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Clinical efficacy of polyethylene glycol as an adjunct therapy for mild spinal injuries in dog

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Abstract

The present study investigated the clinical efficacy of polyethylene glycol (PEG 4000 Da) as an adjunct therapy for mild Spinal Cord Injury (SCI) in dogs. 16 dogs exhibiting clinical signs of SCI were randomly allocated into two groups. Group I received a 20% PEG solution (Four ml/kg IV) along with methylprednisolone sodium succinate (MPSS, 30 mg/kg IV) on the day of presentation, followed by a second PEG dose after 48 hours. Group II received MPSS alone. Both groups were treated with oral prednisolone acetate (1 mg/kg) for 10 days in tapering doses, along with supportive therapy for 30 days. Neurological, radiographic, and epidurographic assessments identified the thoracolumbar region as the most commonly affected site. Hematological and biochemical profiles remained largely unaffected by the treatment protocols, except for elevated alkaline phosphatase (ALP) levels. By end of study period, 87.5% of dogs in Group I regained ambulatory function compared to 62.5% in Group II. PEG administration significantly accelerated and improved recovery, highlighting its potential as an effective adjunct in canine SCI management.

Keywords: Spinal cord injury, Polyethylene glycol, MPSS, Epidurography

Introduction

Spinal Cord Injuries (SCI) are frequently encountered in canine practice and result from trauma or ischemia, leading to significant neurological dysfunction and long-term disability. The canine vertebral column consists of cervical, thoracic, lumbar, sacral, and coccygeal vertebrae, with the spinal cord running through the vertebral canal. SCIs are broadly classified into compressive types, caused by conditions such as intervertebral disc disease and spinal trauma, and non-compressive types, which are typically inflammatory in nature, such as degenerative myelopathy.

High-dose methylprednisolone sodium succinate (MPSS) has been the standard neuroprotective therapy, though its efficacy is limited and associated with significant side effects. Spinal surgeries in dogs are limited due to several factors, including the risks and potential complications associated with spinal cord procedures, the high cost of surgery, lack of owner compliance, and limited surgical expertise. Given these challenges, conservative management with effective therapeutic agents is crucial. Recent advancements highlight polyethylene glycol (PEG), a synthetic polymer capable of sealing damaged axons, reducing edema, and limiting glial scarring, offering promising therapeutic potential. This article focuses on PEG as an emerging treatment modality for canine SCI.

Materials and Methods

The present study was conducted on 16 dogs of varying age, breed, sex, and body weight, presented with clinical signs of spinal cord injury to the Veterinary Clinical Complex, Post Graduate Institute of Veterinary and Animal Sciences, Akola. The affected animals were randomly divided into two equal groups of eight dogs each. Dogs in Group I received an intravenous injection of methylprednisolone sodium succinate (MPSS) at a dose of 30 mg/kg body weight, along with a 20% solution of polyethylene glycol (PEG, molecular weight 4000 Da) at a dose of 4 ml/kg body weight on the day of presentation.

The PEG administration was repeated intravenously after 48 hours. This was followed by oral administration of prednisolone acetate at 1 mg/kg body weight in divided and tapering doses over subsequent 10 days. Dogs in Group II were treated with MPSS intravenously at 30 mg/kg body weight on the day of presentation, followed by oral prednisolone acetate at the same dosage regimen as Group I. All dogs were given supportive therapy with neurotrophic vitamin preparations containing mecobalamin at rate of 1500 µg daily orally and analgesic gabapentin at the rate of 3 mg/kg body weight for 30 days. The dogs of both groups were provided with antibiotic treatment and fluid therapy as and when needed. In animals with urine retention, bladder was catheterized to remove the urine, whenever required.

All dogs included in the study were subjected to physiological, clinical, neurological, haematological, and serum biochemical assessments. Physiological parameters recorded were rectal temperature, pulse rate, and respiratory rate.

