ORIGINAL PAPER

UROLITHIASIS

High-power laser lithotripsy – do we treat or harm? Histological evaluation of temperature effects in an in vivo study with thulium fiber laser

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Introduction The aim of this study was to evaluate the possible histopathological alterations that occur in the kidneys due to a continuous temperature increase above 43°C for one hour of lithotripsy using a newly introduced thulium fiber laser (TFL).

Material and methods Two female pigs were used. After the insertion of a 9.5/11.5 ureteral access sheath, flexible ureteroscopy and laser lithotripsy for one hour were conducted. A TFL laser with a 200-µm fiber was used. The power setting used was 8 W (0.5 J × 16 Hz). A K-type thermocouple was inserted and fixed in the upper calyx of the right porcine kidney to record the temperature in the pelvicalyceal system during the laser activation. Second-look flexible nephroscopy followed by nephrectomy and pathohistological evaluation of the operated kidney was performed one week after the procedure in the first pig and 2 weeks after the surgery in the second pig.

Results Flexible nephroscopy did not reveal significant differences between the 2 porcine kidneys. Nevertheless, the histopathological report demonstrated severe alterations in the kidney of the first pig. Mild changes were reported in the kidney of the second pig. A significant improvement in inflammation and haemorrhagic lesions was demonstrated when comparing the 2 kidneys.

Conclusions The difference demonstrated between the 2 kidneys based on the histopathological report shows that the healing process is capable of improving severe to mild alterations within a one-week time frame. Two weeks after the surgery, only minor changes were observed, suggesting that even temperature increases above the threshold can be tolerated regarding renal damage.

Key Words: thulium fiber laser ‹› temperature ‹› laser ‹› lithotripsy ‹› histology

INTRODUCTION

The recent introduction of the new thulium fiber laser (TFL) in urolithiasis management has created a new field of investigation regarding the comparison of these tools. TFL technology has been shown to be superior to the Holmium:YAG (Ho:YAG) laser in some aspects, and its characteristics make it a promising surgical solution [1]. In vitro studies have demonstrated that the TFL can offer a better ablation rate and the same safety profile regarding the thermal effect in comparison to the Ho:YAG laser [2, 3]. In addition, in a comparative pre-clinical study conducted by Andreeva et al., it was reported that TFL demonstrated less retropulsion [4]. The existing data regarding the thermal effect of laser activation on renal tissue are still insufficient. The effect of TFL activation on the kidney in terms of a lithotripsy procedure is yet to be investigated. Previous studies suggest that the temperature inside the kidney in terms of safety should be less than 43°C because this is the crucial threshold for protein denaturation of the urinary tract [5]. Nevertheless, the real thermal effect of TFL activation on the histopathology of the kidney and the possible healing following the temperature rise has not been investigated. The current in vivo experimental study was designed to evaluate the possible histopathological alterations that occur in the kidneys due to a continuous temperature increase above 43°C caused by laser activation using TFL.

