

Original Article

+Gz-induced post-cholecystectomy syndrome in rabbit model by using a telemetric method

Yalin Kong¹, Gang Zhao¹, Yifeng Li², Dongqing Wen², Hui Zhang¹, Xiaojun He¹, Yuying Zhen¹, Hongyi Zhang¹

¹Department of Hepatobiliary Surgery, Chinese PLA Air Force General Hospital, Beijing 100142, China; ²Institute of Aviation Medicine of Chinese PLA Air Force, Beijing 100142, China

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Abstract: Aviation-related mechanism may exist in the post-cholecystectomy syndrome (PCS) of aircrew patients. The aim of this study was to test this hypothesis on vivo rabbit model and to explore the mechanism by using a novel telemetric method. We constructed a bile duct-to-intestinal bridge bypass on 30 rabbits, with a telemetry implant attached to the Oddi's sphincter. Then a telemetric recording system was used to record the biliary pressure fluctuation through the subcutaneous bridge and the changes of electromyography of the Oddi's sphincter under different +Gz acceleration. Self-control comparison was made before and after cholecystectomy. The fully implantable device was very well accepted by rabbits and the data could reflect the real experimental environment simultaneously. Biliary pressure in common bile duct increased accordingly with +Gz acceleration increased, but bile secretion didn't change. Although +Gz acceleration could increase the frequency of burst of spike potentials in the Oddi's sphincter, the frequency didn't change with the +Gz acceleration increased, and the spike activity didn't change obviously before cholecystectomy. After cholecystectomy, the biliary pressure in common bile duct remained high in 12 rabbits (40%) under +Gz exposure, and the pressure value didn't change as the +Gz acceleration increased. The long-time changes in electromyography of the Oddi's sphincter were observed in the same 12 rabbits, with symptoms of PCS developed in 9 of them. +Gz exposure is an important external factor leading to the biliary physiology disorder, and it may induce PCS in some aircrew patients with individual susceptibility, which means gallbladder maybe a dominant factor in regulating the biliary physiology in these aircrew patients.

Keywords: Acceleration, biliary physiology, telemetry, post-cholecystectomy syndrome

Introduction

Gallbladder disease, such as calculous cholecystitis, polyps, and adenomyoma, is one of the most common organic diseases in aircrew. Due to the more frequent use of abdominal ultrasound examination and the great improvement in diagnostic sensitivity, the incidence of gallbladder disease in Chinese aircrew has increased 30% over the past ten years [1]. In recent years, significant changes have also occurred regarding the therapeutic modus of gallbladder disease. Laparoscopic cholecystectomy (LC) has become a standard operation for surgical treatment of gallbladder disease in aircrew, which has also developed the rate of cholecystectomy in aircrew patients because of its minimally invasive nature [2]. However, post-cholecystectomy syndrome (PCS), including the long-term complications of diarrhea, mild abdominal pain, abdominal distention, and nausea, happened much higher in aircrew than

general population, and one of the most obvious characteristics of PCS in aircrew is that the symptoms occur more often in flight period rather than in postoperative grounding observation period [3]. So it is very important to clarify the mechanism of PCS in aircrew under aviation physiology environment.

In the late 1990s, +Gz-induced biliary system dysfunction and disorders of Oddi's sphincter were observed in some animal models, suggesting that +Gz maybe an important outer factor to induce changes in bile secretion and metabolism [4]. We also guess that +Gz may induce PCS in aircrew by analyzing the clinical features of PCS in aircrew. So it's necessary to dynamically monitor indexes of biliary physiology on vivo animal models to verify our hypothesis. However, the lack of method to observe the biliary physiology on vivo animal models under +Gz exposure restricts critically the further research. Telemetric recording systems have

