CHANGES OF ECG QT INTERVAL IN GERMAN SHEPHERD AND COCKER SPANIEL DOGS DURING PREMEDICATION AND GENERAL ANAESTHESIA

EKG QT INTERVĀLA PĀRMAIŅAS VĀCU AITU UN KOKERSPANIELU ŠĶIRNES SUŅIEM PREMEDIKĀCIJAS UN VISPĀRĒJĀS NARKOZES LAIKĀ

Avdoško Guntars, Birģele Edīte
LLU Veterinārmedicīnas fakultāte, Latvija
Faculty of Veterinary Medicine, LUA, Latvia
guntars_avdosko@apollo.lv

ANOTĀCIJA

Darbā ir izpētīta EKG II standartnovadījuma QT intervāla (mm s^{-1}) dinamika 34 Vācu aitu un 32 Kokerspanieklu šķirnes suņiem premedikācijas (atropīna sulfāta kombinācijā ar acepromazīna maleātu) un vispārējās anestēzijas (ketamīna hidrohlorīda kombinācijā ar diazepamu) ietekmē. EKG QT intervāls suņiem premedikācijas līdzekļu atropīna sulfāta un acepromazīna maleāta ietekmē būtiski pagarinājās, pagarināšanās pakāpe Kokerspanielu un Vācu aitas šķirnes suņiem praktiski bija vienāda. Vispārējās anestēzijas (narkozes) līdzekļu ketamīna hidrohlorīda un diazepāma summārais efekts (uz premedikācijas līdzekļu iedarbības fona) suņiem izpaužas kā QT intervāla būtiska samazināšanās. Kokerspanielu un Vācu aitas šķirnes suņiem, minūti pēc narkozes līdzekļu ievadīšanas ir raksturīgs ļoti krass un būtisks QT intervāla samazinājums. Kokerspanielu šķirnes dzīvniekiem QT intervāla samazinājums ketamīna hidrohlorīda un diazepāma summārajā ietekmē vēl turpinājās līdz 30 – tajai anestēzijas minūtei.QT intervāla dinamika suņiem narkozes līdzekļu, ketamīna hidrohlorīda un diazepāma summārajā ietekmē atsevišķos anestēzijas laika periodos ir būtiski saistīta ar dzīvnieka šķirni, bet nav saistīta ar dzīvnieka dzimumu. Pēdējais novērojums ir būtiski svarīgs praktiskajā veterinārmedicīnā, strādājot ar šķirnes suņiem.

KEY WORDS: dogs; electrocardiography; breed and gender; QT interval dynamics; combinations of agents.

INTRODUCTION

QT interval of electrocardiogram (ECG) shows the time necessary for ventricular depolarisation and relpolarisation during one heart cycle. QT interval reflects the total duration of ventricular systole, during which myocardium is excitated, starting with the first manifestations in the ventricular septum and papillary muscles up to evanescence of excitation in the ventricular myocardium (Antzelevitch et al., 1998; Щварц и др., 2001; Campbell, Atwell, 2002; Мартин, Коркорэн, 2004; Kalvelis, 2005).

It is established that QT interval in humans can be prolonged by various anaesthetics used in surgical manipulations. The same refers to many other exogenous and endogenous factors (Booker et al., 2003; Cucchiaro, Rhodes, 2003; Testai et al., 2004; Sala et al., 2005). As to the dogs, we could not find data of any research on such a premedication model (atropine sulphate in combination with acepromazine maleate) and anaesthesia model (ketamine hydrochloride in combination with diazepam).

The main task of **this work** was: 1. to establish the dynamics of QT interval (ECG standard lead II) in dogs during premedication and general anaesthesia according to the breed and gender of the animal; 2. to determine patterns of QT interval alterations in induced dogs

by premedication agents atropine sulphate and acepromazine maleate, as well anaesthetics ketamine hydrochloride in combination with diazepam .

MATERIALS AND METHODS

Research was performed on 34 German shepherds and 32 cocker spaniels. QT interval dynamics in animals in the initial state, during premedication and during general anaesthesia were registered electrocardiographically together with heartbeat frequency and other cardiac biopotentials.

