Modified Perihepatic Packing; A Creative and Beneficial Method for Management of High Grade Liver Injury

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ABSTRACT

Objective: To evaluate the efficacy of modified perihepatic packing (MPHP) in reducing the rate of re-bleeding rate after packing removal.
Methods: This was an experimental study being performed in Shiraz animal laboratory. High grade liver parenchymal injury was induced in 30 transgenic Australian rabbits which were then divided into two groups. Group A (control) included 14 and group B (experimental) comprised 16 rabbits. The animals in group A underwent standard perihepatic packing (SPHP) and those in group B were subjected to MPHP. Re-bleeding was assessed and compared between the two groups, after removal of perihepatic packings.
Results: There was no significant difference between two study groups regarding baseline and perioperative characteristics. Rabbits in group A had significantly lower rate of postoperative re-bleeding compared to those in group A (57.1% vs. 12.5%; p=0.019). The mean bleeding volume was also significantly lower in group B compared to group A (76.88 ± 22.12 vs. 98.93 ± 33.8 mL; $p<001$). Although the survival rate was higher in group A compared to group B (93.8% vs. 78.6%) but the difference was not statistically significant (p=0.315).
Conclusion: MPHP is a simple and safe procedure for surgical management of high grade liver parenchymal injury concomitant with severe loss of glisson's capsule. This procedure significantly decreases re-bleeding after packing removal in comparison with SPHP.

Keywords: High grade liver injury; Perihepatic packing (PHP); Modified perihepatic packing (MPHP)

Introduction

Trauma is one of the most common life-threatening injuries and among the most prevalent causes of death worldwide. In this context, the abdominal trauma has always been a complicated problem of patients. The trauma to the liver, whether penetrating or blunt, is considered as one of the most common abdominal injuries, which leads to death or high morbidity. Conservative management of patients with trauma to the liver has evoked remarkable interest and led to progressive achievements in recent years. The indications for operative management of liver injuries are laparotomy for penetrating injury, patient's instability, or concomitant internal injury [1]. Those with major hepatic injury, however, often develop hemodynamic instability and therefore operation would be the method of choice for them. Among various methods of liver bleeding control, perihepatic packing has become the most successful procedure. This method is performed to achieve quicker hemostasis by placing surgical pads

around the liver to pack it, so that the wound will be compressed against the pads and between the anterior chest wall, diaphragm, and retro peritoneum [1].

The conventional surgical procedures for management of liver injury are midline incision, primary packing, clot removal and bleeding control. The bleeding of small injuries can be managed by surgical methods and medications. These include finger fracture [1,2], administration of inappropriate haemostatic agents, suturing, fibrin derivatives and in more complicated cases, lobar resection [1,3,4] and liver transplantation [1,5,6]. Unlike low grade liver trauma, the management of high grade (grade III to V) liver trauma is a challenging problem for many trauma surgeons, especially in patients with coagulopathy, acidosis and hypothermia. In presence of high grade liver injury, the patients are usually hemodynamically unstable. Furthermore, manipulation of liver by the surgeon may exacerbate the patient`s condition. In these situations damage control surgery (DCS) is the most reasonable approach to cope with liver trauma [1,2].

Perihepatic packing (PHP) has previously been assessed as a method for DCS in liver trauma. The studies revealed lesser complications when PHP is used appropriately [1,3,5,7,8]. The most important goal of this method, as well as other DCS procedures, is the correction of acidosis, coagulopathy and hypothermia [5]. But there is no study which clearly states the indications of perihepatic packing and its proper duration. Close observation after primary packing, and the need for an experienced surgeon to manage the second surgery are the other shortcomings of this method [3,8]. But because of its simplicity, PHP is available and widely used. In this method, the entire liver surface is packed all around [5] after resection of as many ligaments as needed to immobilize the liver. The patient will be monitored in ICU after the surgery. After correction of acidosis, coagulopathy and hypothermia the patient will undergo the second surgery to remove perihepatic packs.

Some of the complications of this method are sepsis, vascular collapse and re-bleeding after packs removal [3]. Hemobilia and bilovenous fistula are other rare complications of PHP [1,2,9,10]. Packing duration is a controversial issue. Theoretically, 24 to 48 hours is needed to correct acidosis, coagulopathy or hypothermia. On the other hand, the longer the packing time, the higher the risk of sepsis. Less than 7% of complications of liver trauma surgery are due to bleeding. Abdominal swelling, detection of low blood pressure and high pulse rate are signs of re-bleeding. In this condition stable patients can be treated with percutaneous procedures but unstable cases should undergo open surgery to stop bleeding.

