



Anaesthetic responses and reflexes to propofol and its combination in swine

MD. SOHEL RANA¹, MD. MIZANUR RAHMAN² and NASRIN SULTANA JUYENA³

Bangladesh Agricultural University, Mymensingh 2202, Bangladesh

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ABSTRACT

To determine the effectiveness of propofol alone (P), and the combination of xylazine-propofol (XP), xylazine-ketamine (XK), xylazine-thiopentone (XT), anaesthetic protocols were studied in randomly selected 16 healthy indigenous pigs of either sexes, age 12 to 15 months and weight ranging from 12 to 16 kg. The responses of propofol and the combinations in different stages of anaesthesia were closely monitored. Various reflex responses and muscle tenacity were also observed concurrently during the period of anaesthesia. The study found the shortest (0.29 ± 0.02 min) induction period with XT anaesthesia and the longest (2.95 ± 0.21 min) by XK; whereas, induction of anaesthesia with P and XP was 0.4 ± 0.08 and 0.41 ± 0.08 min respectively. The time required for maximum depth of anaesthesia was the shortest in P (7.50 ± 0.65 min) than the combinations. However, the anaesthetic protocol with XP produced the highest (65.25 ± 3.30 min) duration of anaesthesia than the shortest (10.75 ± 1.75 min) extent with P. Moreover, time to recovery from anaesthesia was higher (83.25 ± 2.14 min) in XT and shorter (18.50 ± 1.32 min) in P protocol. Good muscle relaxation was observed in XP, XK and XT combinations. Palpebral, conjunctival, jaw, tail and digital reflexes were almost absent in XP and XT combinations. The study concluded that propofol itself is a safe anaesthetic for short surgical interventions and its combination with xylazine is to be recommended for prolonged surgical procedures in swine.

Key words: General anaesthesia, Propofol, Responses, Reflexes, Swine

Among farm animals, pigs are fast growing and one of the most prolific livestock breeds ((Durranc and Maxson 2008, Phookan *et al.* 2006, Taylor and Roesse 2006). In Bangladesh, pigs are reared mostly by tribal group for meeting up their protein demand and economic benefit and majority of them are poor and landless people (Hossain *et al.* 2012). But, due to difficulties in restraining, the pigs are often being accomplished with local or regional anaesthesia, sedation or general anaesthesia to avoid stress (Ko *et al.* 1993). Anaesthesia is frequently required during the medical management of animals for both therapeutic procedures and experimental models (Toyama *et al.* 2004, Wessler *et al.* 2011). It is also important for major operative procedures without experiencing pain (Arras *et al.* 2001). Immobilization and desensitization of pigs is done by both the injectable and gaseous anaesthetic agents. Among different premedicants, xylazine, an α_2 -adrenergic agonist, has been used routinely as an anaesthetic agent in pigs (Pypendop *et al.* 1996, Lee *et al.* 2010).

Ketamine hydrochloride is frequently used for sedation, induction of anaesthesia and analgesia (Ajadi *et al.* 2008). Xylazine hydrochloride has commonly been used with

ketamine hydrochloride for surgical anaesthesia in pigs (Gaertner 2008). Thiopental is a rapidly acting, ultra-short duration of induction, intravenous anaesthetic used for induction of anaesthesia prior to inhalation anaesthesia or as a sole agent for minor procedures in animals and it seems to be the most suitable induction agent (Tachecí *et al.* 2013). Propofol is another intravenous anaesthetic agent that induces anaesthesia rapidly and smoothly and is associated with a quick recovery and has lower hazards in dogs (Ribeiro *et al.* 2009). Propofol follows xylazine induce quick, smooth and excitement free recovery in camels (Fahmy *et al.* 1995) and ponies (Bettschart-Wolfensberger *et al.* 2001, Flaherty *et al.* 1997). The effects of propofol and its combinations with xylazine on clinical traits is safer during general anaesthesia (Rana *et al.* 2014). However, there is no record on anaesthetic responses of propofol for induction of anaesthesia to recovery processes in swine. Thus, the present experiment was carried out to investigate the responses and reflexes of propofol alone, and the combinations of propofol, ketamine hydrochloride and thiopentone sodium with xylazine hydrochloride as premedication for general anaesthesia in swine.