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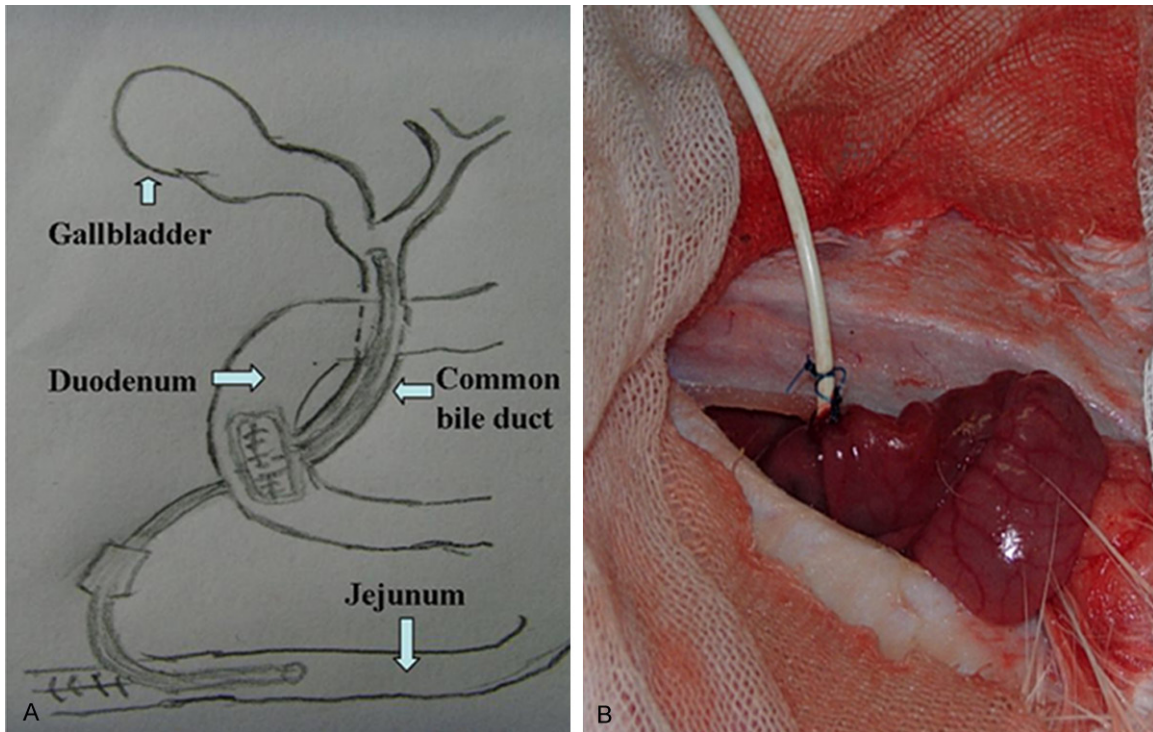


Figure 1. The surgery procedure of bile duct-to-intestinal bridge bypass model. (A) is the illustration of the bile duct-to-intestinal bridge bypass, and it shows that one end of the bridge was inserted into common bile duct and the other into jejunum. (B) shows that the manometry catheter was inserted into the common bile duct through the duodenal papilla of biliary duct.

been used to record physiological parameters (e.g. blood pressure, heart beat, body temperature, brain activity) under relatively natural conditions. They are in many aspects advantageous and more valuable when compared to conventional recording devices used in vivo animal models. Therefore, the characteristics of biliary physiology led us to investigate the feasibility of utilizing the telemetric recording systems.

In this study, we established a kind of novel method to study biliary physiology on vivo animal models. On this vivo rabbit model, we constructed a bile duct-to-intestinal bridge bypass which was put subcutaneously, and attached a telemetry implant to the Oddi's sphincter. Through the bridge bypass, we used the telemetric recording system to record the biliary pressure fluctuation under +Gz exposure. We also used the telemetric recording system to record electromyography of Oddi's sphincter in vitro. So we can dynamically detect the changes of biliary physiology under +Gz exposure on vivo animal models. Just on basis of this method, we firstly found symptoms of PCS on experi-

mental rabbits under +Gz exposure and acquired a better understanding about the nature of +Gz-induced PCS.

Material and methods

Ethics statement

This study was carried out in strict accordance with the recommendations in the Guide for the Care and Use of Laboratory Animals of the Ministry of Science and Technology of China P.R. The protocol was approved by the Committee on the Ethics of Animal Experiments of the Ministry of Health of the Chinese PLA General Logistics Department (Permit Number: 08G047). All surgery was performed under sodium pentobarbital anesthesia, and all efforts were made to minimize suffering.

