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SHORT COMMUNICATION

Effects of Sumianxin's on Liver and Kidney Functions in Rabbits

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ABSTRACT

Sumianxin is a reliable anesthetic agent used in small animal surgery. Thus, the effects of sumianxin on the liver and kidney functions of rabbits were investigated experimentally. To this end, a total of six rabbits were given sumianxin at standard dose rate. Blood samples were collected before the anesthesia as well as 30, 60, 90, 120 minutes post anesthesia. The blood samples were also collected 30 minutes after recovery to measure ALT, AST, CRE and BUN levels. The results showed that Sumianxin administration significantly reduced pain and reflex responses in rabbits, with peak effects observed at 30-45 minutes post anesthesia and partial recovery of responses was noted by 90 minutes. There were no significant differences (P>0.05) in liver and kidney function indicators before and after anesthesia, indicating that Sumianxin has no significant effect on rabbit liver and kidney functions and can be used for general anesthesia in rabbits.

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INTRODUCTION

Anesthesia works to restrain and sedate animals preoperatively and during operations, examinations, or any other procedures that can lead to suffering (Iwanaga *et al*., 2024). There are various categories of anesthetics in veterinary surgery. One of the common agents is Sumianxin, in which xylazine hydrochloride, diazepam, and ketamine hydrochloride are found. It has led to its use by many experimentalists and clinical workers because it is effective in the condition of sedation, pain relief, and muscle relaxation (Kou *et al*., 2022). Additionally, because all anesthetics are equally effective, some side effects to the liver and kidneys are reported. In this context, the use of Sumianxin can have serious implications. Understanding these effects helps all those working with animals who are sensitive to anesthesia (Wang *et al.*, 2021).

The body absorbs the anesthetic, and the liver is responsible for changing and eliminating those drugs. Processed by the liver, xylazine and ketamine (important ingredients of Sumianxin) may quickly alter blood levels of ALT and AST enzymes. High enzyme levels could suggest that something is disturbing or damaging the liver cells, mainly when the drug is taken for a long time in large quantities (Abdulrazaq *et al.*, 2021). Also, due to a special metabolism in the liver, rabbits are more likely to suffer from drug-induced liver problems if given the wrong doses. Other anesthetics have been shown to cause short-term effects, but given regular exposure, they may seriously harm the liver. So, experts suggest checking for signs of liver damage in scientific and treatment research (Nazir *et al.*, 2021).

Likewise, kidneys are crucial for excreting anesthetic waste, and a decrease in kidney function can result in taking too much anesthetic and lengthening recovery or increasing harm. About 55% of ketamine, an active substance in Sumianxin, is cleared by the kidneys, and its metabolites might increase kidney function (Huang *et al.*, 2024). The use of anesthetics can cause hypotension, which may also lower blood flow to the kidneys and risk making pre-existing kidney issues worse. Although Sumianxin is not usually nephrotoxic in healthy rabbits, it may cause delayed clearing of the drug in those with damaged kidneys, resulting in longer or stronger drowsiness. For this reason, the real function should be evaluated ahead of administration, and proper hydration should be ensured (Abdulrazaq *et al.*, 2021). It is proposed that a one-time dose is typically acceptable, continual or inappropriate drug intake can lead to organ strain that is imperceptible except under unique chemical examinations (Yongsheng *et al*., 2023).

Administration of Sumianxin sensitive animals can have serious effects during the surgery protocols. The effects of Sumianxin on the vital organs (liver, kidneys) in small animal models are not well investigated. Thus, during current investigation, an effort is made to find the effects

of any administration of Sumianxin on the functioning of the liver and the kidneys of rabbits by looking at the chemical indicators in their body.

MATERIALS AND METHODS

Experimental animals and study design: For current investigation, a total of six healthy rabbits (male and female in equal ratio) were provided by the College of Animal Science and Veterinary Medicine, Tianjin Agricultural University. Experimental animals were immunized through standard protocols and offered unrestricted access to food and water *ad libitum* before the start experimentation. The experimental animals were weighed and administered intramuscularly with atropine sulfate at rate of 0.01mL/kg (State-owned Luoyang Veterinary Medicine Factory). 15 minutes later, animals were administered with sumianxin at the dose rate of 0.1mL/kg (Jilin Huamu Animal Health Products Co., Ltd.).

