (romifidine, detomidine and xylazine) in the horse. J. Vet. Pharm. Therap. 15(2): 94-201.

Faulkner, W.R. and King, J.W. (1976): Fundamentals of clinical chemistry: determination of creatinine concentration. 2nd Ed., N. W. Tietz (ed.), Saunders, Philadelphia, P. 994.

Fengyun, X.U. Straub, W.O., Pak. W., Su, P., Maier, K.G., Yu, M., Roman, R.J., Paul, R. DeMontellano, O. and Kroetz, D.L. (2002): Antihypertensive effect of mechanism based inhibition of renal arachidonic acid hydroxylase activity. Am. J. Physiol, Regul. Integr. Comp. Physiol, 283: R710-R720

Figueiredo, J.P., Muir, W.W., Smith, J. and Wolfrom,G.W. (2005): Sedative and analgesic effects of romifidine in horses. Intern J Appl Res Vet Med. Vol.3, No., 3.

Forney, Barbara, C., M.V. and V.M.D. (2007): Equine Medications, Revised Ed., Blood Horse Publication, Lexington, KY. Copy right

Freeman, S.L. and England, G.C.W. (2000): Investigation of romifidine and detomidine for the clinical sedation of horses. Vet. Rec. 147: 507-511.

Freeman, S.L.; Bowen, I.M.; Bettschart-Wolfensberger, R.; Alibhai, H.I. and England, G.C.W. (2002): Cardiovascular effect of romifidine in standing horse. Res. Vet. Sci, 72: 123-129.

Gathuys, F., Martens, A. and Goossens, L. (1996): Quantitative and qualitative study of the diuretic effects of romifidine in the horse. J. Vet. Anest., 23:6-10.

Hall, L.W., Clarke, K.W. and Trim, C.M. (2001): Veterinary anaesthesia.10th Ed. W. B., Saunders, P: 83- 91

Hamm, D.; Turchi, P and Jochle, W. (1995): Sedative and analgesic effects of detomidine and romifidine in horses. Vet. Rec., 136:324-327.

Jeffrey, A.N., Deyoung, M.B., Sumpter, T.L., Traynor, J.R., Lewis, J.W. and Wood, J.H. (1999): Opiod Receptor Effects of Butrophanol in Rhesus Monkeys. Pharmacology and Experimental therapeutics, Vol.290, Issue1, 259-265.

Katterman, T., Jaworek, D. and Moller, G. (1984): Multicentre study of a new enzymatic method of cholesterol determination. J.Ciln.Chem.Biochem. 22:245.

Kinjavdekar, P., Aithsal, H.P., Amarpal, Pawde, A.M., Pratap, K. and Singh, G.R. (2006): Potential effects of romifidine with lidocaine administration in goats. Small Ruminant Research, 64:923-304.

Kinjavdekar, P., Singh, G.R., Amarpal, Aithsal, H.P. and Pawde,A.M. (2001): Physiologic and biochemical effects of sub arachonoidally administered xylazine and medetomidine in goats. Small Ruminant Research, Nov.1; 38(3): 217-228.

Kumar, A. and Singh, H. (1978): Xylazine as a sedative and analgesic agent in equine surgery. Ind. J. Health, 17: 7-11.

LeBlanc, P.H. and Caron, J.P. (1990): Clinical use of epidural xylazine in the horse. Eq. Vet. J., 23: 180-181.

Leist, M., Gantner, F., Bohlinger, I., Tiegs, G., Germann, P.G. and Wendel, A. (1995): Tumor necrosis Factor-induced hepaocyte apoptosis procedes liver failure in experimental murine shock models Am.J.Pathol.,146; 1220-1234.

MacDonald, E. Scheinin, H. and Scheinin, M. (1988): Behavioural and Neurochemical effects of Medetomidine, A novel Veterinary Sedative, Eur.J.Pharmacd, 158:119-127.

Marieb, E. 2001): Human Anatomy and Physiology, San Francisco: Benjamin Cummings, 414 ISBN, 8053-4989.

Masaki, T., Chiba, S., Yasuda, T., Noguchi, H., Kakuma, T., Watanabe, T., Sakata, T. and Yoshimatsu, H. (2004): Involvement of Hypothalamic Histamine H1 Receptor in the regulation of feeding rhythm and obesity: Diabetes, 53:2250-2260.

