EVALUATION OF ANAESTHETIC CHARACTERISTICS OF PROPOFOL IN NON-PREMEDICATED RABBITS WITH EXPERIMENTALLY INDUCED POST RENAL UNILATERAL URETERAL OBSTRUCTION

UDEGBUNAM, Rita 1jeoma, OGBANYA, Kenneth Chiedozie, EWUNONU, Uzochi Ihuoma, UDEGBUNAM, Sunday Ositadimma, ONUBA, Austin Chukwudum, UGWU, Nnenna Ebere
Department of Veterinary Surgery, Faculty of Veterinary Medicine, University of Nigeria, Nsukka, Enugu State, Nigeria.

Corresponding Author: Ugwu, N. E. Department of Veterinary Surgery, University of Nigeria, Nsukka, Enugu State, Nigeria. **Email:** nnenna.ugwu@unn.edu.ng **Phone:** +234 8136210721

ABSTRACT

This study was carried out to investigate the anaesthetic characteristics of propofol in rabbits with unilateral ureteral obstruction. Rabbits in two groups (B and C) were anaesthetized respectively with 10 mg/kg propofol intravenously (IV) on days 7 and 14 post unilateral ureteral obstruction (UUO). Healthy rabbits in group A served as the control group and were anaesthetized with propofol (10 mg/kg, IV). Duration of anaesthesia obtained in the control group was significantly ($p<0.05$) shorter compared to anaesthetic duration of groups B and C. Time of recovery from anaesthesia in group A was significantly ($p<0.05$) faster compared to that obtained in group C. Quality of induction, recovery quality and depth of anaesthesia were noted to be good in the three groups of rabbits. Apnoea was observed more in diseased rabbits (groups B and C) compared to the healthy rabbits. Heart rate of rabbits in groups A and B increased but decreased in group C post propofol injection (PPI). Respiratory rates (RR) of rabbits in all the groups decreased PPI with the highest respiratory depression noted in group C. Haematocrit of all rabbits increased though not significantly ($p>0.05$) while white blood cell counts of rabbits decreased PPI. Total serum protein (TSP) and blood urea nitrogen levels of the three groups of rabbits increased PPI though not significantly ($p>0.05$). Serum potassium, chlorine and bicarbonate levels of rabbits in all the three study groups increased PPI. Propofol at the dose used in this study induced rapid induction and recovery from anaesthesia, adequate depth of anaesthesia with no untoward haematologic and serum biochemical effects in UUO rabbits. However it's marked respiratory depressant effect and ability to increase serum potassium levels may preclude its use in advanced UUO.

Keywords: Ureteral obstruction, Propofol, Potassium, Apnoea, Anaesthesia

INTRODUCTION

Obstructive uropathy especially ureteral obstruction remains an important cause of renal insufficiency (Chevalier *et al.,* 1999). Immediate responses to partial or complete ureteral obstruction include reduction in urine flow, renal blood flow and glomerular filtration rate (Cochrane *et al.,* 2005). In long standing cases, interstitial inflammation, tubular atrophy, fibrosis and hydronephroses occurs (Abel El-Hakiem *et al.,* 2011). Ureteral obstruction also alters body electrolyte balance leading to post obstructive diuresis, natriuresis and failure to dilute or concentrate urine (Klahr *et al.,* 1988). Patients with ureteral obstruction may also become hyperkalaeamic and acidotic (Greene and Grauer, 2007).

Renal insufficiency causes haemodynamic instability thus may alter the patients response to anaesthesia (Greene and Grauer, 2007; Wagner and Brentgens, 2010). Furthermore, anaesthesia of patients with renal insufficiency is challenging since nearly every anaesthetic agent decreases renal blood flow and glomerular filtration rate (Greene and

Grauer, 2007; Weils, 2010). Invariably, the use of general anaesthetics that optimise cardiac output with minimal homeostatic alteration are recommended for these patients (Weils, 2010). According to Weils (2010), anaesthesia may be induced using injectable and inhalation agents. Injectable agents such as propofol and ketamine were recommended, while isoflurane and sevoflurane are preferred inhalation agents (Weils, 2010).

