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Comparative evaluation of anaesthetic effects of propofol/etomidate as induction and isoflurane as maintenance anaesthetic agents on clinico-physiological and haemato-biochemical parameters in atropine-diazepam-pentazocine pre-anesthetized dogs

AR Chaudhary, DN Suthar, SK Jhala, VS Dabas and KD Patel

Abstract

A total twelve clinical cases of dogs requiring general anaesthesia for surgical procedures were randomly divided into two groups having six animals in each group. All dogs were premedicated with atropine sulphate @ 0.02 mg/kg b.wt. and pentazocine @ 2 mg/kg b.wt. intramuscularly and diazepam @ 0.5 mg/kg b.wt. intravenously. Induction of anaesthesia was achieved by 1% propofol in group I and 0.2% etomidate in group II intravenously till the effect and maintained by isoflurane upto 50 minutes in both the groups. Clinico-physiological and haemato-biochemical parameters were recorded and evaluated at different time intervals during the study period and found alterations in clinico-physiological and haemato-biochemical parameters within the normal ranges in both the groups; however, pulse rate was significantly dropped in group I after induction of propofol and it remained stable after induction of etomidate up to end of study in group II.

Keywords: Atropine sulphate, dog, diazepam, etomidate, pentazocine, propofol, isoflurane, clinical-physiological, haemato-biochemical parameters

Introduction

Anaesthesia is a basic requirement of any surgical intervention in order to surgeon can succeed surgical procedure with optimum accuracy and shrewdness (Muhammad *et al.*, 2009) [1]. General anaesthesia is considered one of the miracles of veterinary medicine and characterized by unconsciousness, muscle relaxation, amnesia and analgesia. Propofol provides rapid induction of anaesthesia, rapid recovery, lack of excitatory adverse effect and no significant cumulative effect on repeated administration (Ambros *et al.*, 2008 and Aguilera *et al.*, 2020) [2, 3]. Etomidate is commonly used in cardiomyopathy and haemodynamically unstable canine patients (Qin *et al.*, 2015) [4]. Isoflurane is a most widely used volatile inhalant anaesthetic in veterinary practice and number of advantageous properties are low blood solubility, low biodegradability, short induction and recovery time, no catecholamine induced cardiac arrhythmias and hepatotoxicity as compared to halothane (Wade and Stevens, 1981 and Kenna and Jones, 1995) [5, 6]. The present study was undertaken to evaluate the clinico-physiological parameters in balanced anaesthesia using atropine sulphate-pentazocine-diazepam as pre-anaesthetics, propofol/etomidate as induction agents and isoflurane as maintenance anaesthetic in dogs.

Materials and Methods

Total twelve clinical cases of dogs selected for general anaesthesia having six animals in each group were premedicated with atropine sulphate @ 0.02 mg/kg b.wt. and pentazocine @ 2 mg/kg b.wt. Intramuscularly in single syringe and then after 15 minutes, diazepam @ 0.5 mg/kg b.wt. was administered intravenously. Subsequently; 5 minutes after administration of diazepam, induction of anaesthesia was achieved by administration of 1% propofol intravenously till the effect in group I and 0.2% etomidate intravenously till the effect in group II. After achieving desired depth of anaesthesia, endotracheal intubation was carried out with suitable size of endotracheal tube as per body weight under the guidance of laryngoscope in sternal or lateral recumbency and anaesthesia was maintained by isoflurane in all the animals.

The clinico-physiological parameters *viz.*, rectal temperature ($^{\circ}\text{F}$), pulse rate (beats/minute), respiration rate (breaths per minute), systolic, diastolic and mean arterial blood pressure (mm Hg) and saturation of peripheral oxygen (SpO_2) were recorded at 0 minute (prior to administration of any anaesthetic drug), prior to the induction of anaesthesia (PIA), after induction of anaesthesia (AIA) and thereafter at every 10 minutes intervals up to 50 minutes using vital signs monitor or standard technique. 2 ml of venous blood samples were collected in a sterile K_3EDTA vacutainer at 0 minute (prior to administration of any anaesthetic drug), prior to induction of anaesthesia (PIA), after induction of anaesthesia (AIA) and thereafter at every 15 minutes interval up to 45 minutes during maintenance period of anaesthesia for haemato-biochemical study. Haematological parameters *viz.*, haemoglobin (g/dl), packed cell volume (per cent), total erythrocyte count (million/cu.mm), total leucocyte count (thousand/cu.mm) and differential leukocyte count (per cent) were estimated using automatic haemato-analyzer. The blood glucose (mg/dl) was estimated by using glucometer immediately after the blood collection. After haematological examination, remaining volume of blood sample was used for plasma separation for biochemical analysis. Biochemical parameters *viz.*, total protein (g/dl), alanine aminotransferase (IU/L), blood urea nitrogen (mg/dl) and creatinine (mg/dl) were quantified by using semi-automatic biochemical analyzer and standard kits. Statistical data were analysed using R software version 4.0.3 to estimate the means and means were compared using ANOVA and Duncan's New Multiple Range Test (DNMRT).