Animals

Thirty male New Zealand white rabbits with average body weight of 1.5-2 kg were purchased from the Experimental animal center of Military Medical Science Academy of Chinese

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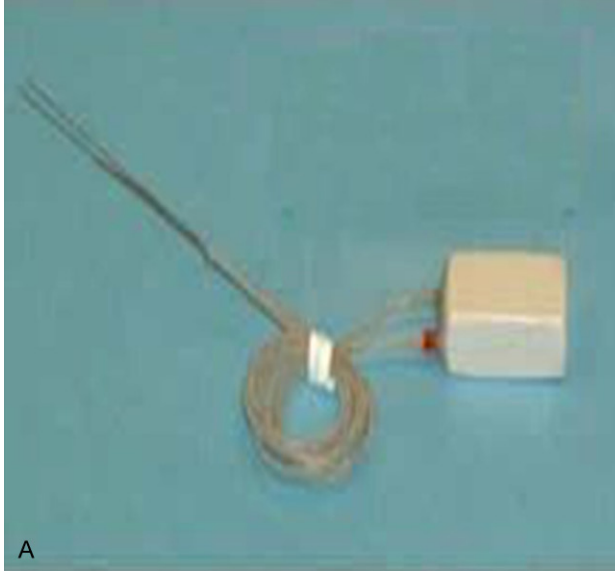


Figure 2. Photograph of the miniature recording telemetric system. This system consists of two separate parts, (A) telemetric implant unit, which can be used inside or outside of the animal body to transmit signal, and (B) wireless receiver, which can amplify and convert the signal.



PLA. These experimental rabbits were housed individually in standard steel cages (45 cm × 50 cm × 35 cm) under a 12 h light-dark (lights on at 7 am). The room temperature was maintained at $21 \pm 2^\circ\text{C}$ and relative humidity at $50 \pm 5\%$. Standard rabbit food and tap water were available without limit.

Apparatus

The miniature telemetric recording system consists of a telemetric implant (Tox-LA implant, Softron Beijing Incorporated) to transmit the signal, and a receiver (DSCF-08, Softron Beijing Incorporated) to amplify and convert the signal via radio transmission over a distance of up to 3 m (Figure 1). The receiver is connected to a computer via a USB connection and the data are displayed, analyzed and saved by software SBP2000 (Softron Beijing Incorporated). The SBP2000 software consists of three independent modules for (1) capturing data, (2) replaying/analyzing data, and (3) software servicing of the control system and the implanted devices.

The animal centrifuge, provided by the Air Force institute of Aeromedicine, was 2 m in radius and was capable of producing acceleration range from +1 Gz to +15 Gz, with an onset rate of 0.1-6 Gz/s. Each rabbit was put into a 30 cm × 20 cm × 10 cm plexiglass box which was clamped to the centrifuge arm with its head facing toward the axis of the centrifuge for +Gz orientation. The onset/offset rate was +1 Gz/s.

Surgical method

The surgery was performed after deeply anesthetizing the animals. Anesthesia was initiated by an intravenous injection of pentobarbital sodium (50 mg/kg) via the marginal ear vein, and then maintained at an appropriate level by continuous intravenous infusion of α -chloralose (16 mg/kg/h) and urethane (100 mg/kg/h) through a catheter inserted into the femoral vein. During the surgery, the animals were intubated and ventilated mechanically with room air mixed with oxygen. Temperature was measured in the esophagus by a thermometer (CTM-303, Terumo, Japan), and was maintained between 38 and 39°C using a heating pad [5].

The rabbit was put in supine position and the area across the abdominal skin were shaved and cleaned with iodine. An incision of 3 cm was made in the right part of the abdomen's mid-line. The duodenum was cut open, and the manometry catheter, made from COOK's 5F tube (outer-diameter 1.6 mm), was cannulated into the common bile duct through the duodenal papilla of biliary duct. The distal jejunum 10 cm from the papilla was cut open, and another COOK's 5F tube was cannulated into the intestinal cavity. A bridge, made of plastic connector, joined the free ends of two tubes. Then we inserted the implant's electrode into the Oddi's sphincter through the serosa of descending duodenum, and fixed the implant onto the abdominal wall. After the incisions of duode-

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num and jejunum were sutured separately, the bridge and the implant's electrode wires were put subcutaneously. So the vivo rabbit model was made (**Figure 2A, 2B**).

For a better recovery, all rabbits were given an antibiotic (IP) (0.1 ml Baytril® 2.5%, Bayer Vital, Leverkusen, Germany) and an analgesic treatment (SC) (0.05 ml Rimadyl®, Pfizer, Karlsruhe, Germany) [6]. Surgery lasted a maximum of 2 h from induction of anesthesia and the success rate was 100% for recovery from anesthesia and surgery. The animals were weighed daily throughout the experiment as an indicator of general health [7].