Propofol (2,6-di-isopropyl phenol) is an alkyl phenol derivative used in veterinary and human medical practice as a general anaesthetic agent (Morgan and Legge, 1989; Pottie and Dart, 2008). In veterinary practice, for example, propofol has been used as a sole anaesthetic or in combination with tranquilizers in dogs (Fonda, 1991; Kusters *et al.,* 1998), goats (Prassinos *et al.,* 2005) and rabbits (Mustola *et al.,* 2000, Allweiler *et al.,* 2010). Assessment of the suitability of propofol, thiopentone and ketamine for anaesthesia in New Zealand white rabbits showed that out of the three intravenous agents investigated, propofol seemed to be the best choice for rabbit anaesthesia (Mustola *et al.,* 2000). The use of propofol for anaesthesia is characterised by rapid induction, satisfactory sedation with good haemodynamic stability (Weaver and Raptopoulous, 1990; Kojima *et al.,* 2002). In humans, IcKx *et al.* (1998) reported that end stage renal disease had no impact on the pharmacokinetics of propofol making this drug a suitable choice in this disease state. Also, according to Martinez *et al.* (2013), propofol is safe for induction and maintenance of anaesthesia during kidney transplantation. Currently, no study has evaluated the use of propofol in animals with pre-existing ureteral obstruction, therefore the need for this study. This investigation specifically studied anaesthetic qualities of propofol in rabbits with UUO. Also studied after propofol injection were changes in the vital, haematologic and serum biochemical parameters of rabbits with pre-existing UUO.

MATERIALS AND METHODS

Animals: Experimental animals were eighteen (18) New Zealand white male rabbits weighing 1.52 ± 0.4 kg. These rabbits were acclimatized for two weeks and housed in stainless steel cages in the animal house of the Department of Veterinary Surgery, University of Nigeria, Nsukka. Rabbits were fed with growers mash, fresh grass (*Centrosima pubescens*) and potato leaves. Water was given *ad-libitum.* Prior to the study, rabbits were assigned to 3 treatment groups, replicated thrice with two rabbits per replicate. The treatment groups were: Group A (control /healthy group), Group B (unilateral ureteral obstruction anaesthetized on day 7 post surgery and Group C (unilateral ureteral obstruction anaesthetized on day 14 post surgery).

Unilateral Ureteral Obstruction: The rabbits in groups B and C scheduled for unilateral ureteral obstruction (UUO) were placed on dorsal recumbency and shaved from the xiphoid region down to the pubic region. Surgical gauze soaked with 0.5 % chlorhexidine gluconate was used for antisepsis of the area shaved. The animals were then restrained using gauze strip and draped as described by (Knecht *et al.,* 1987). Under xylazine hydrochloride (0.2 mg/kg) and ketamine hydrochloride (30 mg/kg) anaesthesia, a ventral midline incision was made 2 cm caudal to the xiphoid region down to 2 cm below the umbilicus cutting through the subcutis, muscle, peritoneum and into the abdomen to expose the right kidney. The ureter was ligated post renally using size 3/0 polyglycolic acid suture (vicryl). Thereafter, the peritoneum, subcutis and muscles were sutured with simple continuous pattern using size 2/0 chromic catgut suture. The skin was sutured with size 2/0 silk using simple interrupted suture pattern. After surgery, tramadol hydrochloride (10 mg/kg) was administered intramuscularly once daily for 3 days. Penicillin and streptomycin at the doses of 0.5 and 1 mg/kg body weight respectively were injected intramuscularly once daily for 5 days post surgery to all the groups.

Propofol Anaesthesia: The rabbits received no premedication and were not deprived of food and water prior to anaesthesia. The skin overlying the left jugular vein were shaved and prepared aseptically for venipuncture. In group B, on day 7 post UUO, anaesthesia was induced with propofol (10 mg/kg) administered intravenously, while rabbits in group C were anaesthetized on day 14 post UUO. Healthy rabbits (without UUO) in group A served as the control group and were anaesthetized with the same dose of propofol used for the UUO groups. Once the animals lost righting reflex, induction time (time from end of injection to onset of recumbency), duration of anaesthesia and time of recovery were determined. Depth of anaesthesia was assessed by blind endotracheal intubation (Prassinos *et al.,* 2005) and pinna reflex testing (ear movement in response to pinching) (Borkowski *et al.,* 1990).

