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Management of secondary hypertension in dogs

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Abstract
Systemic hypertension is recognized as a common problem in elder dogs that results in Target organ damage (TOD). Early and efficient treatment plays a major role to lower the risk of TOD and to avoid hypertensive emergencies. Twelve severely hypertensive (≥ 180 mm Hg) client-owned dogs with chronic kidney disease stage II (Scr. 1.4-2.8 mg/dl) were divided randomly into two groups *viz*., Group I and II with 6 dogs each, and were treated with benazepril (Angiotensin-converting enzyme) and amlodipine (Calcium channel blocker) in group I and with telmisartan (Angiotensin receptor blocker) and amlodipine in group II dogs for 30 days along with other common conventional therapy for all the dogs. Though there was an improvement in both groups, an overall relative improvement in blood pressure along with the clinical signs was seen at a faster rate with complete clinical recovery among group II dogs in comparison with group I dogs.

Keywords: secondary hypertension, chronic kidney disease, antihypertensives, dog

1. Introduction
Systemic hypertension (SHT) is defined as the persistent elevation of systolic arterial blood pressure (SBP) beyond 150 mmHg [1]. Undiagnosed elevations in blood pressure will over-perfuse the organs (barotrauma) thereby affecting multiple organ systems and is usually referred to as Target organ damage (TOD) or end-organ damage and the presence of TOD is typically a significant sign to begin antihypertensive therapy [2]. Hypertension that occurs due to other diseases/conditions is termed as secondary systemic hypertension [2]. CKD has the greatest correlation with SHT. Renal disease is the most typical cause of systemic hypertension in dogs and kidneys were primarily responsible for TOD [3]. SHT was reported to occur in 50% to 93% of dogs with renal failure and approximately 85% of dogs with glomerular disease [4]. Renin-angiotensin-aldosterone system (RAAS) inhibitors and calcium channel blockers (CCB) are the most extensively suggested medications for managing hypertension in dogs. [5]. In general, ACE inhibitors are suggested as the primary treatment option for hypertensive dogs. Alternative RAAS suppression techniques include angiotensin receptor blockers (ARB). However, for treating severely hypertensive dogs co-administration of RAAS inhibitor and CCB is appropriate [2].

2. Materials and Methods
The dogs of various breeds and gender aged over 6 years presented to the Veterinary clinical complex, Rajendranagar, Hyderabad were subjected to blood pressure measurements using a Vet Doppler BP machine. Twelve severely hypertensive dogs (> 180 mm Hg) with CKD stage II (Scr 1.4-2.8 mg/dl) were divided randomly into two groups *viz*., Group I and Group II with 6 dogs each and treated with two different combinations of antihypertensives *viz*., Group I received Benazepril @ 0.5 mg/kg b.wt P/O and Amlodipine @ 0.2 mg/kg P/O whereas, Group II dogs received Telmisartan @ 1mg/kg b.wt P/O and Amlodipine @ 0.2 mg/kg b.wt P/O for 30 days. However, supportive treatment for the underlying cause was also given for both groups. The clinical efficacy of various drugs in the management of hypertension was evaluated by measuring SBP at weekly intervals for 4 weeks along with clinical improvement.

3. Results
The mean SBP of group I hypertensive dogs on day 0 was 197.50±6.05 mm Hg which was significantly (p<0.01) high as compared to apparently healthy (136.80±2.41 mm Hg) adult

dogs. Almost all the dogs were showing similar clinical signs, such as inappetence, epistaxis, vomiting, weakness, halitosis, polydipsia, weight loss, polyuria, pale conjunctival, and buccal mucus membrane. Following therapy with benazepril and amlodipine the mean SBP value decreased non-significantly to 188.50±5.15 mm Hg on day 7, and significantly (p<0.05) to 177.50±3.25 mm Hg, 167.00±3.33 mm Hg and 159.50±2.87 subsequently on day 14, 21 and 28, respectively (Table 1).