Pain Monitoring and biological reflexes: The analgesic effect was tested by needle pricking to the head, neck, abdominal wall and the skin around the hooves of forelimbs and hindlimbs of rabbits. Silver clips were also used on lips, nose, ears, abdominal wall, and hoof areas for assessment. Indicators before anesthesia were used as baseline values and monitoring was performed at 5, 15, 30, 45, 60 and 90 minutes interval during the surgery for monitoring of reflexes as follows.

Eyelid reflex: stimulation of the eyelid causing blinking or flinching was recorded as "+"; Dull or weakened response as "±"; No response as "-".

Corneal reflex: stimulation of the cornea causing eyeball tremors or eye rolling was recorded as "+"; Dull or weakened response as "±"; No response as "-".

Anal reflex: stimulation of the anus causing contraction was recorded as "+"; Dull or weakened response as "±"; No response as "-".

Sample collection and processing: The first cardiac blood sample was collected before the administration of anesthesia followed by 30 minutes after lying down under anesthesia. After recovery from anesthesia stage, blood samples were again collected at 30 minutes, 24 and 72 hours internal, respectively. The serum of the collected samples was obtained and liver and kidney function indicators (ALT, AST, CRE and BUN) were performed according to the reagent instructions.

Statistical analysis: Experimental data were organized using Excel 2017 and ANOVA was performed using SPSS 22.0; $P<0.05$ indicated significant differences, and results were expressed as "mean ± standard deviation".

RESULTS

The differences in the values of liver functions indicators (ALT and AST) of rabbits before and after the administration sumianxin were not significant ($P>0.05$) as depicted in Fig 1. For ALT, pairwise comparisons showed no significant differences between pre-anesthesia levels and those at 30 minutes post-anesthesia ($P=0.142$), 30 minutes post-recovery ($P=0.097$), 24 hours post-recovery ($P=0.115$), or 72 hours post-recovery ($P=0.138$). For AST, no significant variations were observed between pre-anesthesia values and those at 30 minutes post-anesthesia ($P=0.226$), 30 minutes post-recovery ($P=0.189$), 24 hours post-recovery ($P=0.253$), or 72 hours post-recovery ($P=0.271$).

The differences in kidney function indicators (CRE and BUN) levels were also not significant ($P>0.05$) as depicted in Fig 1. For CRE, pre-anesthesia levels versus those at 30 minutes post-anesthesia ($P=0.319$), 30 minutes post-recovery ($P=0.208$), 24 hours post-recovery ($P=0.192$), and 72 hours post-recovery ($P=0.103$) were not statistically significant. For BUN, comparisons between pre-anesthesia values and those at 30 minutes post-anesthesia ($P=0.264$), 30 minutes post-recovery ($P=0.307$), 24 hours post-recovery ($P=0.185$), and 72 hours post-recovery ($P= 0.089$) revealed no significant differences.

Within five minutes after administering Sumianxin, the pain response and biological reflexes (eyelid, corneal and anal) began to dull and weaken. Pain response score as given in Table 1 and illustrated in Fig. 1 show that responses were consistent at 0 and 5 minutes (all marked "a", $P>0.05$). However, there was a marked change at 45 minutes (marked "b") which suggested maximum analgesic effect of Sumianxin ($P<0.05$ vs. 5 min). At the 90 minutes mark, values showed partial recovery (labeled "ab") and there was no significant difference from baseline ($P>0.05$). For reflex responses (Table 2, Fig. 3), the Friedman test suggested significant changes over time. Eyelid reflex scores showed a marked decrease at 30 minutes (b) when compared to the 0-5 minutes range ("a," $P<0.05$), followed by gradual recovery. Corneal reflex had similar results with most suppression occurring at 30 minutes ("b"). The anal reflex was markedly subdued from 30 to 45 minutes (both "b").