Mental status was recorded as alert, depressed, or comatose. Posture was noted as recumbent, sitting, or standing with or without assistance. Gait was assessed by free movement and classified as normal, ataxic, paraplegic (with or without urine retention), or quadriplegic. The test for conscious proprioception and wheel barrowing reaction was conducted in standing animal. Spinal reflexes (Pedal reflex, patellar reflex, perineal reflex, cutaneous trunci reflex, tail wag reflex, hyperpathia) along with the muscle tone were assessed to record upper motor neuron (UMN) and lower motor neuron (LMN) involvement. Bladder function was assessed by abdominal palpation to evaluate bladder filling and ease of urine expulsion. The probable injury site and extent of damage were determined through neurological examinations and graded as proposed by Tartarelli *et al.*, 2005 [24] for each case.

Haematological investigations included haemoglobin concentration (g/dL), packed cell volume (%), total erythrocyte count ($\times 10^6/\text{mm}^3$), total leucocyte count ($\times 10^3/\text{mm}^3$), and differential leucocyte count (%). Serum biochemical parameters evaluated included calcium (mg/dL), phosphorus (mg/dL), alkaline phosphatase (IU/L), blood urea nitrogen (BUN; mg/dL), and creatinine (mg/dL). These assessments were carried out on day 0 (presentation), and subsequently on the 2nd, 4th, and 6th weeks to monitor the response to treatment. Radiographic examination of the vertebral column was performed on the day of presentation in lateral and/or ventro-dorsal views of the suspected lesion site. In cases where spinal lesions were not evident on plain radiographs, lumbosacral epidurography was conducted using Iohexol (300 mg/mL) at a dose rate of 0.2 mL/kg body weight, and lateral radiographic views were obtained for further evaluation.

Data gathered for this study was statistically analyzed using ICAR WASP 2.0 software's Two-Way Factorial Experimental Design and Two Sample t-test.

Results and Discussion

In the present study, a wide variation in age was observed ranging from 2 months to eight years with a mean of 2.8 years. These observations are aligned with the findings of Scott (1997) and Necas (1999) [20, 16] who also reported wide range of incidences of age in dogs with spinal affections. However, Nithina (2012), Abhijith (2017) and Salumol (2021) [17, 1, 18] reported that most paraplegic dogs presented for SCI were between four to six years. This might be due to

the fact that the dogs in 1-4 yr. age group are sexually active and roam frequently, making them more prone to traffic accidents as compared to older animals.

Among the clinical cases included in the study, ten were male (62.5 per cent) and six were female (37.5 per cent). These findings are in accordance with the observation made by Scott (1997), Necas (1999), Tartarelli *et al.* (2005), Chandy (2006) and Nithina (2012) [20, 16, 24, 6, 17] who reported higher incidence of spinal cord affection in male dogs. This might be due to preference of people to keep more male dogs as pets than females.

Among the sixteen dogs studied, seven were non-descript dogs (43.75 per cent), four were Dachshunds (25 per cent), 2 were labrador (12.5 per cent) and the remaining were a Doberman (6.25 per cent) a Spitz (6.25 per cent) and a German Shepherd (6.25 per cent). In the present study, non-descript dogs were presented more. Similar observations are also reported by Chandy (2006), Nagaraja (2007) and Abhijith (2017) [6, 15, 1] who recorded high incidence traumatic paraplegia of in ND dogs. Occurrence of SCI did not show any relation with the breed, especially when the cause was an automobile accident (Bali *et al.*, 2009) [3]. Next to non-descript dogs, Dachshunds were presented more in number. According to Scott (1997), Necas (1999), Brisson (2010), Nithina (2012) and Tartarelli *et al.* (2005) [20, 16, 5, 17, 24] Dachshund was over presented with spinal cord affections. However, the higher incidence of spinal injury in non-descript dogs in the present study might be due to the higher population of these dogs in the Akola locality. These findings are highly variable and subjected to change as per the breed population specific to a particular demography.