Depth of anaesthesia was categorized as good, fair or poor using the criteria: Good - easy tracheal intubation, no response to ear pinch, fair - reflex response to tracheal intubation, sluggish response to ear pinch and poor - inability to intubate trachea, brisk response to ear pinch.

Induction quality scoring: Qualities of induction were evaluated and scored good, fair or poor using the criteria described by Prassinos *et al.* (2005) thus: Good - smooth induction, rapidly assumes recumbency, no sign of excitement; fair - slightly prolonged, mild excitement and poor - obvious excitement, jumps and attempts to stand after recumbency.

Recovery Quality Scoring: Recovery qualities were evaluated and scored good, fair or poor using the criteria (modified) earlier described by Prassinos et al. (2005) thus: Good - smooth easy transition to alertness, stands in a reasonable amount of time and is able to walk with minimal ataxia; fair - transient excitement or whole body movements, some struggling, hyper-responsiveness that disappears once rabbit stands unassisted with moderate ataxia; and poor - stereotypical behaviour such as circling, premature attempts to stand, prolonged recovery. Furthermore, incidence of side effects such as regurgitation, hypersalivation, tympany, apnoea (no spontaneous breathing for more than 20 seconds) and apneustic breathing were recorded.

Haematology and Serum Biochemistry: Blood was collected into plain and heparinized bottles 20 minutes post propofol injection for serology and haematology. Packed cell volume (PCV) and white blood cell counts were determined as described by Tvedten (1994) using heparinised blood. Serum was harvested from blood on clotting and used for serum biochemistry. Blood urea nitrogen was determined by the modified method of Berthelot-Searcy (Fawcett and Scott, 1960), while determination of total serum protein was performed according to the biuret method (Lubran, 1978).

Serum Electrolytes Determination: Serum sodium, chlorine, potassium and bicarbonate were also determined using commercial test kits (Randox). The assay procedures specified on the kits were strictly followed.

Data Analysis: Mean heart rate (HR) and respiratory rate (RR) of each group were compared with their respective pre-induction values using one way analysis of variance (ANOVA). Duncan multiple range test (DMRT) was used to separate variant mean. Mean total serum protein, blood urea nitrogen, white blood cell counts, haematocrit and serum electrolytes of the respective groups obtained after induction of anaesthesia were compared with their respective pre-induction values using t-test. Probability less than 0.05 were considered significant. Results obtained were summarized as mean ± SEM.

RESULTS

Anaesthetic Indices: The duration of anaesthesia obtained in the group A (control) was significantly shorter ($p<0.05$) compared to anaesthetic duration obtained after administering propofol to rabbits in groups B and C on days 7 and 14 post unilateral ureteral obstruction (UUO) (Table 1).

Table 1: Anaesthetic indices in rabbits with experimentally induced post renal unilateral ureteral obstruction after injection of propofol (10 mg/kg)

Anaesthetic indices	Group A	Group B	Group C
Induction time (minutes)	0.0 ± 0.0[a]	0.0 ± 0.0[a]	0.0 ± 0.0[a]
Duration of anaesthesia (minutes)	5.0 ± 0.4[a]	9.0 ± 0.4[b]	10.0 ± 0.7[b]
Time of recovery (minutes)	2.3 ± 0.2[a]	2.0 ± 0.4[ab]	1.3 ± 0.2[b]

Different superscript in a row indicates significant difference between group means (p<0.05)

Time of recovery from anaesthesia in control group was significantly faster (p<0.05) compared to recovery time obtained post propofol anaesthesia in rabbits anaesthetized on day 14 post UUO (group C).

Quality of Anaesthesia: Quality of induction, recovery quality and depth of anaesthesia were noted to be good in both healthy (group A) and obstructed rabbits (groups B and C). Apnoea and apneustic breathing occurred more in diseased rabbits (groups B and C) compared to the healthy rabbits. In the three groups, regurgitation, tympany and hypersalivation were not observed (Table 2).

