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EFFECTS OF AURICULOPALPEBRAL NERVE BLOCK ON OCULAR PARAMETERS IN DOGS

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Abstract

The objective of this study was to compare the effects of two local anesthetics used on auriculopalpebral block on eyelid akinesia, tear production, intraocular pressure (IOP) and tear break-up time (TBUT) in conscious dogs. A blind, randomized, prospective study was conducted to determine the effects of auriculopalpebral block using ropivacaine 0.75% and bupivacaine 0.5% in 12 healthy non-brachycephalic dogs (24 eyes). Threat response and eyelid reflex tests, Schirmer tear test (STT), IOP and tear break-up time were conducted before blockage and at 30, 60, 120, 240 and 360 minutes after application. A difference was observed between the values found at 30, 60, 120 and 240 minutes compared to baseline for threat response and eyelid reflex tests in the two groups evaluated, proving eyelid akinesia after blockages. No difference was found for STT, IOP and TBUT between baseline values and post-anesthesia times or between groups. It was possible to conclude that ropivacaine and bupivacaine on auriculopalpebral block in conscious dogs promoted eyelid akinesia for at least 240 minutes, not altering ocular physiological parameters of tear production, intraocular pressure, and tear break-up time after blockages.

Keywords: Bupivacaine. Dog. Locorregional Anesthesia. Ropivacaine.

1. Introduction

The use of locoregional anesthesia is widely disseminated in veterinary ophthalmology for providing adequate analgesia and akinesia. Among the various existing techniques, eyelid blocks in dogs represent a feasible alternative adjuvant for ocular surgeries (Honsho et al. 2014).

The locoregional anesthesia as a single protocol in ophthalmology may be required for less invasive clinical procedures and diagnostic maneuvers, especially for routines in large-sized animals (Michou and Leece 2012). Therefore, eyelid anesthetic blocks are used in cases resulting from acute painful processes, such as ocular traumas, eyelid lacerations, corneal ulcers, and ocular foreign bodies, providing comfort to patients and assistance to the veterinary physician, and may also be used for the canine species (Mathews et al. 2014).

When the blockage used is able to remove only the motor component, that is, to abolish eyelid movement, the result can be defined as eyelid akinesia. Akinesia means absence of movement. Eyelid akinesia may be required in cases of blepharospasms, in which friction of the eyelids on the ocular surface results in eye lesions or prevents assessment by the veterinary physician (Featherstone and Heinrich 2013).

When injected correctly, the anesthetic agent promotes effective eyelid akinesia resulting from blocking the auriculopalpebral nerve, the facial nerve branch, and the efferent pathway of the blinking act. Eyelid ptosis and cleft eyelid reduction are observed; however, movement of the eye bulb is not compromised, and movement of third eyelid and retraction of eye bulb, mediated by abducent and oculomotor nerves, can also be noticed (Michou and Leece 2012).

Safe anesthesia in ophthalmology should promote stability, or slight decrease of intraocular pressure, absence of corneal sensitivity and absence of eyelid reflexes. Therefore, eyelid blocks can contribute to obtaining safer and more efficient ocular anesthesia when used in combination with general anesthesia, since the suppression of eyelid and corneal reflexes is seen in deep anesthetics planes. Thus, when using eyelid blocks, the total dose of general anesthetics could be reduced. When opting for such blockages, the choice of the anesthetic agent should include characteristics, such as time of action, irritation at injection site and stability of ocular parameters (Shilo-Benjamini et al. 2018; Shilo-Benjamini 2019).

The time of action of bupivacaine in anesthesia is between 360 and 600 minutes (Santamaria et al. 2017; Shilo-Benjamini 2019; Zibura et al. 2019) and the duration of ropivacaine is dose-dependent, however, the literature reports that its analgesic capacity lasts longer than bupivacaine (Bayley and Read 2018; Shilo-Benjamini 2019), which may contribute to more thorough and detailed ocular procedures. The choice for bupivacaine and ropivacaine was due to their time of action since the long duration of their effects as anesthetics would allow the evaluation of their safety or not in the use for longer-lasting ophthalmic procedures.