Data recording

After surgery, a recovery period of 7 days was given to the animals before starting the first recording session, corresponding to the time needed to gain the pre-surgical weight again. All rabbits were exposed to +1 Gz, +3 Gz, +6 Gz for 3 min respectively, and the interval time of each +Gz exposure was 20 min. The onset/off-set rate was +1 G/s. Biliary pressure measurement and electrophysiology of Oddi's sphincter recording were performed within 3 min after each +Gz exposure. The implanted electrode was inserted into the manometry catheter through the subcutaneous bridge to measure biliary pressure. The signal was recorded by the receiver, processed by our software, displayed on computer screen, and saved on the hard-disk. The signal of biliary pressure and electromyography of Oddi's sphincter can appear on the screen respectively via different tunnel without inference. After all the +Gz exposure, the manometry catheter was opened for 12 h to record the amount of bile secretion. We had also measured the biliary pressure and recorded 12 h bile secretion amount of each rabbit before +Gz exposure as self control. We repeated the second recording session of +Gz exposure as the same procedure 7 days later and the third recording session 14 days later.

After data of the first-stage +Gz exposure had been recorded, cholecystectomy was performed in all of these 30 experimental rabbits through the same method of deep anesthesia, and then repeated the +Gz exposure and data recording after complete recovery.

Statistics

Statistical analyses were performed with Systat Version 10 (Systat Software, Erkrath, Germany). Values throughout this report are given as means \pm standard deviation (S.D.) and were analyzed using one-way analysis of variance (ANOVA) followed by SNK methods for post hoc analysis and two-tailed t-test when appropriate. A *P* value less than 0.05 was considered statistically significant.

Results

Recovery of the animals after implantation

All of the implantation surgeries were followed by a lost of weight and the maximum peak was 3 days after the surgery ($92.7 \pm 0.5\%$ of pre-surgery body weight). Six days after the implantation surgery, these rabbits started again to take weight and reached the pre-surgery's weight after 14 days. No infections or mortality due to the implantation surgery were observed on the thirty rabbits used for this study. To test the impact of the system on the animal movements, rabbits were placed for 30 min in an empty open field (150 cm \times 80 cm) and a behavioral recording was made with Etho Vision (Noldus Information Technology, Berlin, Germany). The total distance of moving and the velocity of the rabbits were then compared to non-implanted rabbits (self-control of the same 30 rabbits before implantation surgery) in the same conditions. No significant differences were observed in these two parameters (42.7 ± 2.4 m and 3.8 ± 0.3 cm/s for the control rabbits versus 38.26 ± 2.2 m and 3.3 ± 0.2 cm/s for the implanted rabbits, each group *n* = 30). The device did not restrict limb movements during locomotion. The telemetry device did not cause obvious discomfort to the animals which were still able to eat and sleep. The daily food intake and sleeping posture didn't change.

Manometry of common bile duct and amount of bile secretion

Manometry showed that the biliary pressure in common bile duct without +Gz exposure was 1.54 ± 0.12 Kpa and this result was consistent with what reported in the literature [13]. The biliary pressure in common bile duct increased when the experimental rabbit was under +Gz exposure, and the biliary pressure increased as the +Gz acceleration increased (**Figure 3**). The

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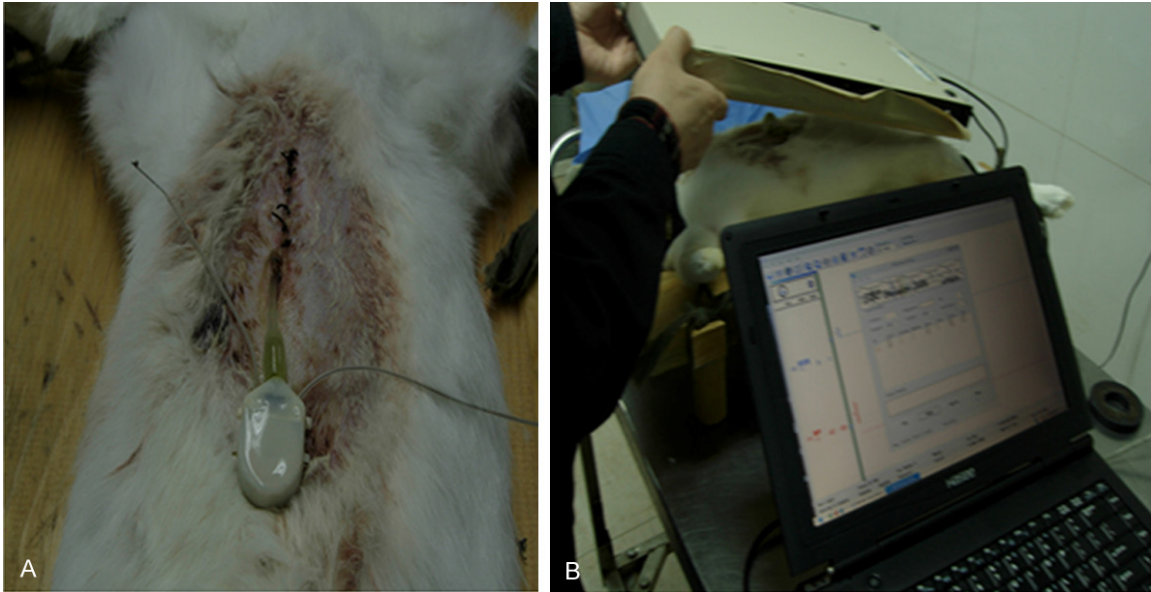