We used the "SCHILLER" electrocardiograph AT–1 produced in Germany. This equipment allows working with 10 ECG leads simultaneously (ECG was registered at the speed of 50 mm s^{-1}). The animals were examined while lying in the dextrolateral position- forelimbs placed parallel to each other and perpendicular to the longitudinal axis of the body, the same as we have described in our previous works (Avdoško, Birģele, 2003a; Avdoško, 2003b; Avdoško, Birģele, 2004; ect.) and following the suggestions of other authors (Rezakhani, 1990; Tilley, 1992; Bernal et al., 1995; ect.). ECG data were registered and simultaneously processed by means of special software. QT interval, duration of particular ECG parameters in seconds (mm s^{-1}) and amplitude in milivolts (mV) were registered automatically.

The premedication was achieved by means of 0.054 % atropine sulphate solution (0.02 mg kg^{-1}) in combination with 1% acepromazine maleate solution (0.06 mg kg^{-1}) administered intramuscularly. ECG record during premedication was preformed 10 minutes after intramuscular injection.

The general anaesthesia (narcosis) was achieved by means of 5% ketamine hydrochloride solution (6 mg kg^{-1}) in combination with 0.5% diazepam solution (0.6 mg kg^{-1}). This combination is widely approved in veterinary medicine. We administered the anaesthetics in the cephalic vein (*v. cephalica)*. Length of ECG QT segment was established immediately after intravenous injection, as well as at the 15^{th}, 30^{th}, 45^{th} and 60^{th} minute.

The dogs were subjected to examination after clinical tests, which included roentgenography of heart and major blood vessels (lateral and dorsoventral projection), as well as morphologic and biochemical blood tests. All dogs involved in the study were clinically sound.

Statistic treatment of ECG data was performed by means of multifactor (here two- "factor" – animal breed and gender) dispersion analysis (ANOVA), as well as t- test for comparison of mutually dependant populations (Williem, 1996; Arhipova u.c. 1998; Miller, 2000).

RESULTS

Detailed alterations of ECG QT interval in dogs of both breeds during premedication and general anaesthesia, as well as statistical significance of these changes is summarized in Table II. It is evident that 10 min after administrations of premedication agents QT interval prolongs – from 0.209 ± 0.0037 mm s^{-1} to 0.215 ± 0.0040 mm s^{-1} in German shepherds and from 0.209 ± 0.0055 mm s^{-1} to 0.219 ± 0.0061 mm s^{-1} in Cocker spaniels ($P < 0.05$).

After administration of anaesthetics the QT interval dramatically shortens in both animals already at the first minute, however the 15^{th} minute brought about certain differences in QT interval dynamics: after administration of ketamine hydrochloride in combination with diazepam the length of QT interval in Cocker spaniels continued decreasing till 0.189 ± 0.0057 mm s^{-1} in average on the 30^{th} minute, whereas German shepherds experienced increase of the segment until 0.203 ± 0.0036 mm s^{-1} on the 30^{th} minute (see Table II). QT interval in the animals of both breeds levelled at the 45^{th} minute after administration of anaesthetics, however the length of QT interval was still different from the one established in the initial

state either in German shepherds ($P < 0.001$), or in Cocker spaniels ($P < 0.05$). The general dynamics of QT interval in dogs of either breed during premedication and general anaesthesia are better revealed in Figure 1.

Table 1

QT segment dynamics (mm s^{-1}) in ECG standard lead II registered in German shepherd dogs and Cocker spaniels during premedication and general anaesthesia

Time observation	German shepherds			Cocker spaniels		
	Mean value± MSE	t – test	*P* value	Mean value± MSE	t – test	*P* value
Initial state	0.209 ± 0.0037			0.209 ± 0.0055		
10 min after premedication	0.215 ± 0.0040	2.106	**<0.05***	0.219 ± 0.0061	2.137	**< 0.05***
1 min after anaesthesia	0.202 ± 0.0038	2.018	>0.05	0.206 ± 0.0057	0.379	>0.25
15 min after anaesthesia	0.205 ± 0.0044	0.800	>0.5	0.196 ± 0.0058	1.578	>0.5
30 min after anaesthesia	0.203 ± 0.0036	1.904	>0.05	0.189 ± 0.0057	2.691	**<0.05***
45 min after anaesthesia	0.198 ± 0.0038	3.378	**<0.01***	0.195 ± 0.0054	2.320	**<0.05***
60 min after anaesthesia	0.199 ± 0.0046	2.934	**<0.01***	0.197 ± 0.0062	1.857	>0.05