MATERIALS AND METHODS

Experimental animals: Anaesthetic sessions (16) were performed in 16 healthy indigenous pigs during January to May, 2013. Age of the pigs ranged from 12 to 16 months

Present address: ¹Veterinary Surgeon (ranasoheldvm06@gmail.com), Upazila Veterinary Hospital, Gangachara, Rangpur, Bangladesh. ^{2,3}Professor (miznih@gmail.com, juyenahabib@yahoo.com), Department of Surgery and Obstetrics, Faculty of Veterinary Science.

and body weight ranged from 12 to 15 kg. The animals were selected randomly regardless of their sex for each anaesthetic session from a nomadic herd. They were scavenged in the pasture for 6–8 h a day and had a free access to water. All animals were routinely examined before anaesthesia. The experiment was conducted at Upazila Veterinary Hospital, Taraganj, Rangpur and Department of Surgery and Obstetrics, Bangladesh Agricultural University, Mymensingh, Bangladesh.

Experimental design: The experimental animals were divided into 4 groups depending on anaesthetic agents and each group consisted of 4 anaesthetic sessions. Group-P pigs were treated with propofol alone (Pofol[®], Popular Infusion Ltd, Bangladesh) @ 4 mg/kg body weight, IV slowly. Pigs of group-XP were treated with xylazine hydrochloride (Xylaxin[®], Indian Innunologicals Ltd, India) @ 1.1 mg/kg, IM. After 5 min, propofol administered @ 4 mg/kg, IV slowly. Group-XK animals were treated with xylazine hydrochloride @ 1.1 mg/kg, IM and ketamine hydrochloride (G-Ketamine[®], Gonoshasthaya Pharmaceuticals Ltd, Bangladesh) administered @ 11 mg/kg, IM after 5 min of premedication and, group-XT pigs were treated with freshly prepared thiopentone sodium (G-Thiopental[®], Gonoshasthaya Pharmaceuticals Ltd, Bangladesh) (5% solution) @ 8 mg/kg body weight slowly IV after 5 min of xylazine hydrochloride injection.

Preparation and anaesthesia of animals: The experimental animals were closely monitored from 72 h prior to anaesthesia. Thoroughly clinical and physical examinations were performed. The animals to be anaesthetized were isolated from others and were kept in starvation for 12 h. Anaesthesia was performed in the morning to avoid the atmospheric temperature and humidity.

Monitoring of anaesthetic stages: The period extending from time of injection up to the onset of recumbence was mentioned as the period of induction. Whereas, the period required from induction to a stage when the mentioned reflexes disappeared was recorded as time for maximum depth of anaesthesia. The duration of anaesthesia is considered between the periods extending from the maximum depth of anaesthesia to a stage when the consciousness started to reappear. Finally, the recovery period was determined as the interval between the stage

of reappearance of consciousness and the pigs resuming in standing position.

Monitoring of reflexes: The depth of anaesthesia was monitored by observing palpebral reflex, conjunctival reflex, corneal reflex, digital reflex, ear pinch reflex, condition of the pupil, contracture of abdominal musculature following pinch and ability to maintain sternal recumbence.

Statistical analyses: Analysis of variance (ANOVA) in completely randomized design (CRD) was applied to analyze data regarding the parameters. Results were assessed by the Least significant difference (LSD) test in MSTAT computer program.

RESULTS AND DISCUSSION

Effects on the induction of anaesthesia: The longest (2.85 ± 0.16 min) induction period was observed in group XK, and the shortest (0.29 ± 0.02 min) in group XT; whereas, induction period in P and XP was recorded as 0.4 ± 0.08 and 0.41 ± 0.08 min respectively. The longest induction period with XK combination in the current study concurred with the findings reported by other researchers (Hall *et al.* 2001, Struck *et al.* 2011). On the other hand, thiopentone is renowned for producing a smooth, rapid induction of anaesthesia in sheep and goats (Gray 1986). Propofol produces effective general anaesthesia in different domestic animals either alone or combination with xylazine (Carroll *et al.* 1998, Bayan *et al.* 2002, Zama *et al.* 2003, Rana *et al.* 2014). The anaesthetic protocol of propofol as induction agent induced a good quality anaesthesia with a short duration of action in dogs (Alkattan and Helal 2013, Ricc6 and Hena0-Guerrero 2014). Induction of anaesthesia is rapid and smooth after administration of propofol alone in goats (Reid *et al.* 1993), sheep (Zama *et al.* 2003), camel (Fahmy *et al.* 1995), ponies (Flaherty *et al.* 1997) and dogs (Bayan *et al.* 2002).