The body weight of the total dogs presented, ranged from 3.4 to 32 kg with an average weight 16.5 kg. These results are corroborated with the findings of Nithina (2012), Abhijith (2017) and Salumol (2021) [17, 1, 18] who also reported that dogs affected with SCI were having wide range of body weight.

In the present study exciting cause was unknown in 68.75 per cent of the cases but remaining had history of trauma. Abhijith (2017) and Salumol (2021) [1, 18] also reported similar findings. Culbert (1998) and Chrisman *et al.* (2003) [9, 7] observed that neurological injury in dogs could arise from number of causes including trauma. According to Bali *et al.* (2009) [3] among traumatic etiologies, motor vehicle accidents (53 per cent) counted more to cause SCI. According to Sulla *et al.* (2018) [23], Hansen type-1 disc disease is the leading cause of acute spinal cord injury in dogs, followed by trauma primarily from traffic accidents (60%) and ischemic infarction.

In the present study, the duration of illness among the dogs varied widely, ranging from one to 21 days, with a mean duration of six days. The majority (68.75%) of dogs with spinal cord injury were presented within the first week of illness. Similar findings have been reported by Gopinathan (2006) and Tikoo *et al.* (2021) [11, 25]. Additionally, Nithina (2012) and Salumol (2021) [17, 18] documented prolonged illness durations of up to two months in dogs with spinal cord injuries. In authors opinion, delayed presentation of cases might be attributed to either owners seeking veterinary assistance elsewhere or negligence.

It was observed that all the physiological parameters (temperature, pulse rate and respiration rate) were within the normal physiological spectrum throughout the observation period. These results are in agreement with the findings of Chandy (2006), Nagaraja (2007), Nithina (2012), Abhijith

(2017), Singh *et al.* (2017) and Salumol (2021) [6, 15, 17, 1, 21, 18] who also reported that spinal cord injury or type of treatment

had no effect on these physiological parameters in dogs.

Table 1: Details of the dogs included in the study of both the groups

Groups	Case no	Age (years)	Breed	Sex	Body weight (kg)	Duration of illness (days)	Aetiology
Group-I	Case-1	7 months	ND	Male	15.8	21	Unknown
	Case-2	1.5	ND	Female	11.4	2	Falling from height
	Case-3	2months	ND	Male	3.4	2	Dog Bite
	Case-4	2	Labrador	Male	26.3	2	RTA
	Case-5	3.5	Dachshund	Female	13.2	3	Unknown
	Case-6	1	ND	Male	15.2	1	RTA
	Case-7	1	ND	Female	17	4	Unknown
	Case-8	4	Dachshund	Male	11.2	3	Unknown
Group-II	Case-1	6	Labrador	Male	32.1	21	Unknown
	Case-2	8	Doberman	Female	25.4	7	Unknown
	Case-3	2	Dachshund	Female	12.3	3	Unknown
	Case-4	4	ND	Female	21	14	Unknown
	Case-5	2	ND	Male	14.3	2	RTA
	Case-6	3	GSD	Male	29.5	7	Unknown
	Case-7	3months	Spitz	Male	7	2	RTA
	Case-8	4	Dachshund	Male	9.6	4	Unknown

Haematological and biochemical parameters assessed at presentation and at fortnightly intervals remained within normal reference ranges in both treatment groups, with no statistically significant alterations attributable to spinal cord injury or the treatment protocols. These findings are consistent with previous reports (Chandy, 2006; Nithina, 2012; Abhijith, 2017) [6, 17, 1]. However, a significant increase in total leucocyte count was observed across time points, likely indicative of a corticosteroid-induced stress leukogram,

as described by Cohn (1997) [8]. Serum biochemical analysis showed that calcium, phosphorus, BUN, and creatinine levels remained within normal limits in both groups throughout the study. However, alkaline phosphatase (ALP) levels were elevated at presentation and exhibited a statistically significant decline over time. These findings align with Ansari *et al.* (2012) [2], who attributed elevated ALP to initial tissue injury and trauma, with subsequent decreases reflecting recovery and resolution of inflammation.