Vital Parameters: The HR of rabbits in groups A and B increased, while the HR of rabbits in group C decreased post propofol injection (PPI). Comparison of mean HR of the groups with their respective pre-induction values (0 minute) showed that in groups A and B, HR obtained at 20, 30, 40 and 50 minutes PPI were significantly higher (p<0.05) than the 0 minute HR of the same group. In group C, HR of rabbits at 10, 30, 40 and 50 minutes PPI were significantly lower (p<0.05)) than 0 minute HR of the same group (Table 3).

The RR of all rabbits in all the groups decreased at 10 minutes PPI with the highest respiratory depression recorded in group C. In group A, RR obtained at 20 minutes PPI was significantly lower (p<0.05) than 0 minutes RR of the same group. In group B, RR obtained at 10, 20, 30 and 50 minutes PPI were significantly lower (p<0.05) than 0 minute RR of the same group. In group C, RR of rabbits at 10, 20, 30 and 40 minutes PPI were significantly lower (p<0.05) than 0 minute RR of the same group (Table 4).

Haematology, Serum Biochemistry and Electrolytes: Haematocrit (HCT) of all groups increased though not significantly different (p>0.05), while WBC of the groups decreased PPI (Table 5). Total serum protein (TSP) and BUN levels of the three groups of rabbits increased PPI though not significantly different (p>0.05) (Table 6). Serum potassium, chlorine and bicarbonate levels of rabbits in all the three study groups increased PPI. Serum sodium level however increased in the control but decreased in the two groups (B and C) anaesthetized post UUO (Table 7).

DISCUSSION

Propofol produces rapid onset of action, a short duration of anaesthesia and smooth recovery in rabbits (Aeschbacher and Webbs, 1993). These features of propofol were again observed in this study in both the healthy and diseased rabbits. More so, rapid recovery even in rabbits anaesthetized on day 14 post UUO suggests that use of propofol can be safely used for induction and maintenance during surgeries to relieve ureteral obstruction. Earlier, Ickx *et al.* (1998) had also reported that end stage renal disease had no impact on pharmacokinetics of propofol making it a suitable choice in patients with renal impairment. In this study also, evaluation of the anaesthetic quality of propofol showed that induction and recovery from anaesthesia were smooth and uneventful while adequate depth of anaesthesia was achieved in all the anaesthetized groups. Likewise, no excitement during induction and recovery as well as adequate depth for intubation was noted in a previous study in rabbits anaesthetized with propofol (Allweiler *et al.,* 2010).

Table 2: Induction and recovery qualities and occurrence of side effects in rabbits with experimentally induced post renal unilateral ureteral obstruction induced with 10 mg/kg propofol

Anaesthetic indices	Group A	Group B	Group C
Quality of induction	Good (6)	Good (6)	Good (6)
Recovery quality	Good (6)	Good (6)	Good (6)
Depth of Anaesthesia	Good (6)	Good (5), Fair (1)	Good (6)
Regurgitation	Good (0)	Good (0)	Good (0)
Hypersalivation	Good (0)	Good (0)	Good (0)
Tympany	Good (0)	Good (0)	Good (0)
Apnoea	Good (5), Fair (1)	Good (6)	Good (6)
Apneustic breathing	Good (5), Fair (1)	Good (6)	Good (6)

Number in parenthesis = number of animals that responded to each anaesthetic index per treatment

Table 3: Heart rates of rabbits with experimentally induced post renal unilateral ureteral obstruction anaesthetized using 10 mg/kg propofol

Groups	Time (minutes)					
	0	**10**	**20**	**30**	**40**	**50**
Control	176.0 ± 1.0^{a}	177.3 ± 4.8^{a}	192.3 ± 6.1^{b}	193.3 ± 6.7^{b}	193.3 ± 6.7^{bc}	186.7 ± 6.7^{c}
UUO 7	177.3 ± 1.3^{a}	190.7 ± 0.1^{b}	196.0 ± 0.1^{c}	200.2 ± 0.4^{c}	194.7 ± 5.3^{c}	200.2 ± 0.1^{c}
UUO 14	197.3 ± 2.7^{a}	185.3 ± 12.7^{b}	200.0 ± 0.2^{ab}	192.1 ± 6.1^{c}	180.1 ± 0.1^{b}	186.7 ± 6.7^{b}

