Fluid heating system (SAF®): effects on clinical and biochemistry parameters in dogs submitted to inhalatory anesthesia[1]

Sistema de aquecimento de fluidos (SAF®): efeitos sobre parâmetros clínicos e bioquímica sérica em cadelas sob anestesia inalatória

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ABSTRACT
Purpose: To evaluate and describe immediate effects of the infusion of saline solution heated by SAF® in bitches submitted to halothane anesthesia. **Methods**: Thirteen bitches were employed and submitted to elective ovariohysterectomy in acclimatized operating room at 22ºC, allocated in two groups: GI, which received non-heated fluid and GII, which received fluid heated at 37ºC by SAF®. The following parameters were evaluated in 30-minutes intervals (M0, M30, M60 and M90): rectal and cutaneous temperatures (TR and TC), cardiac and respiratory frequencies (HR and *f*), mean arterial blood pressure (MAP), serum concentration of urea, creatinin, serum activities of alanin aminotranspherasis (ALT), alkaline phosphatasis (ALP) and also hypnosis parameters. **Results**: There were no significant alterations on clinical and biochemical, but there was group effect on mean arterial blood pressure, urea, ALT, ALP and hypnosis parameters. **Conclusion**: The isolated use of Fluid Heating System (SAF®) was not enough to avoid hypothermia or lead to significant clinical and biochemical alterations in bitches submitted to halothane anesthesia.
Key words: Anesthesia, Inhalation. Hypothermia. Enzymes. Dogs.

RESUMO
Objetivo: Avaliar e descrever os efeitos imediatos da infusão de solução salina 0,9% aquecida pelo SAF® sobre cadelas sob anestesia inalatória. **Métodos**: Foram utilizadas 13 cadelas submetidas a ovariohisterectomia eletiva em centro cirúrgico climatizado a 22ºC, divididas em dois grupos: GI, que recebeu fluido em temperatura ambiente e GII, que recebeu fluido aquecido a 37ºC pelo SAF®. Os parâmetros clínicos avaliados em intervalos de 30 minutos (M0, M30, M60 e M90) foram: temperatura retal (TR) e cutânea (TC), freqüências cardíaca (FR) e respiratória (*f*), pressão arterial média (PAM), tempo de hipnose, concentrações séricas de uréia e creatinina e atividades das enzimas séricas alanina aminotransferase (ALT) e fosfatase alcalina (ALP). **Resultados**: Não foram evidenciadas alterações clínicas e bioquímicas significativas, mas houve efeito de grupo sobre as variáveis PAM, uréia, ALT, ALP e tempo de hipnose. **Conclusão**: O uso isolado do Sistema de Aquecimento de Fluidos (SAF®) não foi suficiente para evitar o estabelecimento da hipotermia em cadelas submetidas a anestesia geral inalatória, ou promover alterações clínicas e bioquímicas significativas.
Descritores: Anestesia por Inalação. Hipotermia. Enzimas. Cães.

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Introduction

In surgical procedures hypothermia results from factors such as reduced organic thermal control due to anesthesia, low temperatures on operating rooms and body heat redistribution. In addition, there is a reduction of body produced heat, inhalation of dry and cold anesthetic gases, evaporation due to antisseptical solutions, lack of adequate thermal insulation, and also through surgical incision which exposes the internal environment to room temperature.[1,2]

Per-operative hypothermia usually leads to adverse events, such as coagulopathies and greater blood loss, surgical wound infection, cardiovascular events, discomfort and shivering, reported by several human patients as worse then the actual surgical pain.