Auriculopalpebral nerve block in dogs is usually used in the routine, combined with general anesthesia techniques (Mathews et al. 2014). However, the knowledge of its application alone is important to evaluate and monitor its effects on the ocular surface, intraocular pressure, and other ocular parameters in awake dogs, besides offering adjuvant methods to the control of blepharospasm and diagnosis aid.

The objective of this study was to evaluate the effects of the use of different local anesthetics, such as bupivacaine and ropivacaine for auriculopalpebral block in conscious dogs, on ocular parameters using Schirmer tear test, tear break-up time, tonometry, and colorimetric test with fluorescein.

2. Material and Methods

Study design

A blind, randomized, prospective study was conducted to determine the effects of auriculopalpebral block using ropivacaine 0.75% and bupivacaine 0.5%. This study was duly submitted and approved by the Ethics Committee on the Use of Animals of the Federal University of Jataí (Protocol nr. 025-17) and conducted at the Veterinary Hospital of the Federal University of Jataí, Goiás, Brazil.

Selection of animals

Twelve non-brachycephalic adult male dogs (24 eyes), proven healthy by previous examinations, were selected from a single kennel in the city, with the consent of the tutor.

Physical (cardiopulmonary auscultation, rectal temperature, capillary filling time), laboratorial (hemogram and leucogram, serum levels of alanine aminotransferase, alkaline phosphatase, urea, and creatinine) and ophthalmic (Schirmer tear test, direct and consensual pupillary reflexes, slit lamp biomicroscopy, tonometry, indirect ophthalmoscopy and fundoscopy, fluorescein dye test and tear break-up time) examinations were conducted.

Auriculopalpebral block technique

Dogs were randomly distributed in two groups of six animals: in one group, the anesthetic auriculopalpebral nerve block was made with ropivacaine 0.75% (Ropi[®], Cristália, Itapira, SP, Brazil) (ropivacaine group – RG) and in the other with bupivacaine 0.50% (Neocaína[®], Cristália, Itapira, SP, Brazil) (bupivacaine group - BG). Blockage was made at the site where the auriculopalpebral nerve is easily accessed along the dorsal region of the zygomatic arch. The needle was placed on the subcutaneous tissue and 1.5mg/kg of local anesthetic was injected on the nerve. The drug was easily applied by palpating the

zygomatic arch using a 3mL syringe and a 25x7mm hypodermic needle, performing trichotomy and prior antisepsis with povidone iodine and alcohol 70%.

The containment of the animals was made physically, with the aid of two people and use of muzzles. The subcutaneous application of local anesthetic did not constitute a painful process requiring chemical containment.

Ophthalmic tests

Tests were conducted in the following order, with the purpose that one test did not alter the results of the others: threat response, eyelid reflex, Schirmer tear test, intraocular pressure, and tear break-up test.

Palpebral kinetics

To evaluate palpebral kinetics, threat response and eyelid reflex tests were used classified as follows: (0) absent – eyelid akinesia; (1) partial – reduced eyelid movement; (2) complete – normal eyelid movement.

For threat response, a threatening gesture was performed with the hand towards the eye to be evaluated and, for eyelid reflex, a digital stimulus on the eyelids was measured.

Aqueous tear production

Aqueous tear production was evaluated using the Schirmer tear test-1 (STT-1), in which a 5mm width and 35mm length commercial millimeter strip of Whatman 41 (Schirmer Test Strips, Ophthalmos, São Paulo, SP, Brazil) was positioned on the lower conjunctival fornix, near the junction of the middle and temporal third of the eyelid, for one minute, without prior instillation of anesthetic eye drops, to measure the production of the aqueous portion of the tear.

Intraocular pressure

Intraocular pressure was measured using a digital applanation tonometer (Tono-Pen[®] XL, Reichert, USA), obtaining only the results with 5% standard deviation measured by the device, with no use of prior anesthetic eye drops after blockage completion. Anesthetic proxymetacaine hydrochloride eye drops (Anestalcon[®], Novartis Biociências S.A., São Paulo, SP, Brazil) were used only in the evaluation before the anesthesia of the auriculopalpebral nerve.

Tear break-up time

Tear break-up time (TBUT) was evaluated by slit lamp biomicroscopy (SL-15, Kowa, Kowa Life Science Division, Tokyo, Japan). A drop of fluorescein sodium eye drops 1% (Colírio Fluoresceína, Allergan, Guarulhos, SP, Brazil) was instilled and tear break-up time, that is, the time spent for the onset of the first dry spot-on ocular surface, was timed.