Different superscript in a row indicates significant difference (p<0.05) between pre-induction mean values at 0 minutes and post induction values of the same group at 10 – 50 minutes

Table 4: Respiratory rates of rabbits with experimentally induced post renal unilateral ureteral obstruction anaesthetized using 10 mg/kg propofol

Groups	Time (minutes)					
	0	**10**	**20**	**30**	**40**	**50**
Control	44.0 ± 1.3^{a}	42.0 ± 4.0^{b}	45.0 ± 6.9^{a}	44.8 ± 8.5^{a}	44.0 ± 12.2^{a}	47.5.0 ± 17.3^{c}
UUO 7	44.3 ± 0.0^{a}	25.3 ± 32.4^{b}	30.7 ± 20.9^{b}	40.5 ± 8.5^{c}	41.0 ± 8.3^{c}	41.0 ± 12.0^{c}
UUO 14	47.3 ± 6.7^{a}	24.3 ± 31.5^{a}	42.0 ± 8.0^{b}	45.3 ± 10.6^{c}	42.7 ± 11.6^{c}	46.0 ± 10.1^{a}

Different superscript in a row indicates significant difference (p<0.05) between pre-induction mean values at 0 minutes and post induction values of the same group at 10 – 50 minutes

Table 5: Haematocrit (HCT) and white blood cell counts (WBC) of rabbits with experimentally induced post renal unilateral ureteral obstruction anaesthetized using 10 mg/kg propofol

Groups	HCT (%)		WBC (10^3/µl)	
	0 minute	**20 minutes**	**0 minute**	**20 minutes**
Control	35.4 ± 0.3^{a}	36.2 ± 1.0^{a}	10.9 ± 3.3^{a}	10.6 ± 2.1^{b}
UUO 7	33.0 ± 1.7^{a}	34.8 ± 1.9^{a}	11.2 ± 8.5^{a}	10.3 ± 1.0^{b}
UU0 14	42.0 ± 0.1^{a}	42.8 ± 1.3^{a}	11.1 ± 4.8^{a}	10.6 ± 3.2^{a}

Different superscript in a row indicates significant difference (p<0.05) between pre-induction mean values at 0 minutes and post induction values of the same group at 10 – 50 minutes

Table 6: Serum total protein (STP) and blood urea nitrogen (BUN) of rabbits with experimentally induced post renal unilateral ureteral obstruction anaesthetized using 10 mg/kg propofol

Groups	TSP (g/dl)		BUN (mg/dl)	
	0 minute	**20 minutes**	**0 minute**	**20 minutes**
Control	7.9 ± 0.2^{a}	8.5 ± 0.8^{a}	7.7 ± 1.2^{a}	**8.5 ± 1.1^{a}**
UUO 7	7.9 ± 0.5^{a}	8.7 ± 0.7^{a}	9.0 ± 0.5^{a}	**10.4 ± 1.5^{a}**
UUO 14	**8.1 ± 0.6^{a}**	**8.7 ± 1.2^{a}**	**4.2 ± 1.5^{a}**	**5.4 ± 2.0^{a}**

Different superscript in a row indicates significant difference (p<0.05) between pre-induction mean values at 0 minutes and post induction values of the same group at 10 – 50 minutes

Table 7: Serum electrolytes of rabbits with experimentally induced post renal unilateral ureteral obstruction anaesthetized using 10 mg/kg propofol