It may also lead to delayed action of anesthetic drugs, as well as delayed recovery, for even mild hypothermia, from 34º to 36ºC, may elevate the drugs anesthetic potency and delay their biotransformation.[2,3,4]

Even if pré-anesthetic exams present normal enzymatic values, hepatic biotransformation may still be compromised in the hypothermic patient. Thiopental's active metabolite, pentobarbital, has a half-life of about 34 hours, and anesthetic recovery occurs after detoxification of 30% to 45% of the applied dose. On the other hand, the solubility of volatile anesthetics is higher in hypothermic tissues; even so, such fact does not mean heightening on anesthetic effect, for its potency is much more determined by partial pressure than by anesthetic concentration. The minimal alveolar concentration (MAC) for halothane is lowered in about 5% for each degree Celsius reduced in central temperature.[3]

The infusion of non-heated fluid may strongly diminish body temperature. For each liter of intravenous fluid infused in room temperature into adult humane patients, or for each blood pack at 4ºC, there is a reduction in body temperature of about 0,25ºC. The infusion of room temperature fluids may lead to central temperature reductions worse than shock situations.[3,4]

The Fluid Heating System (SAF®) was designed to aid on the maintenance of body temperature on the per-operative period. It is a heating and monitoring system for fluid temperature, which consists of a central command unit, a heating pad and its extension, and these last two hold the bottle and the infusion tube containing the solution about to be infused. The central unit determines the heating by tiny resistors and a thermostat inserted along the heating pad, assuring fluid temperature as well as its steadiness.

Although per-operative hypothermia occurs in several species and despite all discussions about the benefits from infusing heated fluids, there are no descriptions in literature concerning the use of SAF®, or its implications, in experimental models. Therefore, the option for employing the dog in this study was based on its frequency as anesthetic experimental model, and also the in frequency of surgical procedures in hospital routine basis for this species.

The aim of this study was to describe and evaluate immediate effects of infusing saline solution heated at 37ºC by SAF® on clinical parameters and serum biochemistry in bitches submitted to halothane anesthesia.

Methods

The experiment was carried out after submission and approval by The Committee of Ethics in Research of Federal University of Goias, under the guidelines of ethics and animal welfare, in an operating room acclimatized at 22º C, as suggested by Bernard *et al.*[5] and Vanni *et al.*[2] Thirteen bitches of several breeds, with mean body weight of 7.55kg ± 2.32, were submitted to ovariohysterectomy, allocated in two experimental groups GI (n=6) and GII (n=7), according to the treatment. The selected animals were considered healthy, according to pré-anesthetic evaluation and laboratory tests.

The animals in GI (control) received 0.9% saline solution in room temperature, whilst those in GII (treatment), received the same solution heated at 37ºC by SAF® (Figure 1).

After water and food fastening of 12 and six hours, respectively, all animals received an intramuscular dose of 0.5 mg/kg of midazolam, as pre-anesthetic medication. After 15 minutes, on anesthetic induction, an intravenous dose of 12.5mg/kg of 2.5% sodium thiopental. Maintenance was carried with halothane in 2V% calibrated vaporizer, during 60 minutes from induction. The surgical procedure and intravenous 0.9% saline solution infusion, of 20mL/kg/h during the procedure. The animals were monitored all along the anesthetic procedure and recovery period by a multiparametric monitor.

Clinical parameters were evaluated in 15-minutes intervals (M0, M15, M30, M45, M60, M75 e M90), where M0 is the moment immediately before administering pré-anesthetic medication, and the remaining moments refer to 15-minutes intervals from M0 on. Rectal temperature (RT) was assessed using a digital thermometer. Using na infrared thermometer, cutaneous temperature was assessed on thoracic and pelvic limbs, modifying the protocol employed by Beck *et al.*[6] in swine. The modification consisted of calculating the mean cutaneous temperature (CT) of the limbs, by the arithmetical mean of the temperature in each limb, on carps and tarsal regions. Heart rate (HR), in beats per minute (bpm), and respiratory rate (*f*), in breaths per minute (bpm), were assessed at all moments.