Results and Discussion

Rectal temperature was decrease non-significantly after premedication and then highly significantly decrease after induction of anaesthesia in both the groups of animals (Table. 1). Similarly, reductions of rectal temperature after administration of propofol or etomidate with different premedications were reported by Perk *et al.*, 2002 [7], Mate and Aher, 2019 [8] and Javdani *et al.*, 2020 [9]. A drop in rectal temperature following anaesthesia might be due to CNS depression, reduction in basal metabolic rate, decrease muscle activity, peripheral vasodilation, increased heat dissipation through respiratory system and combined effects of anaesthetic agents (Khandekar *et al.*, 2015) [10]. Initially pulse rate was non-significantly increased after administration of preanaesthetic drugs in both groups then significantly dropped after the induction of propofol and remained stable; but, lower than the baseline values during entire maintenance period in group I; while, pulse rate remained stable after induction of etomidate up to 50 minutes during maintenance anaesthesia in group II (Table. 1), which indicated minimum adverse effect of etomidate on cardiovascular system as reported by Muir and Mason, 1989 [11] and Branson, 2007 [12]. Initial increase in heart rate might be due to the vagolytic effect of atropine sulphate in the present study as justified by Park *et al.* (2009) [13]. There was a non-significant decrease in respiration rate after administration of preanaesthetic drugs (atropine, pentazocine and diazepam) then it highly significantly further decreased after the induction of the anaesthesia (propofol or etomidate) and remained stable but lower than the base line value up to the end of maintenance anaesthesia (isoflurane) in both the groups (Table. 1) and it might be due to respiratory depressant activity of propofol, etomidate and isoflurane as reported by Mutoh *et al.* (1997) [14] and was further

potentiated by pentazocine, in accordance with the findings of Covey-Crump and Murison (2008) [15].

Mean values of saturation of peripheral oxygen (SpO_2) were increased highly significantly after induction of anaesthesia from baseline value and persisted non-significantly increase up to the end of anaesthesia in group I; while, the mean values of SpO_2 were observed a non-significantly increased from base line value to the end of anaesthesia in group II (Table. 2). Perk *et al.* (2002) [7] and Adediran and Adetunji (2021) [16] recorded non-significant increase in SpO_2 after administration of propofol or etomidate and isoflurane in dogs, respectively. Similar finding was recorded in present study and in addition, endotracheal intubation was carried out in all animals immediately after induction of anaesthesia to maintain airway passage for better ventilation with 100% oxygen supply along with inhalation anaesthetic during maintenance of anaesthesia which improved oxygen level in blood.

The mean values of systolic, diastolic and mean arterial blood pressure were found gradually decreased from base line value (0 minute) up to end of anaesthetic observations at different time interval in both the groups (Table. 2). Suthar *et al.* (2018) [17], Keating *et al.* (2020) [18] and Adediran and Adetunji (2021) [16] observed decrease in blood pressure (SBP, DBP, MAP) after administration of propofol, etomidate and isoflurane and they opined that these anaesthetic drugs produced decrease in peripheral vascular resistance, arterial and venous vasodilatation, myocardial depression effect that caused decreased contractility of the heart and decreased sympathetic outflow which induced hypotension.

