Effect of Anaesthetic Premedication with Medetomidine-Buprenorphine on the Aqueous Tear Production in Dogs

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Abstract

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The Schirmer tear test (STT) was performed in 28 healthy dogs and five dogs with dry-eye syndrome before anaesthesia and 10 and 30 minutes after anaesthetic premedication with medetomidine (20 μg/kg) and buprenorphine (10 μg/kg). All healthy dogs had normal preanaesthetic STT values (16.9 ± 1.08 mm/min). STT values 10 minutes after premedication were highly significantly decreased ($p < 0.01$) from the normal values to critical value (1.7 ± 0.94 mm/min) and after 30 min STT was undetectable (STT 0 mm/min.). Dogs with dry-eye syndrome had preanaesthetic STT 6.4 ± 0.18 mm/min. In comparison with healthy dogs, in this group STT values were undetectable (STT 0) already 10 min after premedication ($p < 0.01$). The age, breed, sex and body weight of the patients did not significantly influence the STT results. Medetomidine (20 μg/kg) with buprenorphine (10 μg/kg) is a good anaesthetic premedication that induces profound sedation and analgesia. STT was recommended as a part of preanaesthetic examination, and eye protection should be performed in each dog premedicated with medetomidine-buprenorphine to prevent corneal damage.

Schirmer tear test, α_2-adrenergic agonist, opioid, sedation

Medetomidine is a potent selective α_2-adrenergic agonist with sedative, myorelaxant and analgesic effects (Clarke and England 1989; Ko et al. 1996; Muir et al. 1999). The level of sedation and analgesia is dependent on the dose administered (Paddleford and Harvey 1999). Increments of the dose do not result in qualitative changes in the effect, only the duration of anaesthesia changes (Pypendop and Verstegen 1998). Following intravenous administration, medetomidine assumes action within 2 minutes; analgesia and sedation last approximately 45 and 60-90 min, respectively. Medetomidine has depressive cardiovascular (bradycardia, cardiac output drop, rise in systemic vascular resistance) and respiratory (bradypnoe) effects. Blood pressure values, however, remain at the same level or are slightly elevated (Pypendop and Verstegen 1998; Pypendop and Verstegen 1999).

Buprenorphine is a partial opioid agonist with good analgesic effects. It induces only mild sedation and has minimum adverse effects on the cardiovascular system. The onset of buprenorphine effects after intravenous administration is delayed (15-30 min) and the analgesic effects last for a longer period (8-10 hours). Apart from good analgesic effect, it is also characterised by mild sedative and cardiovascular depressive actions (Cowan et al. 1977; Martinez et al. 1997).

With combination of α_2-agonists and opioids much lower doses are sufficient for the same sedation effect (Young et al. 1990; Bartram et al. 1993; Bartram et al. 1994; Muir et al. 1999; Pascoe 2000). Dose reductions of both drugs minimize the unfavorable adverse effects.

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Even though there are many reports concerning the side effects of these two drugs, to our knowledge there are no reports on their undesirable side effects on the tear production in dogs. Eye and corneal protection during general anaesthesia is important to prevent the incidence of corneal damage, especially in humans (Grover et al. 1998; Marquardt et al. 1987). In veterinary medicine the eye protection is often overlooked. It was performed routinely only with the use of ketamine (Arnett et al. 1984). However, patients after anaesthetic premedication or under general anaesthesia do not have any conscious blinking reflex to protect the eyes from damage or injuries (Marquardt et al. 1987). Tears play an important role in the defense of conjunctival and corneal surfaces (Eichenbaum et al. 1987; Nečas 1992; Kottman and Nečas 1993). Furthermore, some drugs that can be administered before general anaesthesia, such as atropine (Ludders and Heavner 1979; Vestre et al. 1979), sulfonamide (Collin et al. 1986; Tuntivanich et al. 1997; Soontornvipart et al. 1997), aspirin and furosemide (Thorig et al. 1984), can also reduce the tear production. Temporary tear hyposecretion may be seen in old dogs after surgery due to drug-induced circulatory abnormalities (Ludder and Heavner 1979; Severin 1995). The damage to the eye during sedation or general anaesthesia may occur easily (Krupin et al. 1977; Herring et al. 2000).

Medetomidine alone or in combination with buprenorphine is commonly used for sedation and anaesthetic premedication in veterinary medicine (Robinson et al. 2001; Raušer and Lexmaulová 2002; Raušer et al. 2002). However, to our knowledge there are no data concerning the side effects on tear production available. The aim of our study was to evaluate the effect of this premedication on the tear production in dogs and to emphasize the need of corneal protection when using these drugs.

Materials and Methods

Animals

We performed our study in 33 clinically healthy dogs (17 males and 16 females) of 13 breeds (5 Dachshunds, 5 Poodles, 3 Labrador Retrievers, 3 Golden Retrievers, 3 American Staffordshire Terriers, 3 English Cocker Spaniels, 2 Pointers, 2 German Shepherds, 1 Giant Schnauzer, 1 American Pitbull Terrier, 1 Doberman Pinscher, 1 Mixed Breed, 1 Bulldog, 1 American Cocker Spaniel and 1 Whippet), in the age of 5.9 ± 2.81 years and body weight 4-45 kilograms (21.0 ± 13.03 kg). In all dogs we measured STT (Schirmer tear test) during radiological examinations or preoperative patient preparation. The physical and ophthalmological examinations were performed to exclude any ophthalmologic abnormalities or systemic problems, which can disturb or influence the tear production. The patients with no previous medical treatment, with normal physical and ophthalmological examination results were included in this study.