Table 2: Haemato-Biochemical parameters of dogs under both the groups at different intervals

Parameter		Day 0	Second week	Fourth week	Sixth week
Hb	Group I	12.59±0.37	12.66±0.35	12.69±0.32	12.53±0.16
	Group II	12.58±0.32	12.70±0.34	12.66±0.4	12.49±0.29
PCV	Group I	37.40±0.62	37.60±0.83	37.71±0.56	38.31±0.42
	Group II	35.80±0.86	35.76±0.61	35.56±0.62	35.85±0.61
TEC	Group I	5.98±0.08	6.21±0.14	6.27±0.15	6.60±0.21
	Group II	6.57±0.18	6.73±0.18	6.66±0.12	6.74±0.19
TLC	Group I	12.64±0.58	13.25±0.5	13.29±0.21	13.95±0.21
	Group II	13.19±0.36	13.30±0.24	13.33±0.17	13.84±0.24
Neutrophil	Group I	65.34±2.23	67.08±1.91	66.59±1.12	66.78±0.84
	Group II	38.5±0.8	39.52±0.37	40.05±0.75	40.89±0.80
Lymphocyte	Group I	28.41±1.58	26.90±1.45	26.90±1.45	25.96±0.81
	Group II	26.25±1.24	25.25±1.57	24.48±1.26	25.88±1.75
Calcium	Group I	9.83±0.32	9.98±0.22	9.94±0.21	9.94±0.21
	Group II	9.65±0.31	9.76±0.21	9.84±0.16	9.84±0.16
Phosphorous	Group I	5.08±0.21	4.75±0.21	5.06±0.18	4.98±0.21
	Group II	4.79±0.17	4.75±0.21	4.66±0.22	4.54±0.12
ALP	Group I	336.0±57.57	279.0±53.59	225.5±41.42	217.3±24.88
	Group II	378.5±69.28	291.1±44.23	247.6±29.8	218.13±27.02
BUN	Group I	19.38±2.28	21.13±3.32	21.75±2.99	21.00±3.00
	Group II	23.38±2.59	24.88±2.77	26.63±2.14	26.00±2.50
Creatinine	Group I	1.18±0.05	1.19±0.05	1.28±0.04	1.28±0.04
	Group II	1.24±0.06	1.27±0.05	1.19±0.08	1.18±0.08

Radiographic examination of the suspected region revealed salient features like intervertebral space narrowing, intervertebral disc calcification, and changes of spondylosis deformans like vertebral body beaking, osteophyte formation and ventral bridging of the vertebrae in survey radiographs. In epidurography, filling defects in the epidural space and elevation of ventral margin of contrast column suggesting disc protrusion and spinal compression were identified in different regions. Most of the lesions identified were in thoracolumbar

and lumbar regions which had positive correlation with lesions localized by neurological examination. All these findings are in accordance with Scott (1997), Scharf *et al.* (2004) and Steffen *et al.* (2004) [20, 19, 22] who also recorded similar changes in survey radiographs in dogs affected with various spinal cord injury.

In Group I, seven dogs (87.5%) regained ambulatory function within six weeks, while one dog with a suspected cervical lesion showed no improvement. These findings are consistent

with previous reports demonstrating recovery rates of 71-90% following intravenous or epidural administration of polyethylene glycol (PEG) with methylprednisolone sodium succinate (MPSS) in canine spinal cord injury (Lavery *et al.*, 2004; Nithina, 2012; Abhijith, 2017; Salumol, 2021) ^[12, 17, 1, 18]. PEG facilitates recovery by sealing damaged axonal membranes and restoring nerve conduction (Borgens and Shi, 2000; Luo *et al.*, 2002; Liu Snyder *et al.*, 2007) ^[4, 14, 13]. No adverse effects related to treatment were observed during the study period.