Effect on the time for maximum depth of anaesthesia: Highest time (17.25 ± 1.31 min) for maximum depth of anaesthesia was observed in XK anaesthesia and lowest (7.5 ± 0.65 min) and (10.0 ± 0.91 min) was required for maximum depth of anaesthesia in P and XP anaesthesia respectively. Research related to this parameter is very scanty. However, the depth of anaesthesia may be clinically ascertained by monitoring various reflexes such as,

Table 1. Mean values of induction, time for maximum depth, duration of anaesthesia, recovery period of anaesthesia, quality of anaesthesia and quality of recovery in swine in different groups.

Group	Induction of anaesthesia (min)	Time for maximum depth of anaesthesia (min)	Quality of anaesthesia	Duration of anaesthesia (min)	Recovery period from anaesthesia (min)	Quality of recovery
P	$0.40 \pm 0.08^{**}$	$7.50 \pm 0.65^{**}$	Excellent	$10.75 \pm 1.75^{**}$	$18.50 \pm 1.32^{**}$	Good
XP	$0.41 \pm 0.08^{**}$	$10.00 \pm 0.91^{**}$	Excellent	$65.25 \pm 3.30^{**}$	$77.00 \pm 2.20^{**}$	Excellent
XK	$2.95 \pm 0.21^{**}$	$17.25 \pm 1.31^{**}$	Good	$30.25 \pm 1.60^{**}$	$56.25 \pm 2.14^{**}$	Good
XT	$0.29 \pm 0.02^{**}$	$16.00 \pm 1.58^{**}$	Good	$57.75 \pm 2.39^{**}$	$83.25 \pm 2.14^{**}$	Good

Values are presented as mean \pm SEM. *Significant at $P < 0.05$, **Significant at $P < 0.01$. P, Propofol; XP, Xylazine-Propofol; XK, Xylazine-Ketamine; XT, Xylazine-Thiopentone.

Table 2. Condition of pupil, position of eyeball and muscle relaxation in different groups of anaesthetized swine

Group	Condition of pupil	Position of eyeball	Muscle relaxation
P	Dilated slightly	Initially centrally fixed, then fixed laterally	Slightly muscle relaxation
XP	Dilated	Centrally fixed	Good muscle relaxation
XK	Dilated	Centrally fixed	Good muscle relaxation
XT	Dilated initially, then constricted	Centrally fixed, movement 35 min after induction	Good muscle relaxation, relax of legs and limbs

P, Propofol; XP, Xylazine-Propofol; XK, Xylazine-Ketamine; XT, Xylazine-Thiopentone.

Table 3. Reflex responses during maximum depth of anaesthesia in swine

Name of anesthetic	Palpebral	Conjunctival	Corneal	Digital	Ear pinch
P	-	+ (1)	+ (2)	+ (1)	+ (1)
XP	-	-	+ (1)	-	+ (1)
XK	-	-	+ (1)	+ (1)	+ (2)
XT	-	-	+ (1)	-	+ (1)

+, Present; -, Absent. Number indicates no. of swine manifested signs. P, Propofol; XP, Xylazine-Propofol; XK, Xylazine-Ketamine; XT, Xylazine-Thiopentone.

palpebral reflex (Williams and Wyatt 2007), palpebral and corneal movement in response to clamping claw (Doherty *et al.* 2007). Single reflex should not be used as the sole determinant of anaesthetic depth. Therefore, vital signs (heart and respiration rates, rectal temperature) along with different reflexes should be monitored continuously during anaesthesia to assess depth of anaesthesia.