Maxine, M and Benjamine, B.S. (1985): Outline of veterinary clinical pathology 3rdedition, Colorado State University.

Mollet, A., Lutz, T.A., Meier, S., Riediqer, T., Rushing P.A. and Scherrer, E. (2001): HistamineH1 Receptors Medistee the anorectic action of the pancreatic hormone amylin A J Physiolo Regul. Intergr Comp Physiol.281:R1442-R1448.

Naylor, J.M., Garven, E. and Fraser, L.A. (1997): Comparison of romifidine and xylazine in foals: the effects on sedation and analgesia. Equine Veterinary Journal, V.9, N. 6, P. 329-334.

Nouh, S.R. and Abdel-Wahed, R.E. (2000): Romifidine as sedative premedication before thiopentone and ketamine anaesthesia in donkeys. 7th world Cong. Vet. Anaesth. Berne Sept. 20-23.

Reitman, S. and Frankel, S. (1957): A colorimetric method for dermination of serum glutamicoxaloacetic and glutamic pyruvic transaminase.AM. J.Clin. Pathol., 15:56-63.

SAS (1987): Statistical Analysis System. Users Guide: Statistics. SAS Institute Cary, North Carolina.

Schatzman, M.; Armbrusten, S.; Stuchi, F.; Busato, A. and Kohler, L. (2001): Analgesic effect of butorphanol and levomethadone in detomidine sedated horse. J. Vet. Med. A. Physiol. Pathol. Clin. Med. Aug., 48.

Selmi, A.L., Barbudo- Selmi, G.R., Moreira, C.F., Martins, C.S., Lins, B.T., Mendes, G.M. and McManus,C.(2002): Evaluation of sedative and cardiorespiratory effects of romifidine and romifidine- butrophanol in cats. J. Am. Med. Assoc., 15; 221(4):506-510.

Selmi, A.L.; Barbudo-Selmi, G.R.; Martins, C.S. and Moreira, C.F. (2001): Effect of I.M romifidine/butorphanol administration in cats with and without atropine. World Small. Veterinary Association, World Congress. Vancouver.

Short, C.E. (1987): Principale and Practice of Veterinary Anaesthesia. 1st Ed.,Williams and Wilkins, Baltimore, London, Los Angeles, Sydney.

Short, C.E. (1992): Alpha 2-agonists in animals. Veterinary practice publishing company, Santa Barbara, California, USA.

Strubbe, J.H. (1989): Central nervous system and insulin secretion, Neth. J, Med., 34:154-167.

Taylor, P.M. (1985): Chemical restraint of the standing horse. Equine Vet.J. 17:269-273.

Taylor, P.M., Browning, A.P. and Harris, C.P. (1988): Detomidine-butorphanol sedation in equine clinical practice. Vet. Rec. October; 8(123): 388-390.

Thurmon, J.C.; Tranquili, W.J. and Benson, G.J. (1996): Lumb and Jones. Veterinary anaesthsia. 3rd Ed. Williams and Wilkins Co., Lea and Febiger.

Trinder, P. (1969): Determination of glucose in blood using glucose oxidase with an alternative oxygen acceptor.Ann.Clin.Biochem. 6:24.

Tsuda, K., Yoshimatsu, H., Nijma, A., Chiba, S., Okeda, T. and Sakata, T. (2002): Hypothalamic Histamine Neurons Activate Lypolysis in Rat Adipose Tissue, Experimental biology and Medicine 227:208-213.

Virtanin,R.(1989): Pharmacological Profiles of Medetomidine and its Antagonist, atinpauezole, Acta.Vet. Scand., 85:29-37.

Wagner, A.E.; Muir, W.W. and Hinchcliff, K.W. (1991): The cardiovascular effects of xylazine and detomidine in horses. Vet. Surg., 20(1), 82.

Wasak, A. (1983): Haematological and Electrocardiograaphical Changes in dogs after Xylazine. Med.Weter, 39: 235-237.

Watling, K.J. (1998): The RBI Handbook of Receptor Classification and Signal Transduction, 3rd ED.

Yamashita, K.; Tsubakishita, S. and Futaok, S. (2000): Cardiovascular effectes of medetomidine detomidine and xylazine in horses. J. Vet Med Sci; 62: 1025-1032.

Zijlstra, N.C. (1961): Determination of haemoglobin. Clin.Chem.Acta, 5:719-720.