Groups	Time in minutes	Potassium (mmol/L)	Sodium (mmol/L)	Chlorine (mmol/L)	Bicarbonate (mEq/L)
Control	0	5.4 ± 0.4[a]	234.9 ± 1.8[a]	117.2 ± 1.0[a]	15.0 ± 0.4[a]
	20	9.4 ± 2.3[b]	278.2 ± 12.5[b]	132.7 ± 10.0[b]	30.26 ± 14.9[b]
UUO 7	0	6.6 ± 0.9[a]	271.1 ± 4.2[a]	118.2 ± 6.1[a]	12.5 ± 2.5 [a]
	20	6.8 ± 0.4[a]	236.2 ± 26.9[b]	126.2 ± 3.7[b]	12.5 ± 5.0 [a]
UUO 14	0	9.6 ± 1.6[a]	265.9 ± 16.4[a]	134.9 ± 1.6[a]	60.0 ± 8.7[a]
	20	10.1 ± 0.5[a]	264.4 ± 12.6[a]	150.8 ± 4.8[b]	67.5 ± 11.5[a]

Different superscript in a row indicates significant difference ($p<0.05$) between pre-induction mean values at 0 minutes and post induction values of the same group at 10 – 50 minutes

Propofol have been previously reported to cause an increase in HR followed by a phase of decline in un-premeditated dogs (Bayan *et al.,* 2002; Guzel *et al.,* 2006). In the course of this study, a similar cardiovascular effect of propofol was observed in the control rabbits and in rabbits anaesthetized on day 7 post UUO. On the contrary, instead of incremental change in heart rate PPI, heart rate of rabbits anaesthetized on day 14 post UUO decreased. An earlier study revealed that dogs that were acutely hypovolaemaic showed a significant decrease in blood pressure when propofol was used alone (Ilkiw *et al.,* 1992). This report may explain the finding in this latter group of rabbits since these rabbits may be dehydrated as a result of the long standing duration of obstruction. The observed respiratory effects of propofol during this study in both the healthy and diseased rabbits were respiratory depression, apnoea and apneustic breathing. These are known adverse respiratory effects of propofol in animal species and man (Amarpal *et al.,* 2002; Bayan *et al.,* 2002). Worthy to note is the more pronounced depression of respiratory rate recorded in the group of rabbits anaesthetized on day 14 post UUO. This finding probably suggests an exacerbated sensitivity of the respiratory centre of this group of rabbits to propofol.

In this study, the haematocrit of rabbits increased in all study groups PPI, while the WBC decreased. Three previous studies showed that haematological parameters were within physiological limits during propofol anaesthesia in sheep (Brzeski *et al.,* 1994), reduced in the first 10 minutes of anaesthesia in ewes (Handel *et al.,* 1991) and remained unchanged when used for seven consecutive days in dogs (Kwon *et al.,* 1999). The finding of this present study is at variance with those of Handel *et al.* (1991) and Kwon *et al.* (1999) but similar to that of Brzeski *et al.* (1994).

Notable from this study is that similar haematological responses to propofol were obtained in the control rabbits and in those anaesthetized post UUO.

Immediate responses to partial or complete ureteral obstruction include reduction in urine flow, renal blood flow and glomerular filtration rate (Cochrane *et al.,* 2005). Patients with ureteral obstruction may become hyperkalaeamic and acidotic (Greene and Grauer, 2007). Also, hyperkalaemia is a notable propofol-related infusion syndrome characterised by arrhythmia and metabolic acidosis (Mali *et al.,* 2009; Mike, 2010; Lee *et al.,* 2011). Thus, the implication of increased serum potassium concentration PPI as recorded in this study is that for UUO patients with pre-existing hyperkalaemia and metabolic acidosis, use of propofol should be avoided.

Conclusion: Propofol at the dose used in this study demonstrated a high degree of predictability by inducing rapid induction and recovery from anaesthesia, adequate depth of anaesthesia with no untoward haematologic and serum biochemical effects. However, its marked respiratory depressant effect and ability to increase serum potassium levels may preclude its use in advanced UUO.

REFERENCES

ABEL EL-HAKIEM, M. A. H., ABDELLAH, M. R., YOUSSEF, N. A., SALEL, A. S. and HASSANEIN, K .M. A. (2011). Effect of unilateral ureteral ligation on blood constituents, renal histopathology and ultrasonography in dogs. *Journal of Animal and Veterinary Advances,* 10(3): 356 – 364.

AESCHBACHER, G. and WEBBS, A. I. (1993). Propofol in rabbits 2. Long term anaesthesia. *Laboratory Animal Science,* 43(4): 328 – 335.