Protocol of the experiment

Schirmer tear test (STT) is a quantitative method, which measures the aqueous tear production. A normal STT value is 12-22 mm/min (Severin 1995). Schirmer tear test's paper strip (COLOR BAR, EagleVision, USA) is placed between lower eyelid and cornea and the eyelid is held closed for 1 minute. After paper strip removal, the amount of moisture on the strip is measured in millimeters.

Schirmer tear tests (STT) were performed in 28 healthy dogs (right eye) before and 10 and 30 minutes after intravenous premedication by medetomidine (Domitor, Pfizer, B) – 20 μg/kg with buprenorphine (Temgesic, Schering-Plough, U.K.) - 10 μg/kg. STT values were calculated in mean ± SD mm/min. All patients were prepared for osteosynthesis procedures or for radiography.

Statistical evaluation

Statistical evaluation included comparison of parameters in both groups of animals (age, sex and weight) as well as STT parameters measured before and 10 and 30 min after anaesthetic premedication. All data was reported in mean ± SD. We also compared normal and pathological STT values and their variations between dogs with normal STT. The Student's paired T-test was used to evaluate the difference between the mean of STT before and STT after premedication.

Results

In our experience, medetomidine (20 μg/kg) with buprenorphine (10 μg/kg) administered intravenously is a good preanaesthetic medication. They can produce profound

Table 1
Breed, age, sex and Schirmer tear test before and after medetomidine-buprenorphine anaesthetic premedication

Breed	Age (years)	Sex	Weight (kg)	STT (mm/min)		
				Before premedication	10 min after premedication	30 min after premedication
Dachshund	8	M	11	16	1	0
Dachshund	5	M	10	15	3	0
Mixed Breed	0.5	F	9	17	2	0
Dachshund	4	M	12	14	1	0
Poodle	0.4	M	4	17	2	0
Whippet	1	F	10	17	0	0
Poodle	2	F	5	18	0	0
Labrador Retriever	0.5	M	28	17	7	0
Golden Retriever	0.6	M	32	18	2	0
Doberman Pinscher	5	F	35	17	1	0
English Cocker Spaniel	7	F	14	18	1	0
German Shepherd	6	M	45	16	2	0
Golden Retriever	5	M	40	18	1	0
Poodle	12	F	4	17	2	0
Dachshund	6	F	8	16	1	0
Labrador Retriever	0.4	F	25	18	1	0
English Cocker Spaniel	0.5	M	12	17	2	0
German Shepherd	8	F	39	16	0	0
Poodle	4	F	5	19	3	0
Giant Schnauzer	7	M	38	18	2	0
Pointer	8	M	32	17	3	0
Staffordshire Terrier	0.6	F	35	16	1	0
Staffordshire Terrier	1	M	34	16	1	0
Pitbull Terrier	0.5	M	28	16	0	0
Golden Retriever	5	F	36	18	2	0
Labrador Retriever	0.5	F	28	17	3	0
Staffordshire Terrier	0.6	M	27	16	2	0
Pointer	0.5	F	18	17	2	0

Table 2
Breed, age, sex and Schirmer tear test before and after medetomidine-buprenorphine anaesthetic premedication in dogs with suspected dry-eye syndrome

Breed	Age (years)	Sex	Weight (kg)	STT (mm/min)		
				Before premedication	10 min after premedication	30 min after premedication
English Cocker Spaniel	8	M	14	5	0	0
Bulldog	3	M	32	7	0	0
Dachshund	10	F	8	8	0	0
American Cocker Spaniel	5	M	12	6	0	0
Poodle	9	F	4.5	6	0	0

sedation and analgesia. It is good enough to manipulate with the patients during radiography or patient preparation for the surgery without any problems.

The age, breed, sex and body weight of the patients did not significantly influence the STT results. Although it is reported that long-haired-breed dogs tend to have higher normal STT values than short-haired breeds (Severin 1995; Tuntivanich et al. 2001) there was not any statistical difference in our study.

Twenty-eight dogs had normal STT values (14-19 mm/min; mean 16.9 ± 1.08 mm/min) before medetomidine-buprenorphine premedication. STT had tendency to decrease after administration of medetomidine-buprenorphine. Concretely, the STT values 10 min and 30 min after the premedication were 0-3 mm/min (mean=1.7 ± 1.38 mm/min) and 0 mm/min, respectively. STT values were highly significantly decreased ($p < 0.01$). STT in all dogs 30 min after premedication was undetectable (0 mm/min) (Table 1).

