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RESEARCH ARTICLE

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Comparative evaluation of physiological and haemodynamic effects of zoletil, ketofol, and etofol administered as constant rate infusions in glycopyrrolate and dexmedetomidine premedicated dogs

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The study evaluated the effects of zoletil, ketofol, and etofol as constant rate infusions (CRI) in dogs premedicated with glycopyrrolate and dexmedetomidine. Eighteen dogs were randomly divided into three groups (n=6), all receiving glycopyrrolate (0.01 mg/kg, i.m.) and dexmedetomidine (15 µg/kg, i.v.) prior to anaesthetic induction. Group A animals received zoletil (6.5 mg/kg, i.v.), group B received ketofol (1:1), and group C received etofol (1:1) for both induction and maintenance. All groups showed a significant decrease in heart rate at 15 min, with the lowest rates in group C, followed by groups B and A. Respiratory rate was similar between groups A and B up to 30 min; but overall, group A had the lower values. Rectal temperature remained consistent across groups, except at 45 min where group B showed a significant higher value. Mean arterial pressure was lowest in group A throughout, followed by groups B and C. SpO_2 levels showed minimal variation, with the lowest readings in group B, then group C, and highest in group A. These findings indicate that all three CRI protocols provided satisfactory anaesthetic maintenance with varying effects on physiological and cardiopulmonary parameters.

Keywords: Constant rate infusion, Dexmedetomidine, Dog, Etofol, Glycopyrrolate, Ketofol, Tiletamine-Zolazepam

General anaesthesia is administered to induce unconsciousness, relieve pain and relax muscles. However, it can also inhibit autonomic reflexes, potentially impairing the proper functioning of essential physiological systems like the cardiovascular and respiratory systems (Antognini and Carstens, 2002). Constant rate infusion (CRI) techniques are more effective than intermittent re-dosing for many analgesics and anaesthetic drugs (Lucas *et al.,* 2001; Urquhart, 2001).

Glycopyrrolate is a synthetic quaternary ammonium compound and an anticholinergic agent that does not impact the central nervous system. It effectively reduces saliva production, being about five times more potent than atropine (Hall *et al.,* 2001). Dexmedetomidine is a potent and highly selective alpha-2 adrenoceptor agonist known for its sympatholytic, sedative, amnestic and analgesic properties (Carollo *et al.,* 2008). Tiletamine is a dissociative drug that provides anaesthesia and analgesia. Zolazepam, a benzodiazepine, induces muscle relaxation and counteracts convulsive seizures, especially those associated with tiletamine (Morgan *et al.,* 2012). Ketofol, a 1:1 mixture of ketamine and propofol, is commonly used for procedural sedation and remains physically and chemically stable for up to 3 hours at room temperature (Donnelly *et al.,* 2008). Etofol, a 1:1 mixture of propofol and etomidate, offers improved haemodynamic stability during induction and intubation compared to either drug alone in patients under general anaesthesia. The present study was undertaken with an objective to evaluate the alterations in clinico-physiological and haemato-biochemical parameters induced by zoletil, ketofol and etofol as CRI in dogs.

Materials and Methods

The study was carried out on 18 dogs presented to the Veterinary Clinical Complex, Rewa, for various surgical procedures. Regardless of age, sex, or breeds, the animals were randomly assigned to two groups of six each. Prior to anaesthesia, all dogs were fasted for 12-18 hr and water withheld for 8-12 hr**.** All dogs were premedicated with glycopyrrolate (0.01 mg/kg body weight, i.m.) followed by dexmedetomidine (15 µg/kg, i.v.). Anaesthesia was induced and maintained with zoletil (6.5 mg/kg, i.v.) in group A, ketofol (1:1) in group B, and etofol (1:1) in group C. Clinico-physiological parameters including heart rate (beats/min), respiratory rate (breaths/min), rectal temperature (ºF), peripheral oxygen saturation (%), and mean arterial pressure (mm Hg) were recorded at baseline (0 min, before premedication), at 15 min of pre-anaesthetic administration and subsequently at 30, 45, 60, 75, and 90 minutes following the administration of anaesthetic agents. All the data were analyzed using "SPSS Statistics Version 20" software as per method given by Snedecor and Cochran (1994), and were compared between groups.