The mortality rate of traumatic liver injury is about 10-15%. Type of injury and damage to adjacent organs are factors affecting the mortality rate. Mortality rate of a penetrating trauma to liver only is about 1%, whereas that of hepatic blunt trauma could be as high as 20% [1,2,9,10]. Furthermore, when the liver is the only injured organ, the mortality rate is about 10%, but the injury of two other organs beside liver, increases the mortality rate to about 70% [9,10]. The aim of this study is to evaluate the efficacy of modified perihepatic packing (MPHP) in reducing the rate of re-bleeding rate after packing removal.

Materials and Methods

Animals

All animals were chosen, prepared and handled according to the Ethics committee guidelines. Having approved by a statistician and with reference to relevant studies, 32 genetically homologous, healthy white Australian rabbits (weighing about 10 kg) of either sex with hemodynamically stable condition were obtained from an animal breeding center of Shiraz University of Medical Sciences, as a pilot study, considering ethic limitations imposed on many animal experiments for medical reasons In Iran. However, the bilobar, right-lobe dominant liver of these rabbits was comparable with those of humans, and similarities in consistency, shape, anatomic relations and perihepatic ligaments. Furthermore, the vascular structures and liver segments were also similar to human liver, in number and anatomy.

The exclusion criteria were unhealthy general appearance, abnormal weight, pregnancy, unstable hemodynamics and death during the first surgery or one hour post-surgery. Two animals were later excluded from the study after laparotomy, because of the operation room being unprepared for one rabbit and the pregnancy for another. The remaining 30 rabbits which met the inclusion criteria had become nil per os (NPO) since 6 hours prior to the operation.

Surgical procedure

After a preoperative visit by a vet, the animals were anesthetized with Terazol (6 mg) and Glycopyrrolate (0.1mg), getting intubated and receiving intravenous maintenance fluid followed by close monitoring for blood pressure, pulse rate and O_2 saturation during and one hour post-surgery. The hemodynamic status was intermittently monitored for 48 hours post-surgery. For fluid management, a venous access was established under general anesthesia through a triple lumen (5Fr) placed in external jugular vein. After insertion of the triple lumen, 100-200 ml

dextrose saline was administered initially, and 10-20ml/kg/hr of the same solution were infused as the maintenance fluid.

After the routine prep and drape, the rabbits underwent a midline abdominal incision. To expose the liver, 2 or 3 lowest right ribs were removed and all the perihepatic ligaments hindering access to all surfaces of the liver were cut but vascular structures were preserved. After the exposure of the liver in the surgery field, it was covered with some sterile gauze. The weight of gauze soaked and saturated with blood after induction of trauma to the liver determined the pretreatment blood loss. The injury was induced by a laceration, made with a clamp, and equivalent to the grade IV to V liver parenchymal injury, according to American college of surgeons of trauma classification. The clamp penetrated deeply in the parenchyma of the right lobe of the liver and was displaced toward the inferior vena cava (IVC) to form a 4 in 5 cm star-shaped wound. After primary bleeding control, the wet gauze around the liver was removed, blood clots were collected and surgery field blood was suctioned. These three components determined the pretreatment amount of bleeding. After 15 seconds of bleeding, the rabbits were divided into two groups by flipping a coin. Bleeding was controlled primarily by direct pressure of the surgeon`s finger. In group B (case group), the liver injury was managed by MPHP. The surface of the injured liver was covered with a haemostatic agent (surgicel) followed by wrapping up the liver with a water proof, nonstick plastic. The entire surface of the liver was covered except the liver hilum. The liver was then packed counterclockwise from 6 to 5 to spare the hilum. After MPHP, the surgery field was observed for 15 minutes to detect bleeding. In cases with no bleeding, the abdomen would be closed. Finally, after one hour of observation, the dead rabbits were excluded from the study whereas the living animals were transported to their cages. During the surgery, the animals' blood pressure was maintained above 70 mmHg with fluid administration through the IV access.

In group A (control group), injury induction, primary bleeding control with pressure of the surgeon`s finger and measuring pretreatment blood loss were the same as group B. Contrary to group B, the liver injury was managed with counterclockwise packing of the liver without application of surgical or covering the liver with water proof plastic. The post-op observation and the criteria to transport the animals to their cages were the same as group B.

In both groups, after initial surgery, the surviving animals were observed for 48 hours. The dead animals in the cage period underwent an exploratory laparotomy to detect the cause of probable bleeding. These animals were included in the death group due to re-bleeding.