Premedication: 0.054% atropine sulphate solution (0.02 mg kg^{-1}) in combination with 1% acepromazine maleate solution (0.06 mg kg^{-1}) via intramuscular injection; **General anaesthesia:** 5% ketamine hydrochloride (6 mg kg^{-1}) in combination with 0.5% diazepam (0.6 mg kg^{-1}) via intravenous injection

* The difference it statistically significant ($P < 0.05$)

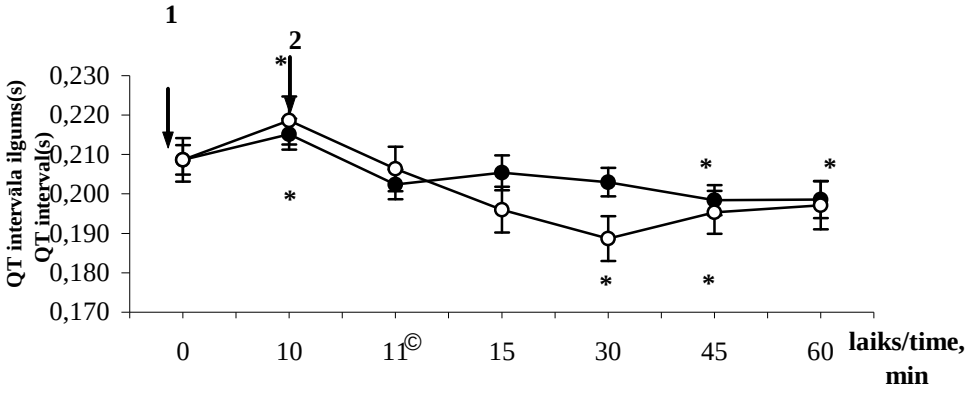

Figure 1. **QT interval dynamics in German shepherd (–●–) and Cocker spaniel (–○–) dogs during: 1 – premedication (atropine sulphate 0.02 mg/kg and acepromazine maleate 0.06 mg kg^{-1}); 2 – general anaesthesia (ketamine hydrochloride 6 mg kg^{-1} and diazepam 0.6 mg kg^{-1}).**

11© - first minute after administration of ketamine hydrochloride and diazempam

* - the differences of QT interval if compared to the initial state are statistically significant ($P < 0.05$)

This shows obvious differences in ECG QT interval registered in German shepherds and Cocker spaniels at the 15th and 30th minute after administration of anaesthetics, as well as levelling of QT interval in dogs of both breeds within one hour after general anaesthesia. It is also apparent that one hour after administration of ketamine hydrochloride and diazepam QT interval still had not regained initial length.

Thus we can conclude that changes in the length of ECG QT interval in dogs during general anaesthesia are to some extent dependent on the breed factor.

DISCUSSION

The effects of premedication agents or general anaesthetics (narcosis agents) on the various organ systems of animal body are studied regularly due to the invention of new pharmacologic preparations suitable for anaesthesia and the introduction of new combinations of anaesthetics.

The traditional premedication agents atropine sulphate and phenothiazine are known to be used to sedate animals and reduce their discomfort and to some extent also pain, as well as to encourage anaesthesia and simultaneously to prevent operative complications (Sawyer, Piermattey, 1992; Хозгуд и др., 2000; Nicholson, Watson, 2001; Щебиц, Брасс, 2001; Мартов, 2003; Pang et al., 2005).

Our previous *in vitro* experimental studies, during which we focused the effect of both premedication agents on the functional parameters of an isolated frog's heart, proved that atropine sulphate together with acepromazine maleate affect these parameters directly (Avdoško, Birģele 2002). Being isolated, the frog's heart could not react to various secondary influences, a characteristic of the central nervous system (CNS) of the animal body. We concluded that atropine sulphate together with acepromazine maleate altered the conduction system of the isolated heart, manifested as changes in either heartbeat frequency, or intensity of myocardial contractions and cardiac rhythm. It must be stressed that changes of the conduction system due to the effect of premedication agents is assumed by other authors (Бондаренко и др., 1999; Хозгуд и др., 2000; Мартов, 2003).