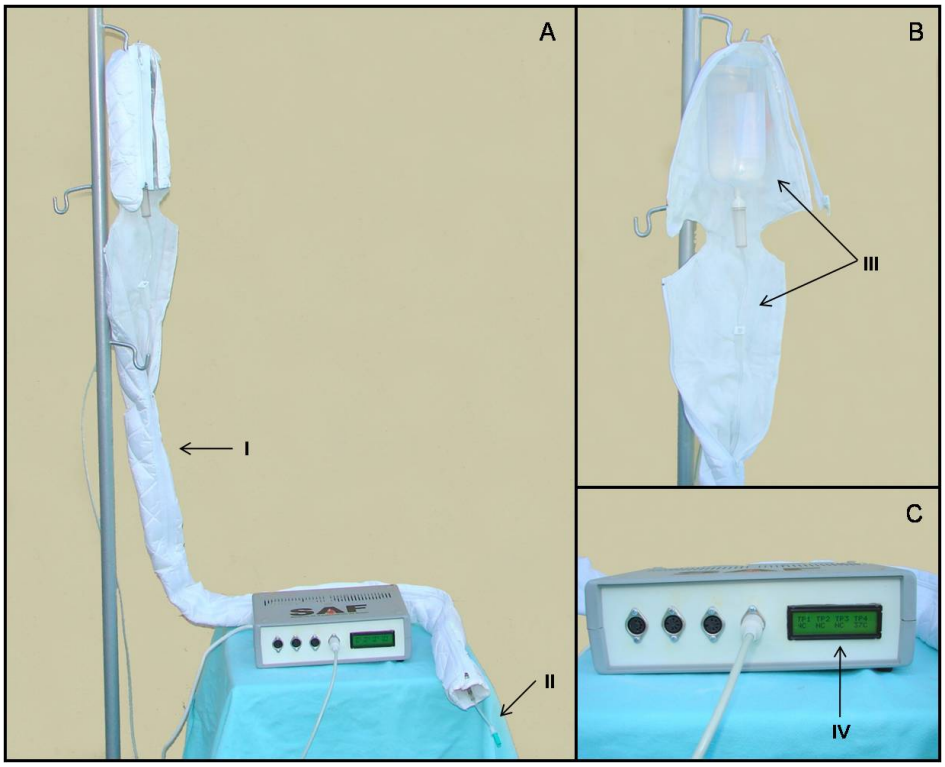

FIGURE 1 – Illustrative representation of Fluid Heating System (SAF®). In **A**, set demonstrating the heating pad around the infusion tube (**I**) and its connection to venopuncture site (**II**); In **B**, zoom image of heating pad indicating (**III**) the sites of resistors; In **C**, central command unit, and visual display, showing the temperature of the fluid to be infused (**IV**)

Mean arterial pressure (MAP) was invasively assessed by canulating the femoral artery and using an aneroid manometer, as described by Rezende *et al.*[7], from M30 on, 15 minutes after anesthetic induction.

The variables for time of hypnosis were: time for postural correction – time elapsed from the administration of pre-anesthetic medication until recovery of postural tonus; and time for returning to esternal decubitus – time elapsed from the administration of pre-anesthetic medication until being able to stay in esternal decubitus.[8]

Concerning biochemical analysis, samples were taken at M0 e M90 to determine serum concentrations of urea and creatinine, and serum activity of alanine aminotransferasis (ALT) and alkaline phosphatasis (ALP), employing commercial kits.[8]

For statistical analysis data were grouped and expressed as mean ± standard deviation and median, employing the software GraphPad InStat, 3.00 version, 1998. For the variables CT, HR, MAP and creatinine ordinary or repeated measures Analysis of Variance (ANOVA) was done, followed by Tukey test. Group and moment effects were calculated. On the analysis of the variables RT, *f*, urea, ALT and ALP, the median was obtained and Friedman test was carried for repeated measures, while Kruskal-Wallis was carried for independent measures. Hypnosis variables were descriptively evaluated. For correlations the Pearson correlation test was used. The significance level of 5% ($p<0.05$) was adopted.

Results

The results for the variables TR and TC are described in Table 1, and the results for the variables FC, *f*, and PAM are described in Table 2. At the end of the observation period, both groups presented reduction in RT, with no significant difference between the groups in any moment. In the bitches from GI, this parameter presented lowest means in the moments M75 ($p<0.05$) and M90 ($p<0.001$), with significant difference when compared to M0 and M15 ($p<0.05$). Similar results were observed in the animals from GII, in the moments M75 ($p<0.05$) and M90 ($p<0.01$). However, in this group, M15 differed only from M90 ($p<0.05$). Moment effect was observed for this variable ($p<0.001$).