The mean values of haemoglobin, packed cell volume and total erythrocyte count were highly significantly decreased in group I and non-significantly decreased in group II after administration of anaesthesia up to the end of the observations as compared to the base line value (Table. 3) and it might be due to pooling of circulatory blood cells in the spleen and lungs or shifting of fluid from the extravascular compartment to the intravascular compartment in order to maintain normal cardiac output after administration of anaesthetic drugs as reported by Wagner and Muir (1991) [19], Tiwari *et al.* (1994) [20] and Hareesh (2016) [21]. A non-significant difference in the mean values of total leukocyte count and differential leukocyte count was observed at different time intervals in both the groups (Table. 3).

The mean values of blood glucose were gradually increased from base value (0 minute) up to 45 minutes of observations in both the groups except in group II, in which non-significant decrease in blood glucose level has observed before and after induction of etomidate anaesthesia (Table. 4). Surgical and anaesthetic stress are also responsible for stimulation of hypothalamus and pituitary gland for increasing secretion of adrenocortical hormone (ACTH). ACTH produces the glucocorticoids which contribute rise in blood glucose level as reported by Dikshit and Prasad (1971) [22] and Mirakur *et al.* (1984) [23].

A non-significant decrease in the mean values of total plasma proteins were recorded between the groups at different time intervals (Table 4). Dewangan *et al.* (2016) [24] also estimated non-significant decrease in total proteins after administration of propofol. It might be due to haemodilution owing to inter-compartment fluid shift as opined by Amaral and Kumar (1995) [25]. The mean values of alanine aminotransferase were found decreased from base line value (0 minute) up to 45th minutes after induction of anaesthesia in both the groups (Table. 4). This might be due to the effect of anaesthesia

which caused decrease cardiac output and proportional effect on decrease in total hepatic blood flow resulting in lower production of liver enzymes as reported by Thomson *et al.* (1986) [26]. The mean value of blood urea nitrogen was increased during entire study period from base line values after administration of anaesthetic drugs in animals of both groups (Table. 4) but, these changes in the mean values were within the normal physiological range, indicated no adverse effect of drugs. Non-significant increase in the blood urea nitrogen level up to end of observation period was noticed in both the groups (Table. 4) which might be due to temporary inhibitory effect of anaesthetic drugs on renal blood flow, changes in cardiovascular and neuroendocrine activities as reported by Jones *et al.* (1981) [27]. No major alternation in the

mean value of creatinine was recorded at different time intervals in both the groups.

In the present study, all clinico-physiological and haemato-biochemical parameters were found alterations within the normal values in both the groups; however, pulse rate was significantly dropped in group I after induction of propofol and it remained stable in group II after induction of etomidate up to end of study. Overall observations showed satisfactory results in both the groups of balanced anaesthetic protocols. Etomidate produced better cardiac stability with minimum fluctuation on clinico-physiological and haemato-biochemical parameters than propofol induced dogs and it is safer induction anaesthetic protocol for surgical interventions in dogs.

Table 1: Mean±SE values of rectal temperature, pulse rate and respiratory rate at different time intervals in dogs

	Time interval (min)	Group I(n=6)	Group II(n=6)	p-value
Rectal Temperature (°F)	0 minutes (Base line)	101.72±0.08 ^a _A	101.40±0.26 ^a _A	0.28
	Prior induction	101.43±0.21 ^a _A	101.40±0.21 ^a _A	0.91
	After induction	101.18±0.18 ^a _A	101.02±0.25 ^{ab} _A	0.59
	10 th minute	100.62±0.18 ^b _A	100.20±0.37 ^{bc} _A	0.34
	20 th minute	100.38±0.22 ^b _A	99.62±0.45 ^{cd} _A	0.15
	30 th minute	99.60±0.23 ^c _A	98.83±0.46 ^{de} _A	0.16
	40 th minute	99.15±0.21 ^{cd} _A	98.08±0.45 ^{ef} _A	0.05
	50 th minute	98.72±0.23 ^d _A	97.57±0.44 ^f _B	0.043
	p-value	0.0001	0.0001	
Pulse Rate (beats/minute)	0 minutes (Base line)	145.83±11.41 ^a _A	144.67±9.42 ^a _A	0.94
	Prior induction	153.50±10.5 ^a _A	154.67±10 ^a _A	0.94
	After induction	116.33±14.42 ^{ab} _B	153.17±7.49 ^a _A	0.047
	10 th minute	115.33±19.84 ^a _A	157.50±9.37 ^a _A	0.08
	20 th minute	131.33±9.81 ^a _A	157.67±8.62 ^a _A	0.07
	30 th minute	128.50±9.21 ^a _A	146.83±5.31 ^a _A	0.11
	40 th minute	129.50±9.93 ^a _A	141.50±7.49 ^a _A	0.36
	50 th minute	129.00±7.83 ^a _A	140.00±9.19 ^a _A	0.38
	p-value	0.35	0.67	
Respiratory Rate (breaths/minute)	0 minutes (Base line)	25.50±2.17 ^a _A	25.50±2.19 ^a _A	1.00
	Prior induction	21.00±1.81 ^a _A	21.17±1.35 ^a _A	0.94
	After induction	13.17±0.91 ^b _A	11.83±0.65 ^b _A	0.26
	10 th minute	12.17±1.9 ^b _A	10.17±0.83 ^c _A	0.36
	20 th minute	12.33±1.23 ^b _A	9.83±0.83 ^c _A	0.12
	30 th minute	12.50±1.31 ^b _A	10.67±0.33 ^c _A	0.20
	40 th minute	14.50±1.65 ^b _A	12.50±1.77 ^c _A	0.43
	50 th minute	14.33±1.69 ^b _A	12.67±1.45 ^c _A	0.47
	p-value	0.0001	0.0001	