As for dogs, our studies demonstrate that the premedication agents atropine sulphate and acepromazine maleate induce prolongation of ECG QT interval. Thus the total effect of both premedication agents on the QT interval in dogs was similar to the one observed in the *in vitro* isolated frog's heart: the heartbeat frequency decreased (Avdoško, Birģele 2002), inducing prolongation of QT interval. This prolongation proceeded in the same way in both German shepherds and Cocker spaniels, with the absolute results of QT interval differing only slightly.

It must be stressed that total influence of the narcosis agents ketamine hydrochloride and diazepam on the ECG QT interval (after administration of premedication agents) was different in both dog breeds we had selected for our research. Initially, at the first minute after administration of the anaesthetics both Cocker spaniels and German shepherds showed a dramatic shortening of QT interval. After that the 15th and 30th minute of general anaesthesia revealed significant dependency ($P < 0.01$) of QT interval dynamics on the breed of animal. Cocker Spaniels demonstrated significant shortening of QT interval up to the 30th minute after administration of narcosis agents. This was followed by a slight increase of the QT interval. At the same time German shepherds experienced prolongation of QT interval already at the 16th minute after administration of narcosis agents. However QT interval in dogs of both breeds one hour after general anaesthesia was still shorter compared to the one established in the initial state (prior to administration of premedication agents).

Thus it must be repeatedly stressed that changes in the length of ECG QT interval at various time points after administration of general anaesthetics (narcosis agents) are more or less connected on the breed factor.

This possible relation of dog's breed to the dynamics of QT interval during non-inhalative general anaesthesia must be taken into account in practical veterinary medicine when working with purebred animals.

And finally we must emphasize that while administering currently widely used models of non-inhalative anaesthesia, one must remember that atropine sulphate and acepromazine maleate lead to bradycardia (Avdoško, Birģele, 2003a; Avdoško, Birģele, 2003c; Avdoško, Birģele, 2002) which is revealed by prolongation of QT interval, whereas a combination of ketamine hydrochloride and diazepam causes an antagonistic effect, tachycardia (Avdoško, Birģele, 2003a; Avdoško, Birģele, 2003c), leading to the shortening of QT interval during general anaesthesia. Moreover during anaesthesia it is always necessary to take into account possible differences of QT interval connecting on the breed of dog. The role of gender in the changes QT interval is not significant.

CONCLUSIONS

1. The premedication agents atropine sulphate and acepromazine maleate lead to significant increase of ECG QT interval in dogs and the degree of increase was practically the same in both Cocker spaniels and German shepherd dogs.
2. The total effect in canines of the general anaesthetics (narcosis drugs) ketamine hydrochloride and diazepam administered after premedication manifests as a significant shortening of QT interval;
3. The dynamics of QT interval in canines due to the total effect of such anaesthetics as ketamine hydrochloride and diazepam at distinct time points of anaesthesia are greatly connected on the breed of animal, but not on the gender of the animal;
4. Cocker spaniels and German shepherds are characterised by dramatic and significant shortening of QT interval one minute after administration of narcosis drugs. In cocker spaniels this shortening of QT interval due to the total effect of ketamine hydrochloride and diazepam continued up to the 30^{th} minute of anaesthesia.