ALLWEILER, S., LEACH, M. C. and FLECKNELL, P. A. (2010). The use of propofol and sevoflurane for surgical anaesthesia in New Zealand white rabbits. *Laboratory Animal,* 44(2): 113 – 117.

AMARPAL, P. J. P., KINJAVDEKAR, H., AITHAL, R., PATHAK, P. K. and SINGH, V. (2002). The arterial blood propofol concentration preventing movement in 50% of healthy women after skin incision. *Anaesthesia and Analgesia*, 85: 414 – 419.

BAYAN, H., SARMA, K. K. and CHAKRAVARTY, P. (2002). Biochemical and haematological changes during propofol anaesthesia. *Indian Journal of Vet Surgery*, 23: 95 – 96.

BORKOWSKI, G. L., DANNEMAN, P. J., RUSSEL, G. B. and LANG, C. M. (1990). An evaluation of three intravenous anaesthetic regimens in New Zealand rabbits. *Laboratory Animal Science*, 40: 270 – 276.

BRZESKI, W., DEPTA, A., JALYNKSI, M. and CHYCZEWSKI, M. (1994). General anaesthesia in sheep with the use of diprivan-propofol. *Medycyna Weteryn-naryjna*, 50: 215 – 217.

CHEVALIER, R. L., KIM, A., THORNHILL, B. A. and WOLSTENHOLME, J. T. (1999). Recovery following relief of unilateral ureteral obstruction in neonatal rat. *Kidney International,* 55(3): 793 – 807.

COCHRANE, A. L., KETT, M. M., SAMUEL, C. S., CAMPANALE, N. V., ANDERSON, W. P., HUME, D. A., LITTLE, M. H., BERTTRAM, J. F. and RICHARDO, S. D. (2005). Renal structure and functional repair in a mouse model of reversal ureteral obstruction. *Journal of the American Society of Nephrology,* 16: 3623 – 3630.

FAWCETT, J. K. and SCOTT, J. E. (1960). A rapid and precise method for the determination of urea. *Journal of Clinical Pathology*, 13: 156 – 159.

FONDA, D. (1991). Continuous infusion of anaesthesia with propofol in dogs; clinically optimized dosages. Pages 159 – 161. *In: Proceedings of the 4th International congress of Veterinary Anesthesia,* Utrecht, Netherlands.

GREENE, S. A. and GRAUER, G. F. (2007). Renal disease. Pages 915 – 919. *In:* TRANQUILLI, W. J., THURMON, J. C. and GRIMM, K. A. (Eds.), *Veterinary Anaesthesia and Analgesia* 4th Edition, Blackwell, Iowa, USA.

GUZEL, O., PERK, E. C. and DEVECIOGLU, Y. (2006). Electrocardiographic and oxygen saturation studies during propofol and etomidate anaesthesia in dogs. *Indian Veterinary Journal,* 83(3): 288 – 289.

HANDEL, I. G., STADDON, G. E., WEAVER, B. M. Q., PEARSON, M. R. B. and CRUZ MADORRAN, J. I. (1991). Changes in packed cell volume during anaesthesia. *Veterinary Anaesthesia and Analgesia*, 18: 347 – 352.

ICKX, B., COCKSHOTT, I. D., BARVAIS, L., BYTTEBIER, G., DE PAUW, L., VANDESTEENE, A. and D'HOLLANDER, A. A. (1998). Propofol infusion for induction and maintenance of anaesthesia in patients with end-stage renal disease. *British Journal of Anaesthesia*, 81(6): 854 – 860.

ILKIW, J.E., PASCOE, P.J. and PATZ, J.D. (1992). Cardiovascular and respiratory effects of propofol administration in hypovalaemic dogs. *American Journal of Veterinary Research,* 53:2323-2327.

KLAHR, S., HARRIS, K. and PURKERSON, M. L. (1988). Effects of obstruction on renal functions. *Pediatric Nephrology*, 2(1): 34 – 42.

KNECHT, C. D., ALLEN, A. R., WILLIAMS, J. and JOHNSON, H. (1987). Celiotomy. Pages 279 – 281. *In: Fundamental Techniques in Veterinary Surgery*. Saunders Company, Philadelphia.