Means bearing same superscripts within the groups and subscripts between the groups differ non-significantly ($p>0.05$)

Means bearing different subscripts between the groups differ significantly ($p\leq 0.05$)

Means bearing different subscripts within the groups differ highly significantly ($p<0.01$)

Table 2: Mean±SE values of SpO₂, systolic, diastolic and mean arterial blood pressure at different time intervals in dogs

	Time interval (min)	Group I(n=6)	Group II(n=6)	p-value
Saturation Percentage of Oxygen (%)	0 minutes (Base line)	93.33±1.63 ^d _A	95.17±2.02 ^a _A	0.5
	Prior induction	94.50±0.72 ^{cd} _A	94.69±1.26 ^a _A	0.8
	After induction	96.83±0.40 ^{abc} _A	95.64±2.56 ^a _A	0.33
	10 th minute	95.67±1.36 ^{bcd} _A	96.17±0.54 ^a _A	0.33
	20 th minute	97.33±0.49 ^{ab} _A	96.49±0.70 ^a _A	0.2
	30 th minute	97.41±0.49 ^{ab} _A	97.08±0.40 ^a _A	0.8
	40 th minute	97.50±0.43 ^a _A	96.54±0.62 ^a _A	0.21
	50 th minute	97.83±0.31 ^a _A	96.12±0.86 ^a _A	0.07
	p-value	0.002	0.11	
Systolic blood pressure (mm Hg)	0 minutes (Base line)	140.33±7.60 ^a _A	142.83±2.47 ^a _A	0.76
	Prior induction	130.67±9.51 ^{ab} _A	131.67±4.96 ^{ab} _A	0.93
	After induction	120.67±4.22 ^{bc} _A	114.67±8.06 ^{bc} _A	0.52
	10 th minute	118.17±7.51 ^{bc} _A	110±9.34 ^c _A	0.51
	20 th minute	119.33±5.46 ^{bc} _A	109.00±4.40 ^c _A	0.17
	30 th minute	109.83±5.68 ^{bc} _A	97.50±6.14 ^c _A	0.17
	40 th minute	108.67±6.50 ^c _A	95.50±5.26 ^c _A	0.15