Effect on the duration of anaesthesia: The shortest duration (10.75±1.75 min) of anaesthesia was found in swine with P anaesthetic protocol. This result corresponds with others result that rapid onset and short duration of anaesthesia makes propofol potentially suitable (Carroll *et al.* 1998, Kinjavdekar *et al.* 2002, Zoran *et al.* 1993). XK causes significantly ($P<0.01$) shorter (30.25±1.60 min) duration of anaesthesia in swine. This result supports the others result that stated XK anaesthetize young pigs without increasing duration of anaesthesia (Ajadi *et al.* 2008). A relatively longer (65.25±3.30 min) and (57.75±2.39 min) duration of anaesthesia was observed with XP and XT anaesthesia respectively. Propofol combination induces higher duration of anaesthesia comparatively than thiopentone sodium in dog (Funkquist *et al.* 1997). However, duration of anaesthesia reflects the presence of anaesthetic agents in plasma level, which in turn depends on concentration and speed of administration, blood volume between injection

site and brain, ionization, degree of protein binding, redistribution to non-nervous tissue, metabolism and excretion of the drug and metabolites (Hall *et al.* 2001).

Effect on the recovery time from anaesthesia: The mean values of time for recovery from anaesthesia with P, XP, XK, XT combination was recorded 18.50±1.32, 77.0±2.20, 56.25±2.14 and 83.25±2.14 min respectively. This revealed that smooth recovery from anaesthesia with P and XP protocol due to less time requirement. The mean recovery times were also found significantly shorter in goats receiving propofol, compared with the other treatments (Carroll *et al.* 1998, Prassinis *et al.* 2005). Similar result was found in dogs that recovery quality and recovery times of propofol was superior to thiopentone sodium (Ko *et al.* 1993). Shorter recovery period is mainly due to elimination of propofol from plasma by rapid metabolism (Zoran *et al.* 1993). Longer recovery times after ketamine treatment were expected in combination with xylazine (Gray 1986) that supports our current study findings. In XT anaesthesia, longer recovery was observed and it might be due to the prolonged sedative effects of xylazine. It is worthy to point out that recovery from anaesthesia is dependent on hepatic and renal function as well as the uptake of the drug by the body fat and detoxification (Hall *et al.* 2001).

Effect on the body condition and muscle relaxation: The eyeball was found centrally fixed in all swine in groups XP and XT. In propofol anaesthesia, there is rotation of eyeball in rostroventral position in light to moderate surgical anaesthesia (Hall *et al.* 2001). When P was used, pupil slightly dilated in all swine. Initially, pupil was dilated and then constricted in all swine anaesthetized with XT. Dilatation of pupil was observed during XP, XK and XT combinations. Results from XK anaesthesia was also observed with dilatation of pupil in calves (More *et al.* 1993). Slight muscle relaxation was found when propofol was used alone in this investigation. Good muscle relaxation was observed in XP anaesthesia. Similar result was reported in dogs (Cullen and Reynoldson 1997, Kim and Jang 1999), goats (Kinjavdekar *et al.* 2002) and horses (Mama *et al.* 1998). Good muscle relaxation was also observed with XK and XT combination anaesthesia in buffaloes (Kumar and Sharma 1986). This muscle relaxant effect of xylazine is a result of inhibition of intramural transmission of impulses in CNS (Marland *et al.* 2013).

Effect on different body reflexes: Corneal, conjunctival and ear pinch reflexes were observed with P anaesthesia. Sluggish to absent corneal reflex was observed after induction of propofol anaesthesia in calves (Kumar *et al.* 2011). Another study reported that apnoea, regurgitation, hypersalivation and tympany, were less common in goats receiving propofol, compared with the other treatments (Carroll *et al.* 1998). However, during XP, XK and XT anaesthesia, palpebral, conjunctival reflexes were absent, while corneal and ear pinch reflexes were present. It was reported that pupillary, palpebral and corneal reflexes are suppressed at deep level of anaesthesia in animals and man (Whelan and Flecknell 1992).

The study concluded that propofol itself and its combination with xylazine is good choice for anaesthesia in swine due to its short induction and smooth recovery. Moreover, the study recommends to use propofol (P) for short-term surgical interventions and propofol-xylazine (XP) combination for prolonged surgical procedures due to its progressive effect on duration of anaesthesia in swine.

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