Figure 3. Photograph of the data collection by the telemetric recording system. (A) shows that the implant's electrode was inserted into the manometry catheter through the subcutaneous bridge to measure biliary pressure. (B) shows that the signal was recorded by wireless receiver, processed by our software, and displayed on computer screen.

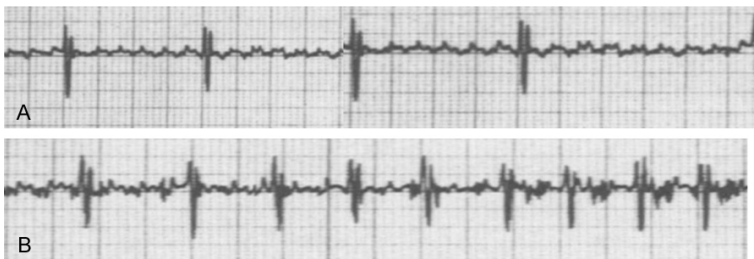


Figure 4. Electromyography of the Oddi's sphincter. The recording apparatus used a paper speed of 1 mm/sec, low frequency cut-off filter of 0.5-1.0 Hz, high frequency cut-off filter of 10-30 Hz, and an overall sensitivity of 25 to 50 mV. (A) shows the Electromyography of the Oddi's sphincter before +Gz exposure. (B) shows Electromyography of the Oddi's sphincter under +Gz exposure.

amount of bile secretion of 12 h after +Gz exposure was 60-75 ml, without obvious difference compared with the self control group before +Gz exposure ($P > 0.05$).

After cholecystectomy, manometry showed that the biliary pressure in common bile duct remained in high level of 2.37 ± 0.16 Kpa in 12 experimental rabbits (40%) under +Gz exposure, and the pressure value didn't change as the +Gz acceleration increased from 1 +Gz to 6 +Gz. While in the other 18 rabbits, biliary pressure data under +Gz exposure remained consistent with that before cholecystectomy. The measure of bile secretion of 12 h after +Gz

exposure showed that the amount was increased to more than 90 ml in 11 of the 12 rabbits with permanent high biliary pressure in common bile duct, while changes in bile secretion were not observed in the other 19 rabbits.

Electromyography of Oddi's sphincter

The frequency of burst of spike potentials increased temporarily in the Oddi's sphincter after +Gz exposure (6.3 ± 1.2 burst of spikes/min after +Gz exposure and 3.7 ± 0.9 burst of spikes/min before +Gz exposure, $P < 0.05$), but the increase in frequency didn't change as the +Gz acceleration increased. During the entire phase, there was no obvious change in the spike activity in the Oddi's sphincter, whether with or without +Gz exposure (**Figure 4**). In 5-7 minutes after +Gz exposure, the electromyography of Oddi's sphincter of all these 30 experimental rabbits restored to pre-acceleration level.

After cholecystectomy, electromyography of Oddi's sphincter after +Gz exposure showed

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the same changes with the electromyography without cholecystectomy. However, the changes lasted above 10 minutes in 12 rabbits (40%), just the same 12 rabbits with permanent high biliary pressure in common bile duct under +Gz exposure after cholecystectomy, and transient unstable waves happened more often in these 12 rabbits. No difference was found in the other 18 experimental rabbits compared with the electromyography before cholecystectomy.