Results and Discussion

At 15 min post-induction, animals of all the groups (A, B, and C) exhibited a significant reduction in heart rate from baseline, attributed to the $alpha_2$-agonist effects of dexmedetomidine, which reduces sympathetic tone (Vishnugurubaran, 2023). In group A, heart

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rate significantly increased at 30 min, probably due to tiletamine's sympathomimetic activity, followed by non-significant decreases at 45 and 60 min, and a significant drop at 75 and 90 min (Singh, 2024). Group B also showed a significant rise at 30 min with minor fluctuations thereafter, reflecting the opposing effects of ketamine (stimulant) and propofol (depressant) (Kalaiselvan, 2018). In group C, heart rate decreased non-significantly at 30 and 45 min, increased slightly at 60 min, and declined again at later intervals, suggesting mild cardiac depression from etomidate, potentially enhanced by dexmedetomidine (Kamble *et al*., 2021).

Respiratory rate in group A significantly decreased at 30 min, followed by non-significant drops at 45 and 60 min, then significant increase at 75 and 90 min. This pattern reflects transient respiratory depression observed with tiletamine-zolazepam (Koli *et al*., 2021). Group B showed a non-significant decline at 30 min and gradual increase through 90 min, with a significant rise at the end, consistent with early respiratory suppression by ketofol followed by recovery (Lee *et al*., 2017). Group C exhibited mild, non-significant decrease initially, followed by steady increase, reflecting the mild and transient respiratory depression induced by etomidate (Kamble *et al*., 2021; Singh, 2024).

Rectal temperature decreased non-significantly at 15 min in all groups, supporting Poonia *et al*. (2022). Group A showed continued non-significant decline until 60 min, with significant reductions at 75 and 90 min, likely due to muscle relaxation and reduced metabolism from tiletamine-zolazepam (Koli *et al*., 2021). Group B exhibited a steady, non-significant decline throughout, in line with reports by Kalaiselvan (2018). Njoku (2015) attributed ketofol-induced hypothermia to suppression of thermoregulation and vasodilation. Group C followed a similar trend, consistent with the hypothermic effects of etomidate and the hypotensive action of propofol, compounded by surgical stress (Jadvani *et al*., 2020; Kamble *et al*., 2021).

Table 1: Mean±SE values of clinical parameters in different groups.

Time (in min)	Heart rate (beats/min)			Respiratory rate (breaths/min)			Rectal temperature (^{0}F)		
	Gr A	Gr B	Gr C	Gr A	Gr B	Gr C	Gr A	**Gr B**	**Gr C**
0	123.50^{CD} ±1.26	121.67^{E} ±2.02	122.83^{B} ±3.52	23.67^{E} ±0.89	24.50^{D} ±1.15	24.50^{C} ±1.15	102.14^{E} ±0.58	102.50^{D} ±0.18	102.07^{B} ±0.34
15	114.17^{A} ±0.60	110.67^{A} ±0.95	111.83^{A} ±2.47	18.50^{Dab} ±0.34	16.83^{Aba} ±1.33	20.50^{ABb} ±0.72	102.02^{E} ±0.16	102.35^{CD} ±0.18	101.88^{B} ±0.34
30	126.67^{Ec} ±1.02	115.67^{CDb} ±0.68	109.33^{Aa} ±1.02	15.33^{Aba} ±1.17	15.17^{Aa} ±1.11	18.83^{ABb} ±1.04	101.78^{DE} ±0.15	102.08^{CD} ±0.10	101.72^{AB} ±0.19
45	124.33^{DEc} ±1.12	118.17^{DCb} ±0.60	107.67^{Aa} ±0.99	14.67^{ABa} ±0.80	16.67^{ABab} ±0.84	17.17^{Ab} ±0.70	101.45^{CDa} ±0.05	101.97^{CDb} ±0.17	101.45^{ABa} ±0.20
60	123.17^{CDc} ±0.95	114.67^{BCb} ±0.61	110.83^{Aa} ±0.91	13.83^{Aa} ±0.40	18.50^{BCb} ±0.88	19.67^{ABb} ±0.71	101.32^{C} ±0.11	101.70^{BC} ±0.18	101.28^{AB} ±0.20
75	121.33^{BCc} ±0.88	111.83^{ABb} ±0.75	109.50^{Aa} ±0.34	16.67^{BCa} ±0.49	20.17^{Cb} ±0.83	21.33^{BCb} ±1.14	100.95^{B} ±0.08	101.17^{AB} ±0.23	101.23^{AB} ±0.31
90	119.67^{Bc} ±0.33	109.33^{Ab} ±0.33	106.67^{Aa} ±0.71	19.50^{Da} ±0.34	23.67^{Db} ±0.92	24.33^{Cb} ±1.08	100.43^{A} ±0.15	100.80^{A} ±0.38	100.85^{A} ±0.41