Eyelid akinesia, intraocular pressure and tear production evaluations were conducted before the anesthesia of the auriculopalpebral nerve and at the 30, 60, 120, 240, 360 subsequent minutes. The tear break-up test was conducted only at the beginning (before the anesthetic block) and after 360 minutes to avoid alterations on the other tests due to the use of fluorescein eye drops, subsequently removed with saline solution. During that time, patients were kept in a ventilated and bright environment, in metal cages suitable for dogs (1.2x0.9m), with comfortable room temperature kept stable by air conditioning (24°C), with no air displacement towards the patient in order to avoid interference on the ocular surface.

Statistical analysis

Data were analyzed using the software SigmaStat for Windows[®], version 12.0. The Shapiro-Wilk test was used to evaluate data normality. ANOVA methods were used for parametric data, followed by the Bonferroni test to evaluate the different times within a same group. The t test was used for evaluation between groups. For non-parametric evaluations, the Mann-Whitney Hank Sum test was used for

comparisons of a same time between the different groups and Friedman for evaluation between times of a same group. A significance level of 5% was used for all evaluations.

3. Results

Study population

The studied population consisted of mixed-breed castrated male dogs between one and six years old, with body weight between 5 and 15kg. This population was chosen as an attempt to standardize the sample within the dogs available at the kennel for this study. It is known that age and breed of the dog can influence STT, however, there is no evidence of interference caused by gender (Hamor et al. 2000; Hartley et al. 2006).

Palpebral kinetics

The results of threat response test evaluations in the ropivacaine (RG) and bupivacaine (BG) groups are shown in Table 1. The absence of threat response was observed in both groups from the second time of the evaluation (30min), however not noticing differences between the two groups evaluated. It is observed that at the last time of the evaluation (360min), most of the animals already showed a complete test response.

Table 1. Table showing the numbers of eyes analyzed in the threat response test in dogs submitted to auriculopalpebral block using ropivacaine (RG) or bupivacaine (BG), according to the evaluation time and classified as absent, partial, or complete reflex.

Т	ROPIVACAINE (RG)			BUF	BUPIVACAINE (BG)		
	Absent	Partial	Complete	Absent	Partial	Complete	
0min	0	0	12ªA	0	0	12ªA	
30min	9	3	0 ^{bA}	12	0	0 ^{bA}	
60min	12	0	0 ^{bA}	12	0	0 ^{bA}	
120min	10	2	0 ^{bA}	10	2	0 ^{bA}	
240min	6	6	0 ^{bA}	3	9	0 ^{bA}	
360min	0	4	8 ^{aA}	1	5	6 ^{aA}	

Different lowercase letters on the same column mean differences between times within a same group ($\alpha < 0.05$). Different uppercase letters on the same line mean differences between groups at the same time ($\alpha < 0.05$).

The RG and BG results for the eyelid reflex test are shown in Table 2. Similarly to the previous analysis, no significant difference between groups was observed in the eyelid reflex test.

Table 2. Table of the numbers of eyes analyzed in the eyelid reflex test in dogs, submitted to auriculopalpebral block using ropivacaine or bupivacaine, according to the evaluation time and classified as absent, partial, or complete reflex.

•						
	ROPIVACAINE			BUPIVACAINE		
I	Absent	Partial	Complete	Absent	Partial	Complete
Omin	0	0	12 ^{aA}	0	0	12 ^{aA}
30min	9	3	0 ^{bA}	12	0	0 ^{bA}
60min	12	0	0 ^{bA}	12	0	0 ^{bA}
120min	10	2	0 ^{bA}	10	2	0 ^{bA}
240min	6	6	0 ^{bA}	3	9	0 ^{bA}
360min	0	4	8 ^{aA}	1	5	6 ^{bA}

Different lowercase letters on the same column mean differences between times within a same group ($\alpha < 0.05$). Different uppercase letters on the same line mean differences between groups at the same time ($\alpha < 0.05$).

Aqueous tear production

During the Schirmer tear test, no difference was observed before and after blockage or when the different groups were compared (Table 3). However, although RG differences were not evidenced compared

to baseline, there was a slight reduction in tear production in the 30 to 360min times. On the other hand, there was increased tear production in BG in the 30 to 360min times.