KOJIMA, K., RYOHEI, N., MOTOH, T., HONG, S. H., MOCHIZUKI, M. and SASAKI, N. (2002). Effects of medetomidine-midazolam, acepromazine-butorphanol and midazolam-butorphanol on induction dose of thiopentone and propofol and on cardiopulmonary changes in dogs. *American Journal of Veterinary Research*, 63(12): 1671 – 1679.

KUSTERS, A. H. A., VIJN, P. C. M., VAN DEN BROM, W. E., HABERHAM, Z. L., VENKER-VAN, HAAGEN, A. J. and HELLERBREKERS, L. J. (1988). EEG-burst suppression-controlled propofol anaesthesia in the dog. *Veterinary Quarterly*, 20(suppl 1): S105 – S106.

KWON, Y. S., JANG, K. H., KIM, J. E., CHAE, H. G., LIM, J. H., LEE, K. W. and JANG, I. H. (1999). Effects of continuous administration of propofol in dogs. *Korean Journal of Veterinary Clinical Medicine*, 16: 363 – 368.

LEE, J. H., KO, Y. S., SHIN, H. J., YI, J. H., HEN, S. W. and KIM, H. J. (2011). Is there a relationship between hyperkalaemia and propofol? *Electrolyte Blood Press*, 9(1): 27 – 31.

LUBRAN, M. M. (1978). The measurement of total serum proteins by the biuret method. *Annals of Clinical Laboratory Science*, 8(2): 106 – 110.

MALI, A. R., PATIL, V. P., PRAMESH, C. S. and MISTRY, R. C. (2009). Hyperkalaemia during surgery: Is it an early warning of propofol infusion syndrome. *Journal of Anaesthesia,* 23(3): 421 – 423.

MARTINEZ, B. S., GASANOVA, I. and ADESANYA, A. O. (2013). Anaesthesia for kidney transplantation - A review. *Journal of Anaesthesia and Clinical Research*, 4(1): 270 doi.org/10.4172/2155-6148.1000270

MIKE, L. A. (2010). Propofol-related infusion syndrome. *Practical Gastroenterology,* 2010: 16 – 25.

MORGAN, D. W. T. and LEGGE, K. (1989). Clinical evaluation of propofol as an intravenous anaesthetic agent in cats and dogs. *Veterinary Record*, 124: 31 – 33.

MUSTOLA, S. T., RORARIUS, G. F., BAER, G. A., ROSENBERG, P., SEPPALA, T. and HARMONIEN, A. (2000). Potency of propofol, thiopentone and ketamine at various endpoints in New Zealand white rabbits. *Laboratory Animals*, 34(1): 36 – 45.

POTTIE, R. G. and DART, C. M. (2008). Choosing an injectable anaesthetic agent: Characteristics of thiopentone, propofol, ketamine and alafaxalone in small animal clinical use. *Australian Veterinary Practitioner*, 38(2): 52 – 72.

PRASSINOS, N., GALATOS, N. and RAPTOPOULOS, D. (2005). A comparison of propofol, thiopental or ketamine as induction agents in goats. *Veterinary Anaesthesia and Analgesia*, 32(5): 289 – 296.

TVEDTEN, H. (1994). The complete blood count and bone marrow examination. General comments and selected techniques. Pages 179 – 218. *In:* WILLARD, M. D., TVEDTEN, H. and TURNWALD, G. H. (Eds.), *Small Animal Clinical Diagnosis by Laboratory Methods.* W. B. Saunders Company, Philadelphia, USA.

WAGNER, G. and BRENTGENS, T. (2010). Anaesthetic concerns in patients presenting with renal failure. *Anaesthesiology Clinic,* 28: 39 – 54.

WEAVER, B. M. Q. and RAPTOPOULOUS, D. (1990). Induction of anaesthesia in dogs and cats with propofol. *Veterinary Record*, 126:617-620.

WEILS, A. (2010). Anaesthesia for patients with renal/hepatic disease. *Topics in Companion Animal Medicine*, 25(2): 87 – 91.