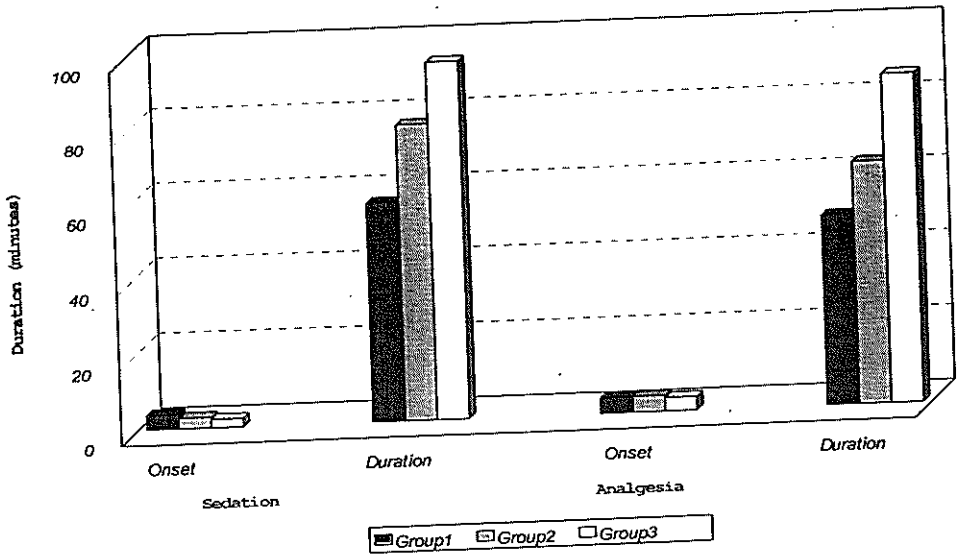

Fig. (1): Showing Onset and duration period of sedation and analgesia pre- and post-i/v injection of 3 different doses of anaesthetic drugs combination.

Table (1): Showing onset and duration period of sedation and analgesia pre- and post- i/v injection of 3 different doses of romifidine- butrophanol combination

Anaesthetic drugs combination	Sedation		Analgesia	
	Onset	Duration	Onset	Duration
	Mean ±SE	Mean ±SE	Mean ±SE	Mean ±SE
Romifidine (40 ug/Kg B. W) + Butrophanol (20 ug/Kg B. W)	3.75±0.10 A	58.25±1.65 C	4.25±0.32 A	50.50±2.10 C
Romifidine (60 ug/Kg B. W) + Butrophanol (30 ug/Kg B. W)	2.83±0.12 B	79.00±1.68 B	4.25±0.32 A	64.50±1.55 B
Romifidine (80 ug/Kg B. W) + Butrophanol (40 ug/Kg B. W)	2.25±0.14 C	95.75±2.17 A	3.58±0.22 A	88.00±1.08 A

Means within the same column carrying different litters are significantly different at ($P < 0.05$)
Number of animal per group = 4

Table (2): Showing rectal temperature, pulse and respiratory rate pre- and post- i/v injection of 3 different doses of romifidine- butrophanol combination.

Anaesthetic drugs combination			Temperature °C	Pulse rate/mint	Respiratory rate/mint
			Mean ± SE	Mean ± SE	Mean ± SE
Romifidine (40 ug/Kg B. W) + Butrophanol (20 ug/Kg B. W)	Baseline		37.60±0.22 CDE	40.00±0.71 BC	27.00±5.69 A
	After	15 minutes	37.80±0.22 ABCD	28.00±0.82 IJ	17.00±1.08 BCD
		30 minutes	37.53±0.19 DEF	29.00±1.08 I	16.00±0.41 CDE
		60 minutes	37.48±0.17 DEF	36.00±1.08 GF	12.00±0.71 EF
		90 minutes	37.33±0.09 EF	41.00±1.08 B	10.00±0.41 F
		120 minutes	37.48±0.11 DEF	44.00±1.22 A	18.00±0.71 BCD
Romifidine (60 ug/Kg B. W) + Butrophanol (30 ug/Kg B. W)	Baseline		37.98±0.09 ABC	40.50±0.65 BC	21.50±0.65 B
	After	15 minutes	37.78±0.09 ABCD	38.75±0.48 BCE	18.50±0.65 BCD
		30 minutes	37.40±0.09 DEF	35.25±0.63 GF	16.00±0.41 CDE
		60 minutes	37.20±0.09 F	36.50±0.65 GFE	15.00±0.41 CDE
		90 minutes	37.50±0.04 DEF	38.50±0.65 CDE	16.75±0.48 BCDE
		120 minutes	37.63±0.09 CDE	39.30±0.24 BC	18.00±0.41 BCD
Romifidine (80 ug/Kg B. W) + Butrophanol (40 ug/Kg B. W)	Baseline		38.05±0.06 AB	40.00±0.41 BCD	21.50±0.65 B
	After	15 minutes	38.15±0.06 A	26.25±0.48 J	18.25±0.48 BCD
		30 minutes	37.75±0.06 BCD	29.25±0.48 I	15.50±0.65 CDE
		60 minutes	37.48±0.09 DEF	31.50±0.65 H	14.00±0.71 DEF
		90 minutes	37.68±0.07 BCDE	34.75±0.85 G	17.75±0.85 BCD
		120 minutes	37.80±0.09 ABCD	37.50±0.65 DEF	19.00±0.41 BC