Т	ROPIVACAINE	BUPIVACAINE
0min	19.33 ± 6.34 ^{Aa}	16.50 ± 2.84 ^{aA}
30min	17.16 ± 3.97 ^{aA}	18.33 ± 5.41 ^{aA}
60min	17.33 ± 4.20 ^{aA}	18.41 ± 5.28 ^{aA}
120min	17.58 ± 4.03 ^{aA}	20.66 ± 5.78 ^{aA}
240min	17.91 ± 3.67 ^{aA}	19.25 ± 5.02ª ^A
360min	18.50 ± 3.60ªA	20.16 ± 5.18 ^{aA}

Table 3. Means and standard deviation of the values found in the Schirmer tear test (mm/min), according to the evaluation time, in dogs submitted to auriculopalpebral block using ropivacaine or bupivacaine.

Different lowercase letters on the same column mean differences between times within a same group ($\alpha < 0.05$). Different uppercase letters on the same line mean differences between groups at the same time ($\alpha < 0.05$).

Intraocular pressure

An IOP reduction was observed during evaluation in both groups for 240 minutes after blockage, however not showing statistical difference between groups or between the times evaluated (Table 4). It is noteworthy that all values remained within normality for IOP in dogs, ranging from 10 to 26mmHg.

Table 4. Means and standard deviation of the values found in the intraocular pressure (mmHg), according to the evaluation time, in dogs submitted to auriculopalpebral block using ropivacaine or bupivacaine.

Т	ROPIVACAINE	BUPIVACAINE
0min	16.58 ± 3.47 ^{aA}	16.75 ± 3.30 ^{aA}
30min	15.08 ± 2.81 ^{aA}	14.33 ± 3.17 ^{aA}
60min	15.00 ± 3.38 ^{aA}	14.66 ± 2.99 ^{aA}
120min	15.16 ± 2.98 ^{aA}	15.25 ± 4.47 ^{aA}
240min	15.75 ± 2.98 ^{aA}	15.66 ± 4.16 ^{aA}
360min	17.33 ± 4.14^{aA}	15.75 ± 3.49 ^{aA}

Different lowercase letters on the same column mean differences between times within a same group ($\alpha < 0.05$). Different uppercase letters on the same line mean differences between groups at the same time ($\alpha < 0.05$).

Tear break-up time

During the tear break-up test, the means and standard deviation found at baseline time were 17.91 \pm 4.12 seconds for RG and 17.58 \pm 3.52 seconds for BG. The second TBUT evaluation was conducted at the end of the experiment, about 360 minutes after blockage, and the values obtained were 16.41 \pm 3.23 seconds for RG and 13.25 \pm 4.26 seconds for BG. Although not statistically significant, tear break-up values showed a subtle drop, more evident in BG.

Other observations

Dry spots were observed in the cornea, by slit lamp biomicroscopy, as of 30 minutes, in all eyes studied. At the end of the procedure, superficial corneal fluorescein dyeing was observed in both eyes in seven of the 12 dogs studied, with no discontinuity of the corneal epithelium, using a slit lamp biomicroscope. A layer of ophthalmic ointment (Regencel[®], Latinofarma, Cotia, SP, Brazil) was applied on those animals. Examination was repeated the next day and there was no corneal fluorescein dyeing.

4. Discussion

The anesthesia of the auriculopalpebral nerve could be conducted on the conscious animal, only with minimal physical restraint, which allowed the evaluation of the effects caused exclusively by local anesthetics, without the possible interferences caused by systemic anesthesia in the physiology of the eye. No reluctance reactions to the application of local anesthetics were observed. However, some animals submitted to the administration of bupivacaine showed discomfort at the time of injection and, in two RG

dogs, sporadic pruritus was observed between the zygomatic arch region and the ear during the first 30 minutes. The literature reports that most of the local anesthetics can cause pain at the time of application and that, for ropivacaine, pruritus can be observed as a response to the pain caused by the drug on the tissue or allergic reaction (Berkun et al. 2003; Calderon et al. 2012; Santamaria et al. 2017; Locke et al. 2018).