REFERENCES

1. Antzelevitch, C., Shimizu, W., Yan, G. X., Sicouri, S. Cellular basis for QT dispersion.- Journal of Electrocardiology. 1998. 30: 168-172.
2. Arhipova, I., Ramute, L., Paura, L. Datu statistiskā apstrāde ar MS Excel. LLU, Jelgava. 1998.- 7-157 pp.
3. Avdoško, G., Birģele, E. EKG PQ intervāla izmaiņas kokerspanielu un vācu aitu šķirnes suņiem premedikācijas un vispārējās anestēzijas laikā. Starptautiskās zinātniskās konferences raksti „Dzīvnieki. Veselība. Pārtikas higiēna". 2004. 1: 21-27.
4. Avdoško, G., Birģele, E. Changes in dogs heart rate frequency during anesthesia.- Proceedings of the Latvian Academy of Sciences, Section B. 2003a. 57: 224-228.
5. Avdoško, G. Changes in Dog's Electrocardiography P- Wave During Anesthesia.- Proceedings of the Lavian Unversity Agriculture. 2003b, 9: 14-19.
6. Avdoško G., Birģele, E. Narkozes līdzekļu ketamīna hidrohlorīda un diazepāma ietekme uz sirds funkcionālo stāvokli.- LLU raksti. 2003c. 7: 40-48.
7. Avdoško G., Birģele E. Atropīna sulfāta un acepromazīna maleāta ietekme uz sirds fizioloģiskajiem rādītājiem.- LLU raksti. 2002. 6: 15-21.
8. Bernal, L. J., Montes, A. M., Fdez del Palazio, M. J., Gutierez, P. C. Electrocardiographic changes in the growing Mastin Espanol.- Journal of Small Animal Practice. 1995. 36: 221-228.
9. Booker, P. D., Whyte, S. D., Landusan, E.J. Long Q-T syndrome and anaesthesia. - Br. J. Anaesth. 2003. 90: 349-366.

10. Бондаренко, С.В., Малкова, Н.В. Электрокардиография собак - М: Аквариум. 1999.- 94 с.
11. Campbell, P. E., Atwell, R. B. Long QT syndrome in dogs with tick toxycity (*Ixodes holocyclus*). Australian Veterinary Journal. 2002. 80: 100-109.
12. Cucchiaro, G., Rhodes, A.L. Unusual presentation of long Q-T syndrome. - Br. J. Anaesth. 2003. 90: 804-807.
13. Хозгуд, Ж.., Хоскинс, Дж. Девидсон, Ж.., Смит, Дж. Терапия и хирургия щенков и котят. - Аквариум ЛТД, М., 2000.- 688 с.
14. Kalvelis, A. Nearitmiskā elektrokardioloģija. - Izdevniecība: SIA Nacionālais apgāds, 2005.- 176 lpp.
15. Мартов, В. Ю. Лекарственные средства в анестезиологи. - Мед. лит., М., 2003. - 304 с.
16. Мартин М. В. С., Коркорэн Б. М. Кардиореспираторные заболевания собак и кощек – Аквариум ЛТД, М., 2004.- 482 с.
17. Miller, R.D. Anesthesia. - Philadelphia: Churchill Livingstone, 2000. - 797 pp.
18. Nicholson, A., Watson, A. Survey on small animal anaesthesia. - Aust Vet J. 2001. 79: 613-619.
19. Pang, D., Rondenay, Y., Hélie, P., Cuvelliez, S.G., Troncy, E. Sudden cardiac death associated with occult hypertrophic cardiomyopathy in a dog under anesthesia. - Can Vet J. 2005. 46: 1122-1125.
20. Rezakhani, A. Electrocardiographic values of german shepherd dogs. - Australian Veterinary Journal. 1990. 67: 307-309.
21. Щебиц, Х., Брасс, В. Оперативная хирургия собак и кощек. - Аквариум ЛТД, М., 2001.- 512 с.
22. Щварц, С., Щайерс, Д., Спенсер, Ф. Клиническая электрокардиография – СПб: Питер, 2001.- 384 с.
23. Sala, M., Vicentini, A., Brambilla, P., Montomoli, C., Jogia, J.R., Caverzasi, E., Bonzano, A., Piccinelli, M., Barale, F., De Ferrari, G.M. QT interval prolongation related to psychoactive drug treatment: a comparison of monotherapy versus polytherapy. - Ann Gen Psychiatry. 2005. 25: 10-20.
24. Testai, L., Calderone, V., Salvadori, A., Breschi, M.C., Nieri, P., Martinotti, E. QT prolongation in anaesthetized guinea-pigs: an experimental approach for preliminary screening of torsadogenicity of drugs and drug candidates. - J Appl Toxicol. 2004. 24: 217-222.
25. Tilley, L. P. In: Essentials of Canine and Feline Electrocardiography: Interpretation and treatment, 3rd edition, Lea & Febiger, Philadelphia, 1992. - 5-49 pp.