Means within the same column carrying different litters are significantly different at (P < 0.05) Number of animal per group = 4

Table (3): Showing the blood picture pre- and post- i/v injection of 3 different doses of romifidine- butrophanol combination

Anaesthetic drugs combination	Group	Treatment	RBCs Million/mm³	WBCs Thousands /mm³	PCV %	Hb g/dl	Lymphocyte %	Neutrophils %	Eosinophils %	Monocyte %
			Mean ±SE	Mean ±SE	Mean ±SE	Mean ±SE	Mean ±SE	Mean ±SE	Mean ±SE	Mean ±SE
Romifidine (40 ug/Kg B. W) + Butrophanol (20 ug/Kg B. W)	Baseline		6.02 ±0.06 C	8.00 ±2.00 G	42.00±0.71 AB	14.00±0.16 A	64.00±0.41 FG	21.00±0.41 G	7.00±0.41 AB	8.00±0.41 CD
	After	15 minutes	5..30 ±0.04 D	10.00 ±1.60 E	39.75±0.63 BC	13.10±0.11 AB	58.00±0.41 I	27.00±0.41 AB	6.00±0.41 BC	9.00±0.41 BC
		30 minutes	5.00 ±0.04 D	7..95 ±1.25 C	37.25±0.48 DE	9.63±2.48 C	67.00±0.41 CD	22.00±0.41 FG	4.00±0.41 DE	7.00±0.41 DE
		60 minutes	4..90 ±0.01 E	9..30 ±1.29 F	34.75±0.63 F	11.20±0.07 BC	65.00±0.41 EF	28.00±0.41 A	4.00±0.41 DE	3.00±0.41 I
		90 minutes	5.40 ± 0.08 D	9.75 ±1.50 C	38.00±0.41 CDE	12.60±0.07 AB	69.00±0.41 AB	23.00±0.41 EF	8.00±0.41 A	6.00±0.41 EFG
		120 minutes	6.00 ±0.08 C	10.75 ±0.06 E	40.00±0.41 BC	13.30±0.11 A	70.00±0.41 A	21.00±0.41 G	3.00±0.41 EF	5.00±0.41 FGH
Romifidine (60 ug/Kg B. W) + Butrophanol (30 ug/Kg B. W)	Baseline		5.80 ± 0.07 D	12.60 ±0.40 C	40.00±0.41 BC	13.30±0.04 A	67.00±0.41 CD	22.00±0.41 FG	5.00±0.41 CD	7.00±1.08 ED
	After	15 minutes	5..30 ±0.07 D	13.00 ±2.0 B	38.00±0.41 CDE	12.60±0.04 AB	60.00±0.41 H	24.00±0.41 DE	6.00±0.41 BC	9.25±0.85 BC
		30 minutes	5.00 ± 0.07 D	7.10±0.40 C	34.00±0.82 F	11.30±0.08 BC	63.00±0.41 G	25.00±0.41 CD	5.00±0.41 CD	6.50±0.65 EF
		60 minutes	5.10 ±0.07 D	9.80 ±0.40 A	33.75±0.85 F	12.00±0.04 AB	66.00±0.41 DE	25.00±0.41 CD	4.00±0.41 DE	4.50±0.65 GHI
		90 minutes	5.40 ± 4.08 D	9.40 ±0.40 C	44.00±1.22 A	12.45±0.05 AB	70.00±0.41 A	24.00±0.41 DE	2.00±0.41 F	3.50±0.65 HI
		120 minutes	6.70 ± 0.02 C	9.60 ±0.40 C	43.25±0.48 A	13.52±0.24 A	68.00±0.41 B	22.00±0.41 FG	4.00±0.41 DE	4.00±0.41 HI
Romifidine (80 ug/Kg B. W) + Butrophanol (40 ug/Kg B. W)	Baseline		6.00 ± 0.02 C	14.00 ±2.7 A	44.00±0.41 A	14.00±0.04 A	65.75±0.48 DE	24.00±0.41 DE	7.25±0.48 AB	9.00±0.41 BC
	After	15 minutes	5..50 ± 0.040 D	11.80 ±3.43 D	40.00±0.71 BC	13.70±0.04 A	64.75±0.48 EF	26.00±0.41 BC	7.00±0.41 AB	10.00±0.41 AB
		30 minutes	5.30 ±0.04 D	11.20 ±3.43 D	38.00±0.41 CDE	13.30±0.08 A	60.00±0.41 H	27.00±0.41 AB	6.75±0.48 AB	11.00±0.41 A
		60 minutes	5.00 ±0.040 D	11.00 ±2.55 D	36.00±0.41 EF	13.00±0.00 AB	63.00±0.41 G	25.00±0.41 CD	5.00±0.41 CD	9.00±0.41 BC
		90 minutes	7.55 ±0.02 B	11.50 ±3.40 D	39.00±0.41 BCD	13.40±0.08 A	64.75±0.48 EF	24.75±0.48 CD	6.00±0.41 BC	8.00±0.41 CD
		120 minutes	9.17 ±0.03 A	11.80 ± 4.82 D	43.25±1.97 A	13.90±0.00 A	67.00±0.41 CD	24.75±0.48 CD	7.00±0.41 AB	7.00±0.41 DE