	50 th minute	100.67±4.83 ^c _A	97.17±6.55 ^c _A	0.68
	<i>p-value</i>	0.004	0.0001	
Diastolic blood pressure (mm Hg)	0 minutes (Base line)	85.67±5.87 ^a _A	81.5±9.92 ^a _A	0.73
	Prior induction	74.33±8.46 ^{ab} _A	81.33±8.74 ^a _A	0.58
	After induction	70.50±9.01 ^{ab} _A	65.33±7.5 ^{ab} _A	0.66
	10 th minute	75.00±7.15 ^{ab} _A	62.00±6.16 ^{ab} _A	0.19
	20 th minute	74.5±3.98 ^{ab} _A	61.17±4.89 ^{ab} _A	0.06
	30 th minute	69.5±4.76 ^{ab} _A	58.16±6.06 ^{ab} _A	0.17
	40 th minute	63.67±4.51 ^b _A	55.33±4.34 ^b _A	0.21
	50 th minute	54.83±4.67 ^b _A	51.17±8.36 ^b _A	0.71
	<i>p-value</i>	0.041	0.036	
Mean arterial pressure (mm Hg)	0 minutes (Base line)	99.33±4.33 ^a _A	99.67±8.40 ^a _A	0.97
	Prior induction	99.17±7.30 ^a _A	100.00±6.19 ^a _A	0.93
	After induction	88.67±6.22 ^{abc} _A	84.33±7.37 ^{ab} _A	0.71
	10 th minute	92.17±6.41 ^{ab} _A	79.00±5.58 ^b _A	0.15
	20 th minute	90.17±4.00 ^{abc} _A	77.67±3.35 ^b _A	0.07
	30 th minute	84.5±5.80 ^{abc} _A	71.83±5.52 ^b _A	0.14
	40 th minute	78.67±4.71 ^{bc} _A	70.17±3.84 ^b _A	0.19
	50 th minute	73.33±3.84 ^c _A	68.00±7.33 ^b _A	0.53
	<i>p-value</i>	0.017	0.002	

Means bearing same subscripts between the groups differ non-significantly ($p > 0.05$)

Means bearing different superscripts within the groups differ significantly ($p \leq 0.05$)

Means bearing different superscripts within the groups differ highly significantly ($p < 0.01$)

Table 3: Mean±SE value of Hb, PVC, TEC and DLC of balanced anaesthetic protocols at different time intervals in dogs

	Time interval (min)	Group I (n=6)	Group II (n=6)	<i>p-value</i>	
Haemoglobin (g/dl)	0 minutes (Base line)	12.05±0.55 ^a _A	12.28±0.9 ^a _A	0.83	
	Prior induction	11.4±0.48 ^a _A	11.65±0.93 ^a _A	0.82	
	After induction	10.52±0.65 ^{ab} _A	11.17±0.92 ^a _A	0.58	
	15 th minute	9.48±0.70 ^{bc} _A	10.63±0.90 ^a _A	0.34	
	30 th minute	9.07±0.47 ^{bc} _A	10.35±0.91 ^a _A	0.24	
	45 th minute	8.65±0.39 ^c _A	10.07±0.89 ^a _A	0.18	
		<i>p-value</i>	0.0005	0.52	
	Packed Cell Volume (%)	0 minutes (Base line)	36.37±1.66 ^a _A	36.65±2.61 ^a _A	0.93
Prior induction		34.28±1.56 ^{ab} _A	35.33±2.60 ^a _A	0.74	
After induction		31.50±1.71 ^{abc} _A	33.48±2.66 ^a _A	0.54	
15 th minute		28.12±1.67 ^{cd} _A	32.30±2.75 ^a _A	0.22	
30 th minute		28.45±0.82 ^{cd} _A	30.82±2.76 ^a _A	0.43	
45 th minute		27.06±0.57 ^d _A	29.83±2.66 ^a _A	0.33	
		<i>p-value</i>	0.0002	0.46	
Total Erythrocyte Count (million/cu.mm)		0 minutes (Base line)	6.20±0.29 ^a _A	6.30±0.46 ^a _A	0.86
	Prior induction	5.81±0.33 ^a _A	6.04±0.46 ^a _A	0.68	
	After induction	5.46±0.32 ^{ab} _A	5.80±0.48 ^a _A	0.57	
	15 th minute	4.90±0.33 ^b _A	5.60±0.46 ^a _A	0.25	
	30 th minute	4.88±0.17 ^b _A	5.40±0.51 ^a _A	0.36	
	45 th minute	4.64±0.11 ^b _A	5.20±0.54 ^a _A	0.33	
		<i>p-value</i>	0.002	0.61	
	Total Leukocyte Count (thousand/cu.mm)	0 minutes (Base line)	13.65±1.98 ^a _A	13.53±1.77 ^a _A	0.97
Prior induction		14.40±2.68 ^a _A	13.22±1.95 ^a _A	0.73	
After induction		13.12±2.23 ^a _A	12.20±1.61 ^a _A	0.75	
15 th minute		13.15±2.59 ^a _A	11.43±1.46 ^a _A	0.58	
30 th minute		11.80±2.04 ^a _A	11.00±1.35 ^a _A	0.75	
45 th minute		11.38±1.85 ^a _A	10.73±1.35 ^a _A	0.78	
		<i>p-value</i>	0.93	0.75	