The survivors of the first surgery underwent the second operation after 48 hours for assessment of post-treatment bleeding and detection of possible re-bleeding. Post-treatment bleeding was considered as the amount of blood loss (clots, suctioned blood, and wet pads weight) detected in the second surgery after opening of abdominal cavity. To assess re-bleeding, the liver was observed and watched closely enough to detect any hemorrhage after removal of the packs. Subsequently, to make sure that there was no hemorrhage, the liver was rinsed with normal saline very gently for 15-30 minutes and the injured site was observed for fresh re-bleeding. Totally, detection of 5ml or more fresh blood in the field was considered as significant re-bleeding. In our study, total bleeding (TB) was determined by summation of blood loss during pre-treatment, post treatment and re-bleeding. After the second surgery, the rabbits were sacrificed according to Ethics committee guideline.

Statistical analysis

Normal distribution of two groups was assessed with Kolmogorov-Smirnov test. *P*-value was calculated with Fisher's and chi-square tests for re-bleeding rate after the surgery, total bleeding volume and survival rate. The average amount of total bleeding in two groups was also compared suing independent t-test. A 2-sided *p*-value less than 0.05 were considered statistically significant.

Results

A total of 32 white Australian rabbits met the inclusion criteria while 2 were further excluded from the study. Thus the final number of rabbits was 30 being randomized to two study groups (group A= 14 rabbits and group B=16 rabbits). The study

Table 1. Comparison of study outcomes between those rabbits that underwent standard (group A) or modified (group B) perihepatic packing.

	Group A (n=14)	Group B (n=16)	*p*-value
Survival Rate (%)	11 (78.6%)	15 (93.8%)	0.315
Re-bleeding Rate (%)	8 (57.1%)	2 (12.5%)	0.019
Bleeding amount (mL)	98.93 ± 33.8	76.88 ± 22.1	<0.001

groups were comparable regarding the baseline and perioperative characteristics.

The study outcomes are summarized in Table 1. Although the survival rate was higher in group B compared to group A (93.8% vs. 78.6%) but the difference was not statistically significant (*p=0.315*). The mean bleeding volume was significantly lower in group B compared to group A (76.88 ± 22.12 *vs.* 98.93 ± 33.8 mL; *p<0.001*). Further bleeding from the injury site after removal of packing, as the main variable of this study, was also measured and evaluated in both groups. Of all 30 rabbits included in the study, 10 (33.3%) had bleeding after removal of wound packing, 2 (12.5%) out of 16 rabbits in group A. In control group, out of 14 rabbits, 8 (57.1%) had significant re-bleeding after removal of packing. The incidence re-bleeding was significantly higher in group A compared to group B (*p=0.019*).

Discussion

This study showed that renewed bleeding after packing removal after 48 hours was significantly less in case group packed with modified dressing perihepatic packing (MPHP) than control group with standard, perihepatic packing (SPHP) gauze. Also there was a significant difference in total amount of bleeding in two groups, about 97 mL in control group and 77 mL in case group. However there was no significant difference in the mortality between two groups.

Increasing application of DCS, an acknowledged method in management of civil trauma, has led to lower mortality rate among the trauma victims [9-15]. In trauma patients, 82% of deaths was due to uncontrollable bleeding of which 50% related to liver laceration hemorrhage [5,6,11]. The control of liver hemorrhage utilizing packing methods is commonly used in level 1 trauma centers and varied from 5% to 36% in different studies.

Trauma teams and surgeons are paying more attention to this method for controlling intractable bleeding from traumatized liver [2,5,11,16]. The control of hemorrhage from liver trauma by packing techniques using surgical pads, along with applied pressure from surgeon's hand has dramatically improved early resuscitation procedure in trauma patients as well as decreasing the incidence of complications and better correction of hypothermia, acidosis and coagulopathy [9-11]. Indeed, some studies have shown that correction of these conditions requires about 12 to 36 hours which is the time needed for removal of packing [3-5]. A study performed by Caruso et al showed that removal of packing in the first 36 hours will increase the possibility of recurrent bleeding which

could be due to manipulation of unstable clots [6].

Utilization of packing method is not free of any inadvertent and unpleasant outcomes and many studies have shown some adverse effects such as inability to control bleeding by packing methods, increasing the rate of liver parenchymal necrosis due to pressure on blood supplies, increasing the rate of abdominal abscess formation and, more importantly, boosting the risk of rebleeding in second surgery. Also the application of packing methods was shown to have some adverse effects on the pulmonary and cardiovascular functions [3,4,17,18], such as inferior vena cava (IVC) collapse, reduction in the amount of blood delivered to the liver and decrease in venous return claimed in the study reported by Meldrum and colleagues [17]. However these consequences barely need early packing removal [17]. In other studies, sepsis, IVC collapse and renewed bleeding have been mentioned as major adverse effects of such packing methods. For Instance, in one study performed by Nicol *et al.*, [3] liver packing could have some detrimental effects such as sepsis, IVC collapse and abdominal compartment syndrome. They also mentioned that IVC collapse and sepsis do not seem time related, where abdominal compartment syndrome happens mostly in first 12 to 24 hours [3].