Means within the same column carrying different litters are significantly different at (P < 0.05) Number of animal per group = 4

Table (4): Showing ALT, AST, Total protein, Albumin, Globulin, Albumin/Globulin ration pre- and post- i/v injection of 3 different doses of romifidine- butrophanol combination

Anaesthetic drugs combination	Group	Treatment	ALT µ/L	AST µ/L	Total protein	Albumin	Globulin	Albumin/Globulin ratio
			Mean ±SE	Mean ±SE	Mean ±SE	Mean ±SE	Mean ±SE	Mean ±SE
Romifidine (40 ug/Kg B. Wt) + Butrophanol (20 ug/Kg B. Wt)	Baseline		10.00±0.41 ED	23.00±1.08 B	7.15±0.06 H	4.00±0.04 H	3.15±0.06 EF	1.27±0.03 FG
	After	15 minutes	16.50±0.29 H	16.50±0.65 EF	7.50±0.04 G	4.20±0.04 G	3.30±0.00 CDE	1.27±0.01 FG
		30 minutes	8.00±0.41 FGH	15.25±1.89 FG	8.50±0.07 C	5.00±0.04 B	3.50±0.04 C	1.43±0.01 DEF
		60 minutes	7.00±0.41 GHI	13.25±0.25 G	8.70±0.04 B	4.50±0.08 ED	4.20±0.11 B	1.07±0.05 H
		90 minutes	5.88±0.24 I	19.00±0.41 D	8.40±0.07 C	3.80±0.04 I	4.60±0.11 A	0.83±0.03 I
		120 minutes	8.50±0.29 EFG	24.00±1.73 AB	6.50±0.11 J	4.20±0.04 G	2.30±0.11 G	1.84±0.09 B
Romifidine (60 ug/Kg B. Wt) + Butrophanol (30 ug/Kg B. Wt)	Baseline		11.50±1.55 CD	23.00±0.41 B	7.60±0.08 FG	5.30±0.04 A	2.30±0.04 G	2.31±0.02 A
	After	15 minutes	7.88±0.52 GH	16.00±0.41 EF	8.20±0.04 D	4.80±0.04 C	3.40±0.00 CD	1.41±0.01 EF
		30 minutes	16.58±0.06H	19.00±0.41 D	7.50±0.08 G	5.10±0.04 B	2.40±0.04 G	2.13±0.02 B
		60 minutes	16.65±0.12H	10.25±0.25 H	6.80±0.11 I	4.80±0.04 C	2.00±0.15 H	2.45±0.22 A
		90 minutes	8.75±0.48 EF	16.00±0.41 EF	7.80±0.04 EF	4.80±0.04 C	3.00±0.00 F	1.60±0.01 CD
		120 minutes	11.25±0.25 CD	19.00±0.71 D	8.00±0.07 DE	5.00±0.04 B	3.00±0.04 F	1.67±0.02 C
Romifidine (80 ug/Kg B. Wt) + Butrophanol (40 ug/Kg B. Wt)	Baseline		12.00±0.41 C	26.00±0.41 A	7.50±0.04 G	4.30±0.04 FG	3.20±0.08 DEF	1.35±0.05 FG
	After	15 minutes	9.00±0.41 EF	20.00±0.41 CD	7.80±0.04 EF	4.50±0.04 ED	3.30±0.00 CDE	1.36±0.01 FG
		30 minutes	8.00±0.41 FGH	22.00±0.41 BC	8.20±0.08 D	5.00±0.04 B	3.20±0.04 DEF	1.56±0.01 CDE
		60 minutes	14.00±0.71 A	18.00±0.41 DE	8.90±0.04 A	4.80±0.04 C	4.10±0.00 B	1.17±0.01 GH
		90 minutes	13.00±0.41 AB	23.00±0.41 BC	8.10±0.04 D	4.60±0.04 C	3.50±0.00 C	1.31±0.01 FG
		120 minutes	11.25±0.25 CD	24.00±0.41AB	7.80±0.04 EF	4.40±0.04 EF	3.40±0.00 CD	1.29±0.01 FG