Perhaps, the discomfort reactions observed with bupivacaine are related to its non-ionized form, since the events were observed in their majority to what would correspond to the latency period of the anesthetic. The pKa of bupivacaine is slightly higher (ropivacaine 8.1 and bupivacaine 8.16), indicating that its latency period could be slightly longer when applied in the same medium, with the same pH (Schroeder 2019). However, in this study, the latency period of the anesthetics used in blockage was not determined.

The fact that auriculopalpebral block was used on the conscious animal also allowed the study of the isolated action of local anesthetics on ocular parameters, since general anesthesia and sedation may alter intraocular pressure, tear break-up time, tear production and neuro-ophthalmic tests (Carareto et al. 2007; Douet et al. 2018).

Threat response and eyelid reflex neuro-ophthalmic tests were used to confirm the duration of local anesthesia. The efferent pathway of those tests is the facial nerve and the main response observed to the stimulus is eyelid closure. Thus, the dog should respond to the tests blinking (Martins and Galera 2011; Featherstone and Heinrich 2013; Ofri, 2013). In turn, it is expected that this efferent pathway is blocked by the local auriculopalpebral anesthesia technique, upon effective anesthetic block. Therefore, the threat response and eyelid reflex tests were considered appropriate to evaluate the efficacy of auriculopalpebral block.

It was observed in both groups the absence of eyelid movement as threat response and eyelid reflex from 30 to, at least, 240 minutes, evidencing the same efficacy of ropivacaine and bupivacaine in promoting eyelid akinesia. The time found for motor block effect was different from that reported by Shilo-Benjamini (2019), who described a motor effect of 360 minutes for bupivacaine and up to 480 minutes for ropivacaine. However, in a study by Honsho et al. (2014), it was observed that ropivacaine and bupivacaine demonstrated to act in similar duration times, as the results found in this study, in which both anesthetics had times of actions shorter than 360 minutes.

Although no statistical differences were evidenced in the Schirmer tear test after anesthetic blocks in both groups, there was a slight reduction in tear production at all evaluation times after the anesthesia of the auriculopalpebral nerve. This result was similar to the one found by Klaumann (2007), who observed tear production reduction compared to baseline in dogs 70 minutes after peribulbar block with ropivacaine 1%.

The reduction of the Schirmer tear test values, even if discreet, draws attention to the need for ocular surface care during trans and postoperative periods, with the purpose that no keratitis and ulcers resulting from this decrease occur, combined to eyelid akinesia. Despite the difference among the species, this result is also similar to the one found by Honsho et al. (2014), who observed that ropivacaine 0.75% showed a greater and more lasting tear production reduction when compared to bupivacaine, when used in retrobulbar block in humans. However, in a study by Visser et al. (2017) evaluating tear production after auriculopalpebral nerve block with lidocaine 2% in horses, increased values were observed in the Schirmer tear test, although not significant.

Although corneal dyeing with fluorescein eye drops was observed, at the end of the experiment no corneal epithelium discontinuity was noted when conducting the examination with the slit lamp biomicroscope. This dyeing possibly occurred due to superficial peeling of the cornea at the contact site of the Schirmer test during evaluations.

No difference was observed in tear break-up time at baseline and after 360 minutes, even in the absence of eyelid movement for at least 240 minutes. As a consequence of eyelid akinesia, there is also decreased tear dispersion on the ocular surface. However, it is probable that the anesthetic block time was not sufficient to create changes in the arrangement of the precorneal tear film, helping to maintain the quality of the corneal surface.

The eye needs the normal movement of the eyelids, mediated by the facial nerve, for protection of the ocular surface and spraying of the tear film, essential in maintaining corneal integrity (Williams 2018). In this way, the duration of an ideal auriculopalpebral block in dogs would be the one that does not compromise

corneal integrity. Thus, blockage duration for 240 minutes corroborated with the preservation of the ocular surface, proven through the conservation of TBUT, which remained within normal limits after blockages.

The decreased tear break-up time was observed by Cullen et al. (2005) in an experiment conducted with healthy cats, evaluating TBUT before and after anesthesia. They report that tear break-up time reduction is closely related to tear production reduction.