Notably, the efficiency of animal models for evaluating severe liver trauma, stable packing methods and assessing the adverse effects of these methods has been proved previously [18,19].

The tendency to finding and producing haemostatic materials and substances for controlling bleeding in severe trauma to solid organs has dramatically increased in recent years. These materials mostly consist of fibrin derivatives, and their production is difficult, time consuming and costly [3,20]. These materials also have to be used under certain environmental circumstances to achieve their maximum performance. However, such settings rarely exist in trauma scenes and emergency conditions [12]. Also the use of haemostatic powders has been assessed in trauma patients with injury to solid organs and bleeding [11]. But utilization of multilayer perihepatic packs has recently been considered for management of such trauma injuries, especially severe trauma to the liver and its consequent hemorrhage [13,14,19].

A well-known type of fibrin derivatives which causes rapid haemostasis is called *Chitosan*. Utilization of chitosan for liver packing has led to successful control of hemorrhage in animal models with severe trauma to the liver and unstable condition. However, the possibility of causing adverse reaction with human tissue and difficulty in retaining the material on the surface of injured liver or wound

against bleeding pressure, are the disadvantages of such powdery materials [19]. Buchicchio *et al.*, [19] achieved a remarkable decrease in mortality by using chitosan in swine models with hypothermia and acidosis after trauma grade V to the liver. Recently the application of a special type of bondage, rapid dressing haemostate (RDH), was shown to cause rapid haemostasis in patient with bleeding due to solid organ injury, and used in Afghanistan by the US army with good results [13]. All three aforementioned methods, and in particular fibrin derivatives, for bleeding control are very expensive.

Jewelewicz *et al.*, [18] compared the standard packing method with a new technique called Miami-modified rapid deployment hemostat. Their study included two groups of pigs made hypothermic with coagulopathic disorders by replacement of 45% of their total blood volume with Hextend solution. Re-bleeding and mortality rates were significantly lower in the case group after removal of modified packing.

In our study modified dressing perihepatic pack (MPHP), as a simple, achievable, practical and cost-effective method is introduced for bleeding control in liver injuries. Wrapping the whole liver with a plastic layer, direct application of haemostatic materials to the laceration and the packing on the plastic layer make packing method very beneficial and highly successful without any unpredictable adverse effect [14]. It seems that using of this method of packing in patients with hypothermia and coagulopathic disorders would lead to an overall decrease in the amount of bleeding and reducing the amount of fluid required for resuscitation, although, This needs to be re-evaluated in further studies.

This kind of study had not been performed on animal models previously. Indeed, primary model of this sort of pack was first introduced and used by Stizman and colleagues [14] in a study on five patients. Compared with that study, due to unavailability of non-stick organic bowel pack which is a sterile and waterproof bag, we used folly bags instead. Folly bags are also sterile, waterproof and flexible to be formed in any shape. Since imposition of excess weight on liver packing methods leads to a decrease in liver blood supply and an increase in liver parenchymal necrosis and mortality, some changes were made in liver wrapping with these folly bags. This was done by cutting and removing a part of folly bag which covered the liver vessels inlet to prevent the pressure effect on vessels and decrease in blood supply. Also using pressure applied by surgeon's hand in our model led to absence of bleeding in injury site and better positioning of pack on the laceration site.

The sole use of fibrin packs has been assessed in some other investigations, such as a study carried out by Parks *et al.* which did not lead to lower mortality and better survival in animal models [11]. But, the inclusion of fibrin derivatives like Surgicel in our model was only a part of the whole packing procedure. Also in our method, the use of plastic layer will impart better effect of fibrin material on liver laceration and a positive pressure effect on the liver to cease bleeding. Also it will decrease the possibility of hemorrhage after removal of packs since unstable clots on the laceration will not be manipulated during packs removal.

We note some limitation to our study. Unfortunately, our animal lab was not properly equipped to measure blood gas status, body temperature, severity of acidosis or coagulation condition of our rabbits. These factors, if measured, would probably provide additional advantages of this method of packing compared to the conventional procedures. These parameters along with administering high amount of fluid needed for resuscitation are risk factors for mortality after liver injury. However, such restrictions do not influence our study, because the total bleeding is an independent factor to determine mortality rate.

In conclusion, utilization of MPHP method seems to lead to a significant decrease in the liver bleeding and also re-bleeding after packing removal. But further studies are required to complete our results and directed toward determining the effects of this modified packing method on the survival, decreasing the mortality and adverse effects. We recommend this method as a simple, rapid and achievable procedure for management of bleeding in patients with trauma to the liver and are used as a substitute for the conventional SPHP.

Conflict of Interest: None declared.

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