Means within the same column carrying different litters are significantly different at ($P < 0.05$) Number of animal per group = 4

Table (5): Showing Glucose, Cholesterol, Triglycerides, Creatine, Urea and Blood urea nitrogen pre- and post- i/v injection of 3 different doses romifidine- butrophanol combination.

Anaesthetic drugs combination			Glucose mg/dL	Cholesterol Mg/dL	Triglycerides Mg/dL	Creatinine Mg/dL	Urea Mg/dL	Blood urea nitrogen Mg/dL
			Mean ±SE	Mean ±SE	Mean ±SE	Mean ±SE	Mean ±SE	Mean ±SE
Romifidine (40 ug/Kg B. Wt + Butrophanol (20 ug/Kg B. Wt	Baseline		122.00±0.71 A	118.00±0.41 K	120.00±0.41 J	1.00±0.0 I 4	58.00±0.41 F	27.15±0.02 EF
	After	15 minutes	131.50±0.65 F	120.00±0.41 J	136.00±0.41 G	1.10±0.04 HI	65.00±0.41 C	30.38±0.07 C
		30 minutes	148.00±0.41 B	130.00±0.71 I	122.00±0.71 I	1.40±0.07 EF	62.00±0.41 D	28.97±0.00 D
		60 minutes	152.00±0.61 E	140.00±0.41 G	124.00±0.82 H	1.28±0.06 GH	50.00±0.41 I	23.36±0.01 I
		90 minutes	147.00±0.65 GI	165.00±0.41 C	125.00±0.41 H	1.20±0.08 GH	54.00±0.41 H	25.23±0.00 HG
		120 minutes	130.00±0.71 L	148.00±0.41 E	150.00±0.41 C	1.10±0.08 HI	48.00±0.41 J	26.43±0.00 F
Romifidine (60 ug/Kg B. Wt + Butrophanol (30 ug/Kg B. W)	Baseline		116.00±0.41 C	112.00±0.71 L	120.00±0.41 J	1.10±0.04 HI	49.00±0.41 IJ	26.17±0.01 FG
	After	124.00±0.41 IG	97.00±0.41 IG	133.00±1.08 H	142.00±0.82 E	1.90±0.04 A	56.00±0.41 G	30.37±0.01 C
		134.00±0.41 D	114.00±0.41 D	135.00±0.71 H	154.00±0.71 B	1.70±0.11 BC	65.00±0.41 C	32.71±0.00 A
		155.00±0.65 O	78.00±0.41 O	173.00±1.08 A	138.00±1.08 F	1.60±0.07 CD	70.00±0.41 B	24.77±0.00 H
		148.00±0.54 M	90.00±0.41 M	173.00±0.41 A	100.00±0.41 L	1.50±0.04 DE	53.00±0.71 H	22.80±0.00 I
		137.00±0.41 N	84.00±0.41 N	168.25±0.48 B	98.00±0.41 M	1.20±0.07 GH	65.00±0.71 C	30.37±0.01 C
Romifidine (80 ug/Kg B. Wt + Butrophanol (40 ug/Kg B. Wt	Baseline		119.00±0.41 B	122.00±0.82 J	110.00±0.41 K	1.30±0.04 FG	60.00±0.41 E	28.00±0.82 ED
	After	15 minutes	130.00±0.41 G	140.00±0.82 G	122.00±0.71 I	1.80±0.04 AB	66.00±0.71 C	33.00±0.82 A
		30 minutes	142.00±0.48 E	143.00±1.22 F	136.00±0.41 G	1.90±0.04 A	70.00±0.41 B	31.00±0.41 B
		60 minutes	148.00±0.41 I	152.00±0.82 D	144.00±0.71 D	1.60±0.04 CD	75.00±0.82 A	32.00±0.82 AB
		90 minutes	153.00±0.65 GK	148.00±0.82 E	156.00±0.41 A	1.70±0.04 BC	69.00±0.82 B	29.00±0.41 D
		120 minutes	132.00±0.41 KL	141.00±0.82 FG	150.00±0.41 C	1.50±0.04 DE	66.00±0.82 C	27.00±0.41 E