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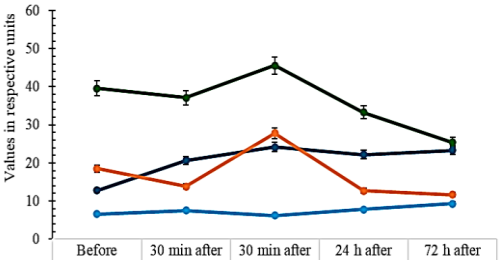

	Before anesthesia	30 min after anesthesia	30 min after recovery	24 h after recovery	72 h after recovery
ALT (Karmen units)	12.83	20.67	24.17	22.17	23.33
AST (Karmen units)	18.5	13.83	27.83	12.67	11.67
CRE (µmol/dL)	39.6	37.13	45.56	33.28	25.4
BUN (mmol/L)	6.62	7.48	6.23	7.8	9.35

Fig 1: Effects of Sumianxin on renal and hepatic function markers evaluated at different time interval post administration

Table 1: Individual pain response scores in rabbits following Sumianxin administration at different time intervals

Item/Time		Normal value	5	15	30	45	60	90
Pain response	1	+	+	+	±	±	±	+
	2	+	+	+	±	-	-	+
	3	+	+	+	-	-	-	+
	4	+	+	+	±	-	-	+
	5	+	+	±	+	-	-	+
	6	+	+	±	±	-	±	±

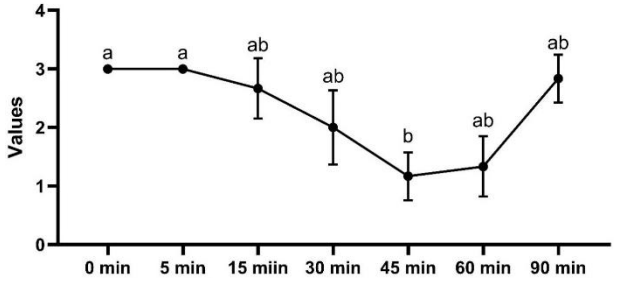

Fig. 2: Graphical representation of temporal changes in pain response in rabbits following Sumianxin administration. Bars or data points marked with different letters (a, b) differ significantly (P<0.05); values sharing a letter (ab) are not significantly different.

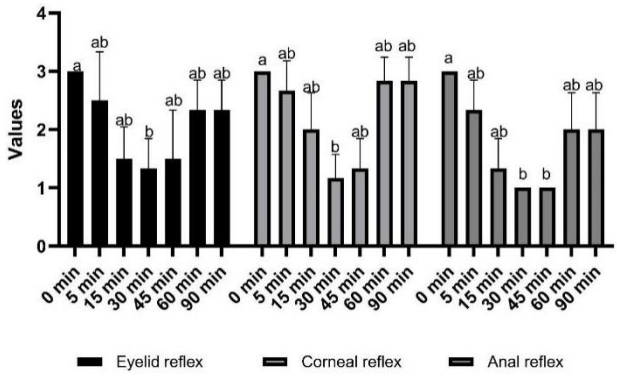

Fig 3: Visual summary of reflex response trends (eyelid, corneal, and anal) in rabbits over time after Sumianxin administration. Different superscript letters (a, b) indicate statistically significant differences between time points (P<0.05); shared letters denote no significant difference.

Table 2 Evaluation of reflex responses in rabbits at various time intervals following Sumianxin administration

Time/min		Normal value	5	15	30	45	60	90
Eyelid reflex	1	+	+	±	±	+	+	+
	2	+	+	±	-	-	±	±
	3	+	+	-	-	-	±	±
	4	+	±	±	-	-	±	±
	5	+	-	-	±	-	+	+
	6	+	+	-	-	±	±	±
Corneal reflex	1	+	+	±	±	±	+	+
	2	+	+	±	-	-	+	+
	3	+	+	-	-	-	+	+
	4	+	+	±	-	-	+	+
	5	+	±	+	-	-	+	+
	6	+	±	±	-	±	±	±
Anal reflex	1	+	±	±	-	-	±	±
	2	+	±	±	-	-	±	±
	3	+	±	-	-	-	+	+
	4	+	+	-	-	-	-	-
	5	+	+	-	-	-	±	±
	6	+	±	-	-	-	±	±