+Gz exposure-related symptoms in the post-cholecystectomy rabbits

After the experiment of +Gz exposure, symptoms including loose stools, decreased appetite, and light weight loss (weight loss < 10%) occurred in 9 experimental rabbits after cholecystectomy (9/30, 30%). The 9 rabbits just belonged to the 12 post-cholecystectomy rabbits which had abnormal variation in biliary pressure and electromyography of Oddi's sphincter under +Gz exposure as mentioned above. These symptoms were relieved gradually without special management and all of these 9 rabbits reached their pre-surgery weight in 4-6 weeks. Such +Gz-related symptoms didn't occur in the other 21 rabbits after cholecystectomy.

Discussion

LC is now the most commonly performed gastrointestinal operation in Chinese aircrew, with approximately 1000 performed each year in civil or military aviation aircrew for various gallbladder diseases [8]. Surveys of LC in aircrew patients showed that about 40%-50% of the aircrew patients suffered from chronic abdominal symptoms with no obvious cause, much higher than the incidence of 5%-20% in general population after LC, and these chronic abdominal symptoms are usually classified as PCS [9, 10]. PCS includes a heterogeneous group of diseases, usually manifested by the presence of abdominal symptoms following gallbladder removal [11]. Although this term is used widely in the medical literature, it is rather inaccurate, because it encompasses a large number of biliary and non-biliary disorders [12]. In general population, the symptoms of PCS usually occur within a few weeks after surgery and may last for months, so a temporary grounding time for aircrew after LC is regulated. However, the non-specific symptoms of PCS reoccur in some air-

crew during aviation work period so that the temporary grounding time has to be prolonged for a few months even for years, and cases of permanent grounding because of serious PCS symptoms and/or heavy psychological burden caused by them are not rare [13, 14]. On one hand, gallbladder disease can lead to aircrew's incapability in flight and is an important indication for LC [15], and on the other hand, the high incidence of PCS makes surgeons very reluctant to perform LC for aircrew patients with gallbladder disease. Up to now, the etiology of PCS is still not clear. Aviation-related mechanism may exist in the PCS of aircrew and it's very necessary to establish a vivo animal model to study such mechanism.

Telemetric recording system offers several advantages compared with the routine method to study the biliary physiology in animal. The relatively small size and weight of the fully implantable device is very well accepted by adult rabbits which do not show any kind of behavior impairments or sign of discomfort. Data can be processed by software and displayed on the computer screen simultaneously, allowing the data to reflect the real experimental environment. The experiment can be repeated on the same rabbit so that self control can be made. Another advantage of our system is that no particular precautions be taken in order to limit any kind of external electromagnetic interferences. In addition the relatively long lifetime of the batteries, due to the low power consumption of the system and possibility to switch on and off by external control, permits experiments lasting 6 to 8 weeks. Finally after sacrificing the implanted animal and extracting the transmitter, the system can be reused several times after changing batteries and electrodes. We recorded the biliary pressure and electromyography of Oddi's sphincter before +Gz exposure as blank control to judge the reliability of this method, and the results were consistent with the data reported in literature [16]. So this proved the reliability of the method.

The +Gz exposure experiment before cholecystectomy showed that, with +Gz acceleration increased, the biliary pressure in common bile duct increased accordingly. But it's difficult to tell whether there is a linear relationship between the +Gz acceleration and biliary pressure from this experiment. There used to be a kind of hypothesis developed by some physi-

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cians engaged in clinical aviation medicine, who thought that +Gz acceleration flight could caused fluctuations of extrahepatic or intrahepatic biliary pressure and the fluctuations in biliary pressure may be connected with the occurrence of primary sclerosing cholangitis [17]. But agreement couldn't be reached on whether +Gz increased or decreased biliary pressure. In this experiment, we observed the increase of extrahepatic biliary pressure caused by +Gz exposure on vivo animal model, and provided direct proof for this hypothesis. We also observed +Gz-induced electromyography changes of Oddi's sphincter. We found that although +Gz acceleration can increase the frequency of spike potentials in the Oddi's sphincter, the frequency didn't increase with the +Gz acceleration increases, and the spike activity didn't change obviously during the whole experiment. It is interesting that while the unparalleled change of the biliary pressure and electromyography of Oddi's sphincter, the bile secretion remains stable. So, we guess some mechanisms may exist in regulating the biliary physiology and keep the bile secretion stable in vivo animal.