Means within the same column carrying different litters are significantly different at ($P < 0.05$) Number of animal per group = 4

الملخص العربى

تقييم التأثير المهدئ و المسكن وصورة الدم الفسيوبيوكيميائية للحقن الوريدي لخليط عقار الروميفيدين و البيتروفينول في الخيول

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استهدفت هذه الدراسة تقييم التأثير المهدئ و المسكن للألم وصورة الدم الفسيوبيوكيميائية لخليط منبهات الفا٢(الروميفيدين) و البيتروفينول عند حقنهم في الوريد. تم إجراء هذه الدراسة على عدد ١٢ من الخيول السليمة إكلينيكيا بحقنها في الوريد بخليط الروميفيدين و البيتروفينول بجرعات مختلفة . قسمت الخيول علي حسب الجرعة إلي ثلاث مجموعات شملت كل مجموعة عدد ٤ خيول و هي كالتالي:-

المجموعة ألا لي: تم حقنها بخليط الروميفيدين (٤٠ميكروجرام \ كيلوجرام من وزن الحيوان) و البيوتورفانول(٢٠ميكروجرام \ كيلوجرام من وزن الحيوان).

المجموعة الثانية: تم حقنها بخليط الروميفيدين (٦٠ميكروجرام \ كيلوجرام من وزن الحيوان) و البيوتورفانول(٣٠ميكروجرام \ كيلوجرام من وزن الحيوان) .

المجموعة الثالثة: تم حقنها بخليط الروميفيدين(٨٠ميكروجرام \ كيلوجرام من وزن الحيوان) و البيوتورفانول(٤٠ميكروجرام \ كيلوجرام من وزن الحيوان) .

وقد تم ملاحظة التغيرات الإكلينيكية مثل معدلات التنفس والنبض ودرجه حرارة الجسم قبل وبعد الحقن وكذلك تم قياس معدل التغير في إنزيمات وظائف الكبد خصوصا إنزيم اسبرتيت أمنيو ترانسفيراز وكذلك ألانين أمنيو ترانسفيراز و مستوى البروتين الكلي والآلبيومين و الجلوبيولين وجلوكوز الدم وكذلك مستوى الكولسترول و البولينا و نيتروجينات البولينا في الدم ونسبة الهيموجلوبين و حجم الخلايا المرصوصة وكذلك عدد خلايا الدم الحمراء و البيضاء ونسب خلايا الدم البيضاء المختلفة. ظهرت علامات الهدوء والسكينة لخليط منبهات الفا٢(الروميفيدين) و البيتروفينول عند حقنهم في الوريد مباشرة.

و كانت علامات الهدوء أكثر وضوحا مع زيادة في الترنح وزيادة ملحوظة في تدلى الرأس .

أما فترة التخدير (فقد الألم) فكانت أطول لخليط الروميفيدين مع البيوتورفانول في المجموعة الثالثة.و لوحظ أن هناك نقص معنوي في نبض وتنفس الحيوانات.وكذالك تغيرات معنوية واضحة في نتائج تحاليل الدم الفسيوبيوكيميائية و لكنها عادت إلي طبيعتها التي قبل الحقن.