Mean±SE values within a row with different lower-case superscripts (a,b,c) differ significantly (P≤0.05) between the groups; Mean±SE values within a column with different upper-case superscripts (A,B,C,D,E) differ significantly between intervals within groups (P≤0.05).

Table 2: Mean±SE values of haemodynamic parameters in different groups.

Time (in min)	Mean arterial pressure (mmHg)			Oxygen saturation (SpO_2; %)		
	Gr A	Gr B	Gr C	Gr A	Gr B	Gr C
0	88.17^{A}±0.87	89.67^{A}±2.48	91.20^{A}±1.72	96.17^{C}±0.91	97.33^{C}±0.42	97.17^{C}±0.54
15	91.27^{ABa}±1.19	93.83^{ABCab}±1.50	98.29^{Bb}±1.97	93.83^{AB}±0.75	93.83^{AB}±0.75	94.17^{AB}±0.70
30	97.70^{C}±2.13	98.68^{CD}±1.79	95.67^{B}±0.92	92.67^{A}±0.95	92.50^{AB}±0.92	92.50^{A}±1.02
45	95.05^{BCa}±2.50	101.18^{Db}±2.06	103.6^{Cb}±0.94	93.83^{AB}±0.87	93.33^{AB}±1.26	93.17^{AB}±0.65
60	93.10^{ABCa}±1.04	97.13^{BCDa}±2.60	105.3^{Cb}±1.10	95.50^{BC}±0.88	94.83^{ABC}±0.75	94.33^{AB}±0.77
75	92.48^{ABC}±1.92	93.50^{ABC}±1.98	97.28^{B}±0.61	96.50^{C}±0.50	96.33^{BC}±0.56	95.17^{B}±0.60
90	91.65^{AB}±1.61	92.02^{AB}±1.96	95.31^{B}±0.50	97.17^{C}±0.30	97.50^{C}±0.34	97.50^{C}±0.22

Mean±SE values within a row with different lower-case superscripts (a,b,c) differ significantly (P≤0.05) between the groups; Mean±SE values within a column with different upper-case superscripts (A,B,C,D,E) differ significantly between intervals within groups (P≤0.05).

Mean arterial pressure (MAP) in group A significantly increased at 30 min, followed by non-significant decrease, indicating mild hypertensive effects of dissociative anaesthesia (Singh, 2024). Group B showed a similar, albeit non-significant, pattern of elevation and decline, likely due to ketamine's sympathomimetic action (Furuya *et al.*, 2001; Singh, 2024). In group C, MAP declined at 30 min, peaked significantly at 45 min, and then decreased at 75 and 90 min, consistent with variable MAP responses reported for etomidate-propofol combinations (Bansal *et al.*, 2020).

SpO2 levels significantly decreased at 15 min across all groups, likely due to dexmedetomidine-induced respiratory depression (Pascoe, 2015). In group A, SpO2 declined slightly at 30 min, followed by gradual recovery, mirroring observations with tiletamine-zolazepam (Jee *et al.*, 2010). Group B followed a similar trend with steady improvement, consistent with ketofol-related respiratory effects (Singh, 2024). In Group C, SpO2 improved progressively after an initial dip, with a significant rise at 90 min, supporting the stabilizing effects of the etofol combination (Hareesh, 2018; Karthik *et al.*, 2019).