CT did not present significant difference among the values between and in the groups ($p>0.05$). Nevertheless it was demonstrated positive correlation between RT and CT ($r=0.501$).

As for HR, results were similar in GI and GII, with no significant difference ($p>0.05$) along the moments between the groups. On the other hand, when comparing the moments in the groups, there was difference in GII amongst M90 and ($p<0.05$), M15 ($p<0.05$) and M30 ($p<0.01$). Besides this finding, there was also positive correlation between HR and RT ($r=0.397$).

There was no significant difference ($p>0.05$) in or between the groups for the variables *f* and MAP during all the observation period. Nonetheless, there was group effect ($p=0.01$) for MAP.

TABLE 1 - Distribution of means ± standard deviations and medians, according to the group (GI – control and GII – SAF) for the clinical parameters rectal temperature (RT) and cutaneous temperature (CT) in bitches submitted to general inhalatory anesthesia

Variables	RT‡ (°C)		CT (°C)	
	GI	GII	GI	GII
M0	39,18±0,55	38,64±0,75	34,07±2,45	33,16±2,65
	38,95[a]	38,7[a]	34,26	33,75
M15	38,32±0,67	38,23±0,38	34,47±2,88	34,46±2,09
	38,55[a]	38,2[ab]	35,57	35,90
M30	37,42±0,93	37,44±0,81	34,26±2,53	34,72±1,40
	37,4	37,8	34,68	35,18
M45	36,80±1,58	36,96±0,53	33,61±2,69	34,67±1,34
	37,05	37,0	33,94	35,00
M60	36,23±1,68	36,24±0,48	33,79±2,13	34,27±1,31
	36,7	36,0	33,58	34,58
M75	35,87±1,84	35,93±0,24	33,00±2,79	34,31±1,08
	35,95[b]	35,9[bc]	33,54	34,58

[abc] Significant differences among moments within each treatment ($p<0,05$); * Significant differences between treatments along the moments ($p<0,05$);† Group effect for the given variable ($p<0,05$); ‡Moment effect for the given variable ($p<0,05$).

TABLE 2 - Distribution of means ± standard deviations and medians, according to the group (GI – control and GII – SAF) for the clinical parameters heart rate (HR), respiratory rate (*f*) and Mean arterial pressure (MAP) in bitches submitted to general inhalatory anesthesia

Variables	HR ‡ (beats/min)		*f* (breaths/min)		MAP† (mmHg)	
	GI	GII	GI	GII	GI	GII
M0	133,67±21,56	136,57±29,82[a]	38,00±15,13	27,43±7,81	-	-
	126,00	120,00	42,00	24,00	-	-
M15	137,67±26,85	136,86±26,63[a]	25,67±14,45	25,86±7,93	-	-
	140,00	150,00	24,00	24,00	-	-
M30	136,33±14,56	145,43±23,63[a]	22,50±20,99	22,43±6,92	83,33±25,03	87,86±21,19
	138,00	160,00	16,00	20,00	70	90
M45	131,33±29,36	127,43±30,35	18,83±14,03	20,86±9,08	86,67±28,75	92,86±17,99
	131,00	116,00	14,00	20,00	80	100
M60	121,33±20,62	117,43±24,78	18,67±7,45	22,29±6,87	83,33±16,33	98,43±29,04
	115,00	130,00	16,00	24,00	85	90
M75	107,33±27,62	111,43±25,76	21,33±6,02	23,43±7,81	86,67±17,80	104,29±24,12
	99,00	112,00	20,00	24,00	87,50	100

[abc] Significant differences among moments within each treatment (p<0,05); * Significant differences between treatments along the moments (p<0,05);† Group effect for the given variable (p<0,05); ‡Moment effect for the given variable (p<0,05).

