

Study on occurrence of aldosterone breakthrough in dogs

Abstract of Doctoral Thesis

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Aldosterone breakthrough (ABT) is observed during renin-angiotensin-aldosterone system (RAAS) suppression therapy using angiotensin-converting enzyme inhibitor (ACEI) and angiotensin II receptor blocker (ARB). Therefore, in human patients, a mineralocorticoid receptor antagonist (MRA) has been used in combination with an ACEI or ARB to prevent the adverse effects caused by excess aldosterone. However, there are few study that investigate the usefulness of MRA in dogs. Therefore, the objective of the present study was to determine if alacepril or telmisartan has a long duration of suppressive effects on drug-induced RAAS activation in dogs. In addition, this study investigated whether MRA has organ-protecting actions on drug-induced RAAS activation in dogs. Finally, this study investigated whether ABT occurs in dogs with proteinuric kidney disease during telmisartan therapy.

Firstly, the objective of this study was to determine if alacepril has a long duration of action for inhibition of drug-induced RAAS activation in normal dogs. As a result, alacepril temporarily suppressed drug-induced RAAS activation but its clinical application may be limited by its duration of action. In light of this decrease in RAAS inhibitory activity with time, it is possible that ABT occurred.

Secondly, this study investigated whether telmisartan has suppressive effects on drug-induced RAAS activation in dogs. As a result, telmisartan did not fully suppress drug-induced RAAS activation. Therefore, it is necessary to consider the existence of ABT during the ARB therapy in dogs.

Thirdly, the objective of this study was to investigate whether MRA (spironolactone, eplerenone) has organ-protecting actions on drug-induced RAAS activation in dogs. As a result, spironolactone (2 mg/kg, at either q24 h or q12 h, PO) temporarily decreased serum galectin-3 concentration as a biomarker for tissue fibrosis in dogs with drug-induced RAAS activation. Therefore, administration of spironolactone at this dosage could be useful for the organ-protecting actions.

Finally, this study investigated whether ABT occurs in dogs with proteinuric kidney disease during telmisartan therapy. As a result, ABT occurred in dogs with proteinuric kidney disease during RAAS suppression therapy.

In conclusion, this study confirmed that ACEI or ARB dose not fully suppress drug-induced RAAS activation in dogs. Moreover, it becomes clear that ABT is associated with these results. In addition, this study indicated that administration of spironolactone could be useful for the organ-

protecting actions in dogs with drug-induced RAAS activation. Finally, the present study revealed that ABT occurred in dogs with proteinuric kidney disease during RAAS suppression therapy.