Five dogs with dry-eye syndrome had abnormal STT value (STT 5-8 mm/min, 6.4 ± 1.14 mm/min) before premedication. These values were significantly lower than STT in normal healthy dogs. None of these 5 dogs had severe clinical ophthalmic sign (3 dogs had purulent ocular discharge, 2 dogs had mild conjunctivitis) before premedication. STT values in comparison with healthy dogs at 10 and 30 min after medetomidine-buprenorphine premedication were highly significantly decreased ($p < 0.01$) (Table 2).

Discussion

The α_2-adrenergic agonist medetomidine produces good sedation, analgesia and myorelaxation, sufficient for use in many procedures such as radiological examination and preoperative patient preparation. According to its effects on central α_2-adrenoreceptors, it can produce analgesic and sedative effects. Low dose of α_2-adrenergic agonist (medetomidine) and opioid (buprenorphine) combination results in a synergistic CNS depressive response with decrease of unlikely side effects of both drugs (Paddleford and Harvey 1999). Medetomidine-buprenorphine combination is commonly used in veterinary practice to produce profound sedation and analgesia in healthy dogs (Bartram et al. 1994; Pypendop and Verstegen 1998; Raušer and Lexmaulová 2002).

The lacrimal gland and third eyelid gland are the primary sources of serous tear film in dogs (Severin 1995). The aqueous tear components are responsible for corneal health due to decreased eyelid shearing forces and providing corneal antibacterial and optic activity (Wilkie 1996). Aqueous tear components also provide corneal or conjunctival metabolic requirements such as glucose or oxygen, removing waste products and provide lubrication for the eyelids. Tear film is the most important part of nonspecific defense of the ocular surface (Eichenbaum et al. 1987).

According to our study, STT in 28 healthy dogs was significantly decreased after administration of medetomidine-buprenorphine premedication (in comparison with normal value) ($p < 0.01$) at all observing periods. Within 30 min after premedication, STT in all dogs was undetectable (STT 0 mm/min). We concluded that aqueous tear production was decreased after medetomidine-buprenorphine premedication. It is probably due to temporary hyposecretion caused by circulatory disturbances (Ludder and Heavner 1979; Severin 1995) after premedication. Medetomidine has a rapid onset of action and produces smooth muscle-mediated vasoconstriction and endothelial-dependent-mediated vasodilation after intravenous application (Paddleford and Harvey 1999). Buprenorphine has minimal cardiovascular effect and onset of its action is delayed (15-30 min) (Cowan et al. 1977; Martinez et al. 1997). In our opinion, 10 and 30 min after administering medetomidine-buprenorphine, the major cardiovascular effects and the effects on tear production are mainly influenced by medetomidine.

When the aqueous tear production is decreased, cornea and conjunctiva are easily damaged (Tuntivanich et al. 2001). It is significant especially in dogs affected with KCS. Any procedures after preanaesthetic medication with medetomidine-buprenorphine should be considered for the corneal and conjunctival damage. The corneal protection with artificial tears or ointments should be performed in all of these cases.

Furthermore, in dogs with dry eye syndrome (STT 5-8 mm/min), we found that after premedication all 5 patients had a mild degree of corneal and conjunctival injuries (corneal erosions and conjunctivitis).

We did not measure the post-anaesthetic STT values because of the large difference in duration of anaesthesia. Other anaesthetic medications may also take effect on the tear production (Severin 1995).

The eye ointment or artificial tears should be used before administration of preanaesthetic medication with medetomidine-buprenorphine in all dogs, especially those with dry eye syndrome to prevent eye injuries. Schirmer tear test should be performed as a part of preanaesthetic examination (Tuntivanich et al. 2001).

Vliv anestetické premedikace medetomidin-buprenorfin na produkci vodní složky slz u psů

U 28 zdravých psů byl prováděn Schirmerův slzný test (STT) před a 10 a 30 minut po anestetické premedikaci medetomidinem (20 μg/kg) a buprenorfinem (10 μg/kg). Všichni zdraví psi měli normální preanestetické hodnoty STT (16,8 ± 1,05 mm/min). Deset minut po premedikaci však byly hodnoty STT významně nižší ($p < 0,01$) oproti normálním hodnotám a dosahovaly kritické úrovně (1,7 ± 1,38 mm/min). Třicet minut po premedikaci byly hodnoty STT neměřitelné (STT 0 mm/min). Pět psů mělo před premedikací suspektní syndrom suchého oka (STT 6,4 ± 1,14 mm/min). V porovnání se zdravými psy byl STT u této skupiny 10 minut po premedikaci významně snížen ($p < 0,01$) (STT 0 mm/min). Po 30 minutách byly hodnoty STT také neměřitelné (STT 0 mm/min). Věk pacientů, plemeno, pohlaví a hmotnost neměly vliv na hodnoty STT. Medetomidine (20 μg/kg) s buprenorfinem (10 μg/kg) je dobrá anestetická premedikace, která navozuje kvalitní sedaci a analgezii. Schirmerův slzný test je doporučován jako jedno z mnoha preanestetických vyšetření. Pro prevenci poškození rohovky by měla být prováděna ochrana očí u každého psa, u kterého je použita anestetická premedikace medetomidin-buprenorfin.

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