The +Gz exposure experiment after cholecystectomy showed that the symptoms of PCS didn't occurred in all these experimental rabbits, and the incidence of PCS was 30% in this study. Considering only objective symptoms were chosen to reflex the occurrence of PCS and the subjective symptoms such as abdominal pain and abdominal distention were ignored, incidence of PCS should be higher than 30% in this model and this result was very similar to the real condition in aircrew patients. Especially it reflected the most important characteristic of PCS in aircrew patients, that the individual susceptibility in the occurrence of PCS. All of the experimental rabbits with obvious symptoms of PCS induced by +Gz exposure had two common features in biliary physiology. One was the abnormally high biliary pressure in common bile duct under +Gz exposure, and the other one was the permanently frequent burst of spike potentials and transient unstable waves on the electromyography of Oddi's sphincter. Because more than 20% patients with PCS have a functional abnormality in the Oddi's sphincter which is referred to as sphincter dyskinesia and ampullary spasm, and an elevated sphincter pressure on biliary manometry with a dilated common bile duct was the characteris-

tic endoscopic finding in patients with PCS (endoscopic retrograde cholangiopancreatography remains the criterion standard for diagnosing Oddi's sphincter disorders), some physicians presume that the factors leading to functional abnormality of the Oddi's sphincter and increase of biliary pressure may be connected with PCS [18, 19]. Correlated with the previous findings, we think that +Gz exposure is just one of the important external factors leading to biliary physiology disorders, and when cholecystectomy weakens the body's self-regulation ability, which manifests as functional or motility disorders of the Oddi's sphincter and abnormal elevation of biliary pressure, the clinical symptoms of PCS appear.

The individual susceptibility of some aircrew patients to PCS symptoms suggests that some people mainly rely on the gallbladder to regulate biliary physiology, while the other people also rely on other mechanisms to maintain the normal biliary physiology function even when cholecystectomy had been performed. It was reported that Oddi's sphincter dysfunction was often associated with other functional gastrointestinal disorders such as irritable bowel syndrome and visceral hyperalgesia, which could be relieved by calcium channel blockers or long-acting nitrates [20]. This suggested that neurohumoral factor and ion channel factor may be the co-existing regulating mechanisms of biliary physiology, and this hypothesis is consistent with what we found in the +Gz exposure experiment before cholecystectomy, and further research should be carried out to prove this hypothesis.

Conclusion

This study provided a kind of novel and reliable telemetric method to study the effects of +Gz exposure on biliary physiology on vivo rabbit model. The telemetric recording systems showed that there was obvious relationship between biliary physiology and +Gz acceleration. +Gz exposure could lead to increase of biliary pressure in common bile duct and frequent bursts of spike potentials of Oddi's sphincter. For some rabbits after cholecystectomy, the changes in biliary physiology were enhanced by +Gz exposure and manifested as clinical symptoms of PCS. The relationship indicates that +Gz exposure is an important external factor leading to biliary physiology disorder.

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ders, and it can induce symptoms of PCS in some aircrew patients with individual susceptibility which means gallbladder maybe the dominant factor in regulating the biliary physiology in these aircrew patients. Other mechanism may also exist in maintaining the normal biliary physiology, and further research should be carried out to prove this hypothesis.

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Disclosure of conflict of interest

None.

Address correspondence to: Hongyi Zhang, Department of Hepatobiliary Surgery, Chinese PLA Air Force General Hospital, 30 Fucheng Rd, Haidian District, Beijing 100142, China. Tel: 86-010-66928312; Fax: 86-010-66927612; E-mail: kjzyg-dwk@163.com