DISCUSSION

Sumianxin is a compound anesthetic agent commonly used in veterinary surgery. It is composed of some sedative, tranquilizer, analgesic and stabilizing compounds. This combination produces rapid onset of deep anesthesia with effective analgesia and muscle relaxation, making it suitable for use in animals (Yongsheng *et al*., 2023). This paper assessed the biochemical effect of an xylazine/ketamine combination with Sumianxin on hepatic and renal functions of healthy rabbits. Since the liver and kidneys play a primary role in drug metabolism and excretion, even a temporary condition can affect these enzymatic markers, such that it becomes clinically relevant in healthy individuals. The results obtained in our study revealed an elevation of ALT and AST, 24 hours after the induction of anesthesia, but the levels of the enzymes returned to normal 72 hours after the induction of anesthesia. These findings are also in close correspondence with previous studies: when New Zealand White rabbits were treated with ketamine xylazine, elevated ALT, AST, BUN and creatinine rates were recorded in 10-120 minutes of drug administration, but the rates did not exceed the normal level (Gil *et al*., 2002). In more recent research, Chen *et al*. (2020) applied the methods of imaging to demonstrate hepatic perfusion alterations and transient steatosis in rodents subjected to ketamine-xylazine anesthesia, which again confirms our findings about the presence of subclinical hepatotoxicity, which can be temporarily reversed.

The processes behind such changes to the liver may include -α2-adrenergic mediated vasoconstriction, lowering hepatic perfusion (Maan *et al*., 2018), and increased activity of cytochrome P450 metabolism to metabolize ketamine (Martinez-Lopez *et al*., 2023). Although the elevation of enzymes in our subjects was not above species-specific normal cut-offs, it represents physiological stress. This was in alignment with an examination, which established that there was greater change in hepatic enzymes in Xylazine-Ketamine (XK) anesthesia in contrast to isoflurane anesthesia, but just temporarily (Maan *et al*., 2018). The findings emphasize the need to monitor the hepatic function during the perioperative period, particularly when dealing with animals.

This experiment recorded modest rises in BUN and creatinine at 24 hours, which had resumed baseline at 72 hours. Gil *et al*. (2002), also revealed the biochemical renal changes associated with anesthesia during XK anesthesia in rabbits. In rodent models, these results were extended by Scurt *et al*. (2024), who demonstrated that HAVCR1 and other urinary proteins were indicators of mild ischemic stress following ketamine xylazine, without histological injury. It was shown that XK anesthesia in goats resulted in glomerular filtration rate decreases and increases in the concentrations of BUN, demonstrating that the renal vasoconstriction caused by α2-agonists can temporarily exert a negative effect on the ability of the kidneys to filter. Since in our study fluid homeostasis was maintained, the mild reversible renal effects should come as no surprise and prevent complications associated with dehydration.

According to the study conducted by Maan *et al*. (2018), there was also a significant difference in the levels of ALT, AST and BUN in the case of XK as compared to isoflurane, a steady level of creatinine, and intensified cardiovascular depression. A 2023 comparative analysis of XK and a combination of xylazine, fentanyl, and ketamine revealed that injectables prolonged the length of anesthesia and also affected clinical chemistry indicators, such as albumin, creatinine (Akter *et al*., 2023). The overall evidence indicates that although Sumianxin is suitable in procedures of short duration, it requires more perioperative monitoring than inhalant regimens.

The safety of Sumianxin was satisfactory when tested on healthy rabbits, as all induced biochemical perturbations were only transient and thus corrected quickly. However, temporary increases of enzymes emphasize the need for serial evaluation-baseline, 24 and 72-hourly measures of

ALT, AST, BUN, and creatinine should be done. This practice is consistent with the new patterns of risk stratification of anesthesia in lagomorphs that stress the concept of personalized monitoring of animals with comorbidities or on a repeat basis (Duan et al., 2017).

Conclusions: This study demonstrates that Sumianxin anesthesia causes predictable, transient alterations in hepatic and renal biomarkers. These effects are generally reversible in healthy rabbits at recommended doses. Although, the effects on the liver and kidneys recorded during the current investigation are not significant. However, the findings reinforce the importance of proper dosing, physiological monitoring and individualized risk assessment of Sumianxin administered animals. By contextualizing the current results within this extensive framework of previous research, current findings can help to improve clinical practice and future research in rabbit anesthesia and pain management.

Conflicts of interest: The authors have no conflicts of interest to declare.

Authors contribution: CY, ZW and YW carried out study design and conceptualization; Administrative support by YW and BJ; Provision of study materials or animals by JW and XS; data collection and assembling by CY, ZW and YY; Data analysis and interpretation by CY, ZW and XS; manuscript writeup and final approval by all authors.

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