The findings of this study indicate that all three CRI protocols provide satisfactory anaesthetic maintenance with minimal and transient effects on physiological and cardiopulmonary parameters.

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OBITUARY

Dr. N S Jadon
(24 Jan. 1958 - 7 July 2026)

It is with profound grief and a deep sense of loss that we mourn the untimely demise of Dr. Narendra Singh Jadon, a distinguished veterinary surgeon, academician, teacher, researcher and able administrator, who passed away suddenly on 7 July 2026 while serving as the Dean, Mahatma Gandhi Veterinary College, Bharatpur, Rajasthan.

Dr. Narendra Singh Jadon was born on 24 January 1958 in Aligarh district of Uttar Pradesh. He began his professional education at G.B. Pant University of Agriculture & Technology, Pantnagar, in 1976 and obtained his BVSc & AH degree in 1981, MVSc in Veterinary Surgery & Radiology in 1983, and PhD in 1991. He joined his alma mater in 1984 as an Assistant Professor in Veterinary Surgery & Radiology and rose through the academic ranks, becoming Associate Professor in 1997 and Professor in 2001. He headed the Department of Surgery and Radiology from 2005 to 2020.

During his distinguished career, Dr. Jadon also served as Consultant Surgeon, Government of Abu Dhabi, UAE, from 2000 to 2002. At G.B. Pant University, he held several important administrative responsibilities, including Coordinator of Examination, Admission Cell, Test & Selection, and NCC. He served as Dean, College of Veterinary and Animal Sciences, Pantnagar, from February 2020 until his superannuation on 31 January 2023.

Dr. Jadon was a highly respected member of the veterinary surgical fraternity. Throughout his long and dedicated career in Veterinary Surgery and Radiology, he made significant contributions to veterinary education, research and clinical practice. He guided 25 MVSc and 8 PhD students and published more than 150 research papers in journals of national and international repute. He also presented more than 150 research papers at national and international conferences. His contributions to extension and field veterinary services included more than 50 semi-technical articles, 30 folders and 5 monographs for field veterinarians and extension workers. He was also the author of seven books.

Dr. Jadon successfully completed five externally funded and eight university-funded research projects. His major areas of research included anaesthesia, therapeutic applications of neuroganglionic blockade, gene therapy, tissue engineering, and regenerative medicine. He worked extensively on the isolation, differentiation, redifferentiation and characterization of mesenchymal stem cells from different sources and evaluated their regenerative potential in animals.

In recognition of his outstanding contributions to veterinary science and research, Dr. Jadon was elected Fellow of the National Academy of Veterinary Sciences (2005), Fellow of the Indian Society for Veterinary Surgery (2006), and Fellow of the Indian Society for Advancement of Canine Practices (2012). He was also a life member of more than 10 professional societies. Among his many honours were the Dr. Bir Bahadur Singh Outstanding Research Award (2015) conferred by G.B. Pant University of Agriculture and Technology, the Hari Om Ashram Trust Award by ICAR (2015), the Pashudhan Samridhi India Gaurav Ratna Award (2022), and the Best Teacher Award of the College of Veterinary and Animal Sciences (2006–07).

Dr. Jadon will be remembered for his academic excellence, scientific contributions, clinical expertise, administrative leadership and unwavering commitment to veterinary education and service. His sudden demise is an irreparable loss to the veterinary profession and, in particular, to the fraternity of Veterinary Surgery and Radiology. His contributions and legacy will continue to inspire generations of veterinary professionals, teachers, researchers and students.

On behalf of the Indian Society for Veterinary Surgery, we extend our deepest condolences and heartfelt sympathies to his wife, daughter, son and all members of the bereaved family. We stand with them in this hour of profound sorrow and pray that the Almighty grants them strength and courage to bear this irreparable loss.

May his soul rest in eternal peace.