References

- [1] Luan FM, Ge CL, Ma N, Li YZ, Hu CJ. The contribution for the diagnosis of the tumor-like polypoid lesions of the gallbladder by SELDI-TOF-MS. *Zhonghua Wai Ke Za Zhi* 2008; 46: 525-527.
- [2] Ball CG, Kirkpatrick AW, Williams DR, Jones JA, Polk JD, Vanderploeg JM, Talamini MA, Campbell MR, Broderick TJ. Prophylactic surgery prior to extended-duration space flight: is the benefit worth the risk? *Can J Surg* 2012; 55: 125-131.
- [3] Farr RW, Kane PD. Clinical outcomes of naval aviation personnel with cholelithiasis. *Aviat Space Environ Med* 2002; 73: 681-683.
- [4] Yang CM, Chen Y, Mao GP, Ma LN, Wang Z, Zhang YH. Effects of acute hypobaric hypoxia on gastric emptying and intestinal propulsion: experiment with rats. *Zhonghua Yi Xue Za Zhi* 2006; 86: 2391-2394.
- [5] Silva A, Ferreira DA, Venâncio C, Souza AP, Antunes LM. Performance of electroencephalogram-derived parameters in prediction of depth of anaesthesia in a rabbit model. *Br J Anaesth* 2011; 106: 540-547.
- [6] Abramov Y, Webb AR, Miller JJ, Alshahrour A, Botros SM, Goldberg RP, Ameer GA, Sand PK. Biomechanical characterization of vaginal versus abdominal surgical wound healing in the rabbit. *Am J Obstet Gynecol* 2006; 194: 1472-1477.
- [7] Sitges-Serra A, Hernández R, Maestro S, Fernández N, Girvent M, Sancho JJ. Influence of parenteral nutrition on postoperative recovery in an experimental model of peritonitis. *Clin Nutr* 2001; 20: 439-443.
- [8] Li LJ, Zheng XM, Jiang DZ, Zhang W, Shen HL, Shan CX, Liu S, Qiu M. Progress in laparoscopic anatomy research: a review of the Chinese literature. *World J Gastroenterol* 2010; 16: 2341-2347.
- [9] Kokhan VE, Bagaudinov KG, Ovakimian GS. Experience of the 7th Central Military Clinical Aviation Hospital in early diagnostics, treatment, rehabilitation, and expert evaluation of cholelithiasis in flying personnel. *Aviakosm Ekolog Med* 2003; 37: 50-51.
- [10] Kokhan VE, Ovakimian GS, Aleksakhin SA. Laparoscopic cholecystectomy in the treatment, rehabilitation and clinical health certification of the flying personnel with cholelithiasis. *Aviakosm Ekolog Med* 2000; 34: 56-58.
- [11] Schofer JM. Biliary causes of postcholecystectomy syndrome. *Emerg Med* 2010; 39: 406-410.
- [12] Beckett D. Imaging patients with "post-cholecystectomy syndrome": an algorithmic approach. *Clin Radiol* 2005; 60: 728-729.
- [13] Chadha DS, Sharma S, Sivasankar R, Kudva N, Sabhiki G, Behl A. Abdominal sonography in the medical evaluation of aviation aspirants. *Aviat Space Environ Med* 2010; 81: 965-969.
- [14] Vasil'ev Alu. The current aspects of diagnosis and expertise in flight personnel with gallstones. *Aviakosm Ekolog Med* 1996; 30: 43-44.
- [15] Bagaudinov KG, Abaraimov NV, Garilevich BA, Kokhan VE, Vasil'ev Alu, Aleksakhin SA, Fidarov EZ. Current problems in the diagnosis, treatment and prevention of cholelithiasis in flight personnel. *Aviakosm Ekolog Med* 1995; 29: 44-46.
- [16] Zhang XY, Cui GB, Ma KJ, Wang S, Wei YN, Du P, Chen BY, Guo W, Wang XJ, Huang HD, Wang JH, Huang XF, Wang CM, Wang YM, Wei JG. Sphincter of Oddi dysfunction in hypercholesterolemic rabbits. *Eur J Gastroenterol Hepatol* 2008; 20: 202-208.
- [17] Newton JL, Hudson M, Tachtatzis P, Sutcliffe K, Pairman J, Burt JA, Jones DE. Population prevalence and symptom associations of autonomic dysfunction in primary biliary cirrhosis. *Hepatology* 2007; 45: 1496-1505.
- [18] Girometti R, Brondani G, Cereser L, Como G, Del Pin M, Bazzocchi M, Zuiani C. Post-cholecystectomy syndrome: spectrum of biliary find-

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- ings at magnetic resonance cholangiopancreatography. *Br J Radiol* 2010; 83: 351-361.
- [19] Shah OJ, Dar MA, Wani NA, Robbani I, Zargar SA. Biliary ascariasis as a cause of post-cholecystectomy syndrome in an endemic area. *Dig Surg* 2004; 21: 108-113.
- [20] Abu Farsakh NA, Stietieh M, Abu Farsakh FA. The postcholecystectomy syndrome: a role for duodenogastric reflux. *J Clin Gastroenterol* 1996; 22: 197-201.