The results obtained for creatinine, urea, ALT and ALP are described in Table 3. Serum alterations were not observed in any of the metabolites assessed, when compared between the groups. As for the comparison among the moments, differences were evidenciated with decrease on serum concentration of creatinine in GII animals (p<0.05) and in ALT serum activity e na atividade sérica de ALT in GI (p<0.05). There was group effect for the variables urea (p<0.01), ALT (p<0.01) and ALP (p<0.001).

Concerning the evaluation of hypnosis parameters, the mean time for postural correction was 138 ± 26.72 minutes for GI animals and 120 ± 10.41 minutes for GII animals. On the time for returning to esternal decubitus, GI mean was of 165 ± 58.35 minutes, whilst in GII it took the mean of 135 ± 37.6 minutes.

TABLE 3 - Distribution of means ±standard deviations and medians, according to the group (GI – control and GII – SAF) for biochemistry variables (creatinine, urea, ALT and ALP) in bitches submitted to general inhalatory anesthesia

Variable	Groups	M0	M90
Creatinine (mg/dL) ‡	GI	0.85±0.10	0.77±0.07
		0.85	0.76
	GII	0.87±0.16	0.74±0.13
		0,8	0.7*
Urea † (mg/dL)	GI	26±11.58	24.6±11.51
		25.5	19.8
	GII	35.29±11.48	30.00±13.45
		30	24
ALT † (UI/L)	GI	28.17±9.79	21.33±7.47
		28,5	20*
	GII	38.29±14.03	36.00±19.50
		31	24
ALP † (UI/L)	GI	68.33±38.70	52.67±17.53
		65	54.5
	GII	111.71±41.12	113.14±95.41
		125	92

* Significant differences among moments within each treatment (p<0, 05); [abc] Significant differences between treatments along the moments (p<0, 05); † Group effect for the given variable (p<0, 05); ‡Moment effect for the given variable (p<0,05).

Discussion

In both groups, variations concerning RT were considered clinically significant, indicating the onset of mild hypothermia, characterized in the canine species by temperatures between 32º and 37ºC, as reported by Armstrong *et al.*[9] Such alterations may be explained by peripheral vasodilatation and reduced thermoregulatory vasoconstriction, which occur after induction of general anesthesia, even so in this case such loss has overcome the 1.5ºC decrease in the first 60 minutes due to thermal redistribution of central temperature, as mentioned by Deakin[1] and Vanni *et al.*[2] Another factor directly related to the results relates to the operating room temperature, established at 22 ºC, which contributed for the patients' heat loss, since room temperature is, as quoted from Vanni *et al.*[2] a known predictor of central temperature in anesthetized patients. As said those authors, assays considering average temperature in operating rooms, 20º to 23º C, revealed and average of 50% of hypothermic humane patients, despite pre and/or trans operative heating.

A similar pattern of RT reduction was described by Matsubara *et al.*[10] in dogs under, respectively, venous and volatile anesthesia, however, they have not aimed to adopt measures to avoid hypothermia or temperature variations in the operating room, factor which influence TR determination. The adoption of such measures should receive more attention in the methodology of experiments, especially in those which evaluate physiologic parameters in early postoperative period, due to the alterations which may occur, as reported by Felies *et al.*[11] in a study employing rats under anesthesia, separated by ages, heating system use and circadian rhythm.

The modification of the protocol used by Beck *et al.*[6] was based on the impossibility of access to some sites used by the author, mainly on mammary, crural and gastrocnemius regions, due to surgical act disturbance. This author states that CT values aid on the inferences of body heat loss.

In both groups CT was always inferior to RT, finding that may be attributed to room temperature effect, having the lower values presented on GI animals. The acclimatized environment may have contributed to CT reduction, in spite of the compensatory effect of room temperature and surgical focal lamps, which heated adjacent structures. Thus, even in face of positive correlation between RT and CT, the latter may not precisely reflect the animal's temperature, for they refer to different compartments, central and peripheral, respectively. The same observation was reported by Beck *et al.*[6] in a study employing swine, in which CT and RT were different in pre and postoperative periods.