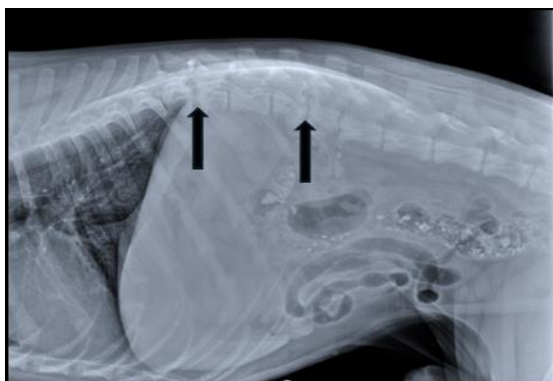


Fig 1: Vertebral end plate lysis

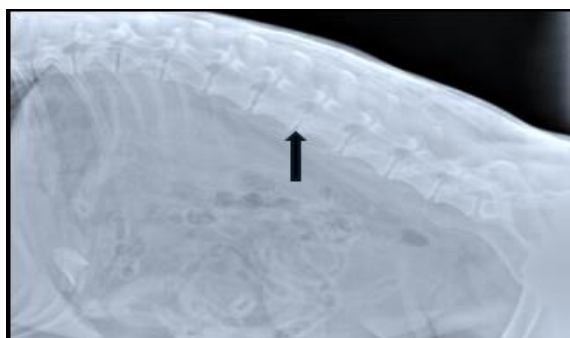


Fig 2: Intervertebral disc space calcification



Fig 3: Epidurogram-dorsal deviation of ventral margin



Fig 4: Blocked vertebra and severe spondylosis

In Group II dogs, five (62.5 per cent) dogs regained their normal ambulatory function within the observation period of 6 weeks. From the current study, it was observed that the treatment regimen was found to be effective in dogs which were brought early after showing the clinical signs. Comparable results have been documented by Abhijith (2017) ^[1] who obtained recovery rate of 62.5 percent in dogs treated with MPSS intravenously. The enhanced sensorimotor reflex in intensive, high dose MPSS therapy can be attributed to improved blood flow, facilitation of neuronal excitability and impulse conduction and, preservation of cord ultrastructure by reducing free radical-catalyzed lipid peroxidation as described by Edward and Mark, 1982 ^[10]. Any adverse effects other than mild gastritis in a single dog were not reported in group II cases.

All the dogs included in the study received neurotropic vitamin Mecobalamin at rate of 1500 µg daily orally and analgesic gabapentin at the rate of 3 mg/kg body weight for a period of one month. To *et al.* (2002) ^[26] substantiated by their research that gabapentin offers an effective therapeutic alternative for the alleviation of neuropathic pain following SCI. Analogously Singh *et al.* (2017) ^[21] validated from their research that treatment with oral gabapentin and methylcobalamin contributed to the functional recovery of spinal cord injury in dogs, particularly those that were ambulatory. In light of these research data, it is speculated that supplementation with these therapeutic agents might have augmented reacquisition of motor function in dogs from both groups. Enhanced recovery rate of 25 percent obtained in Group I dogs compared with Group II dogs can be attributed to sealant effect of PEG maintaining the electrical conductivity of damaged nerves, reducing oedema and preventing cascade of events of auto-destruction.

Clinical improvement of dogs of Group I



Fig 5: Day 0



Fig 6: Day 7



Fig 7: Day 0



Fig 8: Day 7

Clinical improvement of dogs of Group II



Fig 9: Day 0



Fig 10: Day 21

Conclusion

Although both treatment protocols were found effective in treating spinal cord injury in dogs, treatment protocol containing PEG produced an enhanced recovery by early return of spinal reflexes and ambulation in dogs affected with SCI than the treatment protocol involving MPSS alone, in the absence of vertebral instability and space occupying lesions.

Conflict of interest

Not available

Financial support

Not available

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