CHAPTER V

DISCUSSION AND CONCLUSIONS

Central α_2 adrenoceptors, once activated by their selective agonists, decrease norepinephrine release leading to CNS depression (10). Sedative effect of these drugs benefits in reduction of anesthetic consuming and side effects in veterinary practice. Alpha$_2$ adrenergic agonists are practically used as equine chemical restraint and premedication for decades. However, differences in anatomy, behavior, physiology and also pharmacology amongst equine species are recognized. Thus, a protocol for horse anesthesia is not entirely suitable for mules. It is also much more unpredictable with feral animals such as untrained-young mules. While there are number of published data of using xylazine and detomidine in horse premedication, very limited information is available for this horse-donkey hybrid species. Detomidine is much more selective to α_2 adrenoceptors than xylazine (65), hence; it has more potent in sedation and analgesia (38). At equivalent sedative dose to xylazine, detomidine is known for its longer lasting effect (15). For these reasons, comparing between xylazine and detomidine in mules premedication was investigated in this study aiming to establish a suitable premedication protocol for mules.

The study was conducted with mule stallions undergoing castration as it was a repeated, standardized procedure which allowed comparison of the two drugs. The age and body weight between groups were not differences. Doses of both α_2 agonists were assigned based on 1.5 times of those recommended with equality of

their sedative action in horses (18-21). Most of the results revealed similar quality of sedation prior to thiopental induction and quality of thiopental anesthesia between the two drugs. Although the sedation score was given higher, the head fell down more, and the induction time was found significantly slightly shorter in group XY compare to group DET, this has no clinical significance to the author's point of view as it did not affect to the qualities of induction, maintenance, and recovery. Head lowering ratio result in this study was in agreement to a previous report (66) that the group XY significantly dropped the head lower than the group DET.

Changes in cardiopulmonary system are one of the major adverse effects of α_2 agonists reported in mammals. Activating α_2 adrenoceptors centrally and presynaptically reduces sympathetic tone and subsequently causes bradycardia and hypotension (34, 43, 67). CNS depression after administration of α_2 agonists causes bradypnea (34, 43, 67). In our study, the baseline values of HR, PR and RR were measured while the mules were in the resting stage one day before the operation. It was very difficult to measure indirect MABP because of the mule's excitement with the procedure at their rear and it was impossible to measure direct MABP during their consciousness. Thus there was no MABP baseline data in our study. HR, PR, RR and MABP were also unable to perform during sedation stage as the procedures would interfere the sedation quality and the consequent anesthetic induction. Therefore, cardiovascular parameters were obtained under unconscious condition after the mules were under general anesthesia except MABP. Whilst xylazine induced more profound bradycardia, detomidine have no such an effect but, instead, slightly tachycardia and tachypnea after 20 minutes of lateral recumbency. Because of unavailable baseline MABP data, it is impossible to define whether the mules were in hypo- or

hypertension. However, when compared to the conscious horse MABP (22), our anesthetized mules were seemed to be hypertension, especially in group DET that had higher MABP than group XY at every time point. If this was true, the MABP result would not in agreement to the previous reports in horses that both xylazine and detomidine suppress cardiopulmonary function including blood pressure (61, 68). However, the elevation of MABP parameters in both groups could result from, firstly, stimulation of α_1 adrenoceptors in case of excessive doses of the α_2 agonists, and secondly, visceral pain induction during the operation. To the authors' view, the dose of detomidine (0.03 mg/kg) in this study was not too excessive as it is still in the range that was acceptable to use in horses while xylazine dose was far more than the recommendation for horses. Thus elevation of MABP in group DET through the activation of α_1 adrenoceptors by excessive detomidine was not reasonable. It was possible that the castration procedure without local or regional anesthesia caused visceral pain that overcame analgesic effect of xylazine and detomidine at these doses because both RR and MABP data were higher during the operation.

It has been reported that donkeys have higher metabolic activity for several drugs than horses such as sulfamethoxazole. This may result from the different cytochrome P450 isoenzyme of hepatic metabolism, the drug plasma protein binding, and hepatic blood flow between the two species (69-70). Mules are crossbred between horses and donkeys, it is reasonable to consider that the metabolic rate of several drugs, including α_2 agonists, in mules may also be higher than in horses although there has not yet been any confirmation.

Additional sedative may be considered in combination with α_2 adrenergic agonists. Phenothiazines such as acepromazine at dose of 0.04 mg/kg IV has been recommended to tranquilize horses before premedication (18, 71). In case that the acclimatization is not possible, administration of acepromazine may be helpful to calm down the animal before premedication. In case of excited mules, they may need higher dose of sedatives similarly to exercising horses because of lower peak plasma drug concentration and slower rate of elimination when compared to the horses in resting stage (72). Higher cardiac output during and after exercise alters drug delivery to target tissues such as the brain by increasing blood flow to skeleton muscles (73) and reduced the drug plasma concentration (72, 74). Thus the drug delivers to the target organs is less than 30% of which in the resting stage (73). Therefore exercising horses need more dose requirements drugs for rapid acting of central nervous system (72, 75).

In overall, xylazine at 1.6 mg/kg and detomidine at 0.03 mg/kg delivered satisfied and comparable premedication effects for thiopental anesthesia in mules. Detomidine at this dose apparently had slightly cardiopulmonary suppress less than xylazine at this dose but perhaps not as good in analgesia as xylazine based on the increasing of cardiopulmonary parameters during the operation. Higher premedicative doses of detomidine should be further investigated to find an optimum point for a better analgesia with minimal cardiopulmonary effects. Another option is combination of other protocols for pain management concomitant to α_2 agonists premedication.