Means bearing same superscripts within the groups and subscripts between the groups differ non-significantly ($p > 0.05$)

Means bearing different superscripts within the groups differ highly significantly ($p < 0.01$)

Table 4: Mean±SE values of blood glucose, total protein, ALT, BUN and creatinine at different time intervals in dogs

	Time interval (min)	Group I(n=6)	Group II(n=6)	<i>p-value</i>
Blood Glucose (mg/dl)	0 minutes (Base line)	106.00±11.50 ^a _A	105.83±4.88 ^a _A	0.99
	Prior induction	106.83±9.41 ^a _A	104.17±5.63 ^a _A	0.81
	After induction	106.50±9.38 ^a _A	101.00±5.70 ^a _A	0.63
	15 th minute	109.33±10.90 ^a _A	119.83±22.33 ^a _A	0.68
	30 th minute	111.00±11.70 ^a _A	125.33±22.47 ^a _A	0.58
	45 th minute	115.50±11.83 ^a _A	124.83±13.02 ^a _A	0.60
		<i>p-value</i>	0.99	0.71
Total Protein (g/dl)	0 minutes (Base line)	7.67±0.27 ^a _A	7.68±0.37 ^a _A	0.98

	Prior induction	7.45±0.24 ^a _A	7.42±0.29 ^{ab} _A	0.94
	After induction	7.32±0.31 ^a _A	7.31±0.24 ^{ab} _A	0.99
	15 th minute	6.88±0.36 ^{ab} _A	6.78±0.18 ^{bc} _A	0.82
	30 th minute	6.40±0.36 ^b _A	6.53±0.21 ^c _A	0.76
	45 th minute	6.12±0.22 ^b _A	6.19±0.16 ^c _A	0.80
	<i>p-value</i>	0.004	0.001	
Alanine Amino Transferase (IU/L)	0 minutes (Base line)	33.20±2.21 ^a _A	33.12±2.33 ^a _A	0.98
	Prior induction	32.12±1.79 ^a _A	31.78±1.68 ^a _A	0.89
	After induction	30.60±1.55 ^{ab} _A	29.34±1.97 ^{ab} _A	0.63
	15 th minute	26.99±0.63 ^{bc} _A	27.52±1.81 ^{ab} _A	0.79
	30 th minute	25.81±0.59 ^c _A	24.90±1.77 ^b _A	0.64
	45 th minute	24.30±0.57 ^c _A	24.35±1.43 ^b _A	0.97
<i>p-value</i>	0.0002	0.01		
Blood Urea Nitrogen (mg/dl)	0 minutes (Base line)	13.48±1.70 ^a _A	13.66±1.97 ^a _A	0.95
	Prior induction	14.35±1.87 ^a _A	14.42±2.12 ^a _A	0.98
	After induction	15.60±1.97 ^a _A	15.72±2.31 ^a _A	0.97
	15 th minute	18.13±2.94 ^a _A	17.28±2.62 ^a _A	0.83
	30 th minute	19.17±2.86 ^a _A	18.14±2.44 ^a _A	0.79
	45 th minute	19.39±2.97 ^a _A	19.33±3.01 ^a _A	0.99
<i>p-value</i>	0.39	0.55		
Creatinine (mg/dl)	0 minutes (Base line)	1.20±0.08 ^a _A	1.21±0.08 ^a _A	0.87
	Prior induction	1.16±0.05 ^a _A	1.15±0.08 ^a _A	0.76
	After induction	1.26±0.03 ^a _A	1.23±0.07 ^a _A	0.65
	15 th minute	1.27±0.03 ^a _A	1.26±0.05 ^a _A	0.80
	30 th minute	1.30±0.03 ^a _A	1.23±0.06 ^a _A	0.27
	45 th minute	1.33±0.03 ^a _A	1.27±0.05 ^a _A	0.27
<i>p-value</i>	0.06	0.82		

Means bearing same superscripts within the groups and subscripts between the groups differ non-significantly ($p>0.05$)

Means bearing different superscripts within the groups differ significantly ($p\leq 0.05$)

Means bearing different superscripts within the groups differ highly significantly ($p<0.01$)

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