Table 1: Mean SBP alterations of apparently healthy and hypertensive dogs with chronic kidney disease group I on different days

Parameter	Apparently healthy (n=6)	Group-I (n=6)				
		0th day	7th day	14th day	21st day	28th day
SBP (mm of Hg)	136.80±2.41	197.50± 6.05**	188.50 ±5.15	177.50 ±3.25*	167.00 ±3.33*	159.50 ±2.87*

*Significant at (p<0.05)
**Significant at (p<0.01)

The mean SBP of group II hypertensive dogs on day 0 was 199.50±6.10 mm Hg which was significantly (p<0.01) high as compared to apparently healthy (136.80±2.41 mm Hg) adult dogs. Following therapy with telmisartan and amlodipine for 4 weeks the mean SBP value decreased significantly (p<0.01) to 179.50±4.81mm Hg on day 7 and further showed a significant (p<0.05) decline to 163.50±1.87 mm Hg, 158.50±1.87 mm Hg, and 152.50±1.65 mm Hg on day 14, 21 and 28, respectively (Table 2). Similarly, the improvement in clinical signs was also noticed early in group 2 dogs from day 7 and with a complete absence of signs by day 28.

Table 2: Mean SBP alterations of apparently healthy and hypertensive dogs with chronic kidney disease Group II on different days

Parameter	Apparently healthy (n=6)	Group-II (n=6)				
		0th day	7th day	14th day	21st day	28th day
SBP (mm of Hg)	136.80±2.41	199.50± 6.10**	179.50± 4.81**	163.50 ±1.87*	158.50 ±1.87*	152.50 ±1.65*

*Significant at (p<0.05)
**Significant at (p<0.01)

4. Discussion

According to Acierno *et al.* (2018) [2] RAAS inhibitors and CCB are administered together for the treatment of severely hypertensive dogs. In dogs with severe hypertension (SBP>180 mmHg) multidrug therapy was taken into consideration as a single drug is not sufficient for efficient SBP control (Choi *et al.*, 2022) [6]. In the present study the dosage used for various drugs *viz*., benazepril @ 0.5 mg/kg q12-24h, telmisartan @ 1 mg/kg q24h, amlodipine @ 0.2 mg/kg q24h were according to Acierno *et al.* (2018) [2]. However, all the dogs of Group I and Group II received common conventional therapy for chronic kidney disease.

Following treatment, hypertensive dogs of group I showed a significant (p<0.05) decrease in SBP on day 14 whereas hypertensive dogs of group II showed a significant (p<0.01) decrease in SBP as early as on day 7. These findings were in accordance with Priyanka *et al.* (2012) [7], Caro-Vadillo *et al.* (2018) [1], Miyagawa *et al.* (2020) [8], Fowler *et al.* (2021) [9] and Choi *et al.* (2022) [6]. ACEIs partially inhibit the production of angiotensin II leading to a phenomenon known as 'aldosterone breakthrough'. This occurs due to the continued release of angiotensin II from other sources, resulting in challenges in controlling high blood pressure [1]. In contrast, telmisartan, operating through a distinct mechanism, specifically attaches to the AT1 receptor and blocks the impact of angiotensin II, leading to the prevention of angiotensin II-induced narrowing of blood vessels and allowing for vasodilation. As a result, peripheral resistance decreases, leading to a subsequent reduction in blood pressure [10]. Choi *et al.* (2022) [6] also concluded that the combination therapy of telmisartan and amlodipine led to a more substantial decrease in SBP, especially within the first week of beginning the treatment. Although both groups have shown significant reduction in SBP along with clinical improvement during a 4-week treatment period, mean values of SBP on days 14, 21, 28 of group II improved more effectively when compared to the mean values of group I and thereby, indicating that the treatment given to group II was more effective in correcting the blood pressure.

5. Conclusion

This study suggests the utilization of different antihypertensive medications for managing severe hypertension in dogs. From the current study, it can be inferred that the combination of telmisartan and amlodipine is highly effective in the management of hypertension in dogs.

6. Acknowledgment

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