Therefore, other factors can be listed to justify the maintenance of TBUT in this study, citing the preservation of the production of the aqueous portion of the tear film, proven by the STT values and characteristics common to auriculopalpebral block, such as eyelid ptosis and maintenance of retraction of eye bulb and movement of third eyelid. It is known that the retraction of eye bulb and the movement of third eyelid. It is known that the retraction of eye bulb and the movement of third eyelid are mediated by the abducent and oculomotor nerves, and the auriculopalpebral block in dogs only reach branches of the facial nerve, responsible for palpebral movement. Consequently, the animal could still retract the eyeball and move the third eyelid when detecting discomfort in the ocular surface, which, in its turn, has as its afferent pathway the trigeminal nerve, which is not affected by auriculopalpebral block (Michou and Leece 2012). The trigeminal nerve, in turn, when stimulated from the ocular surface, is able to induce tear production (Esteves et al. 2009; Park et al. 2019).

Therefore, even in the face of auriculopalpebral block, the retraction of the eyeball, the movement of the third eyelid, the maintenance of aqueous production of tear film and eyelid ptosis contributed to preserve TBUT in this study.

Even with no difference, we could observe IOP reduction in both groups, for 240 minutes after blockage. However, all values are within normality for IOP in dogs, ranging from 10 to 26mmHg. Those results are similar to those found by Klaumann (2007), who reported discrete IOP variation, however the values remained within the normality range for IOP in dogs. IOP decrease can be attributed to the action of anesthetic agents in the trigeminal nerve, since it is known that the stimulation of this nerve causes IOP increase. Those results differ from those found by Honsho et al. (2014), in which there was a significant reduction in the retrobulbar block conducted with ropivacaine, far beyond those observed when blockage was conducted with bupivacaine and other anesthetics. They report that this effect is related to the greater capacity of ropivacaine in producing relaxation of the musculature extrinsic to the bulb, which contributes to intraocular pressure reduction.

Surprisingly, there was IOP reduction, even if discrete and without statistical significance, during the effects of auriculopalpebral nerve block, in both groups, measured without prior instillation of anesthetic eye drops. It is known that IOP is influenced by painful stimuli to the cornea, mediated by the abducent and oculomotor nerves, and the force exerted by the eyelids on ocular surface, mediated by the facial nerve (Evangelho et al. 2019; Sanchez and Martin 2019). In this study, despite blockage in eyelid movement, the stimulus to cornea touch, generated by measuring IOP with tonometer and the force exerted on eye bulb, as a reflex to this manipulation, still remained. Thus, it is probable that the relaxation of eyelid during blockage supplanted the stimulus by tonometer and the force exerted by the extraocular muscles in the retraction of the eye bulb, showing the importance of the eyelid component on the IOP.

No articles on the effects of auriculopalpebral block on IOP were found for comparison, however, Honsho et al. (2014) showed a significant reduction of IOP in the retrobulbar block conducted with ropivacaine far beyond those observed when blockage was conducted with bupivacaine and other anesthetics. They report that this effect is related to the greater capacity of ropivacaine in producing relaxation of the musculature extrinsic to the bulb, which contributes to intraocular pressure reduction.

As limitations of this experiment, it is possible to observe the time used for the beginning of measurements, since the onset of anesthetic action may have occurred before the 30 minutes, which was the first evaluation. We can also mention the time used between one evaluation and the other. A shorter time between one measurement and the other would provide more accuracy about the end of the anesthetic action. Another limitation was the difficulty of finding current literature describing the same tests with the same type of blockage used. Thus, it is necessary to deepen the studies and reports of this same procedure for the theoretical basis of other researchers.

5. Conclusions

It was possible to confirm with this study that the local anesthetics ropivacaine and bupivacaine confer eyelid akinesia, not altering ocular physiological parameters of tear production, intraocular pressure, and tear break-up time after blockage. Thus, the technique used in this experiment may contribute to patients with blepharospasm or diagnostic assistance.

Authors' Contributions: LUZ, L.C.: conception and design, acquisition of data, analysis and interpretation of data, drafting the article; AMARAL, A.V.C.: conception and design, analysis and interpretation of data, drafting the article; SILVA, A.C.A.: acquisition of data, analysis and interpretation of data; NEVES, C.A.: acquisition of data, analysis and interpretation of data; NEVES, C.A.: acquisition of data, analysis and interpretation of data; REGALIN, D.: analysis and interpretation of data, drafting the article. All authors have read and approved the final version of the manuscript.

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