The difference between RT and CT, called Delta T, was always greater in GI, but in both groups it was reduced along the moments, as RT also was reduced, reflecting the bitches' peripheral constriction degree and consequent peripheral perfusion. In GI, Delta T was greater than 3.5ºC until M45, and in GII such difference was reduced in M30. Despite such temperature gradient, it is not possible to state that peripheral perfusion has been compromised, for room temperature played a role on the establishment of such magnitude of a gradient in so little time. For Sessler *et al.*[12] this evaluation may be extended to surgical environments and other situations of hypothermia, whilst the critical value would be of 4ºC.

The Standard Deviations of RT means were noticeably inferior in GII from M45 on, as well as on CT means from M15, also in GII. Standard Deviation is a measure of variation among the individuals, therefore it reflects the homogeneity of results, and its lower values in GII indicate that the animals from this group presented more homogeneous or uniform results.

HR was kept within the species' physiological limits[13] during the entire evaluation period, and no significant clinical alterations were evident. Although there was no bradicardia (<60bpm), the animals from GII presented a significant difference among M90 and the initial moments (M0, M15 and M30). The reduction in HR means may be partially attributed to the drugs effect, since halothane may lead to dose-dependant reduction of HR, as described by Preckel.[14]

The values for the variable *f* remained within the species' reference interval during the entire observation period. There were no significant alterations on the comparison of MAP values along the moments, although means from GI were slightly below the values considered as normal for dogs under general anesthesia.

In spite of the reduction of HR and exposure of the bitches to a hypothermic environment (22ºC), the compensatory raise expected from MAP was not significant, probably due to the vasodilator effect of the drugs, and to the inhibition of vasoconstriction caused by hypothermia, with consequent alterations on peripheral vascular resistance. Nevertheless, the group effect observed corroborates the observation of higher MAP values in GII, even though there were no significant differences between groups in the individual moments' evaluation, indicating the influence of SAF® on this variable.

There were no clinical significant alterations concerning the variables creatinine, urea, ALT and ALP, and their values remained within the reference limits for the species. Such fact may be attributed to the short observation period, for most of the alterations related to this variable are described in periods greater than that established on this present study. The reduction on the creatinine values on GII animals was not considered clinically important, since only the increase of its serum concentration would be of relevance, directly connected to glomerular filtration rate.

ALT values decreased along the moments, a patter similar to that encountered by Mello and Cordeiro[8] in adult dogs under venous anesthesia. The significant reduction found only in GI may be attributed to the group effect observed. In the present study it was not perceived the increase in serum activity of ALT, described by Siqueira *et al.*[15], probably for not achieving the magnitude of hypothermia they described. Despite the occurrence of group effect, alterations were not observed in ALP values, a fact similar to that described by Mello and Cordeiro[10] in dogs under venous anesthesia.

Postural correction took place 18 minutes earlier, in average, in GII than in GI. GII also presented earlier return to esternal decubitus, 30 minutes in advance of GI, denoting the influence of using SAF®. Although RT values have not shown significant differences, there may have been some kind of difference in the patients' metabolism and on its biotransformation of the anesthetic drugs. Thus, despite the correlation described in literature,[3] RT may not have reflected circulatory temperature in a reliable manner, since the infusion of heated fluid has an impact directly on blood temperature, which, in lack of such circumstances, is determined only by the balance between the temperatures of central and peripheral compartments.

Despite the fact that significant clinical and biochemical alterations were not evident, the group effect on the variables MAP, urea, ALT, ALP, and hypnosis time point to probable effects determined by the use of SAF® in anesthetic procedures. Finally, there remains the belief that the use of this system may beget benefits to the patient under anesthesia, as evinced in this study, pointing to the necessity of future research.

Conclusion

The isolated use of the Fluid Heating System (SAF®) was not enough to avoid the establishment of hypothermia in bitches submitted to general inhalatory anesthesia, or to provide clinical and biochemical significant alterations.

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