MATERIAL AND METHODS

Preparation of pigs and operative set-up

The study was carried out in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. The pigs were managed according to the available veterinary protocols. Female pigs were selected because endoscopic access to the pelvicalyceal system is easier to perform. The ureteral catheterization was conducted as described in a previous study of our experimental team [6]. After the insertion of the ureteral catheter, each pig was moved into the prone position. A small skin incision was implemented for the insertion of a thermocouple into the kidney. The bull's eye technique (fluoroscopy-guided technique) was used for the direct insertion of the K-type thermocouple in the upper calyx of the right kidney. A guidewire was again inserted through the ureteral catheter. The ureteral catheter was then replaced by a dual-lumen ureteral catheter (Cook Medical, Cook Ireland Ltd., Limerick, Ireland), which was used for the insertion of a second guidewire inside the collecting system. The dual-lumen ureteral catheter was retracted, and one of the guidewires was held as a safety wire while the other one was used for the insertion of a 9.5/11.5 ureteral access sheath (Flexor® Ureteral Access Sheath with AQ® Hydrophilic Coating, COOK Medical, Cook Ireland Ltd., Limerick, Ireland), which was used to facilitate the insertion of a Pusen PU3022a flexible ureteroscope (Zhuhai Pusen Medical Technology Co., China). Manual pump irrigation (COOK Medical, Cook Ireland Ltd., Limerick, Ireland) was used for both surgeries at a rate of one pump every 3 seconds. The irrigation bags were placed one meter above the operating table and were kept at room temperature (approximately 25°C), the same as in real-life circumstances in our department. For controlled temperature generation we used a TFL laser (Quanta Fiber Dust, Samarate, Italy) with a 200-μm fiber. The power settings used were 8 W (0.5 J × 16 Hz). This combination was preferred after in vitro testing, being the most efficient power setting for the maintenance of the temperature at specific limits. Two flexible ureteroscopies on the right kidneys of 2 different pigs were conducted. The laser activation time depended on the temperature developing in the porcine renal pelvis during the procedure. The time from the initial laser activation until the last laser activation was 60 minutes. The intrarenal fluid temperature during both ureteroscopies was between 44°C and 46°C. No nephrostomy or pigtail drainage was applied in either of the pigs. After each surgery, the pigs were gradually aroused and monitored until their recovery and kept in their individual lodgings. On the 7th post-operative day, the first pig (pig A) was again anaesthetised. A right kidney renoscopy was conducted following the same operational technique as mentioned above. After the renoscopy, the pig was immediately sacrificed, and a right nephrectomy was conducted. The second pig (pig B) underwent the same procedure on the 14th postoperative day. The kidneys underwent histopathological evaluation. The parameters evaluated were the creation of fibrotic tissue and scars, the presence of haemorrhagic injuries or necrotic tissue, and signs of inflammatory reaction.

RESULTS

Postoperative period

Both pigs recovered normally from the anaesthesia. Broad-spectrum antibiotics were added to their meals for the first 5 postoperative days. The administration of non-steroidal anti-inflammatory drugs was avoided so as not to affect the histopathological report.

Flexible ureteroscopy

The right kidney renoscopy of pig A demonstrated the presence of mildly hyperplastic mucosa with the presence of fibrotic tissue, probably due to the direct laser activation. Mildly hyperaemic areas were formed inside the pelvicalyceal system, demonstrating signs of a typical inflammation image. The endoscopic images from the renoscopy of pig B presented some differences in comparison to those of pig A.

The hyperplasia of the mucosa and some fibrotic areas could be seen, although the inflammation signs were fewer and were more sparsely located.

Figure 1. *Macroscopic image of the right kidney of the pig A. Mucosal redness and oedema of the renal pelvis are demonstrated.*

Microscopic evaluation

The removed kidneys underwent hematoxylin and eosin staining for further evaluation by the pathologist. The report of the first porcine kidney (pig A), which was sent on the 7th post-operative day, demonstrated severe alterations (Figure 1). Haemorrhagic areas, detachment of the urothelium, fibrin deposition, oedema, and mild inflammation in the lamina propria were observed (Figure 2). The histopathological report of the second porcine kidney (pig B), which was sent on the 14th post-operative day, revealed only minimal changes such as mild oedema in the lamina propria. Haemorrhagic lesions were present but to a lesser extent in comparison to the first porcine kidney (Figure 2).

DISCUSSION

The TFL is a newly introduced technology that is increasingly being adopted by endourologists [7]. The theoretical advantages of this device seem innovative. Nevertheless, crossing the line between safety and effectiveness can be easy, and data for the optimal use of the new TFL laser systems are still insufficient. The aim of this in vivo experimental study was to provide more information about the effect of a prolonged temperature increase inside the porcine pelvicalyceal system on the kidney for one hour. The temperature was maintained at between 44°C and 46°C throughout the surgery. The 2 pigs were sacrificed 7 and 14 days after the initial experiment. The endoscopic image performed before the nephrec-

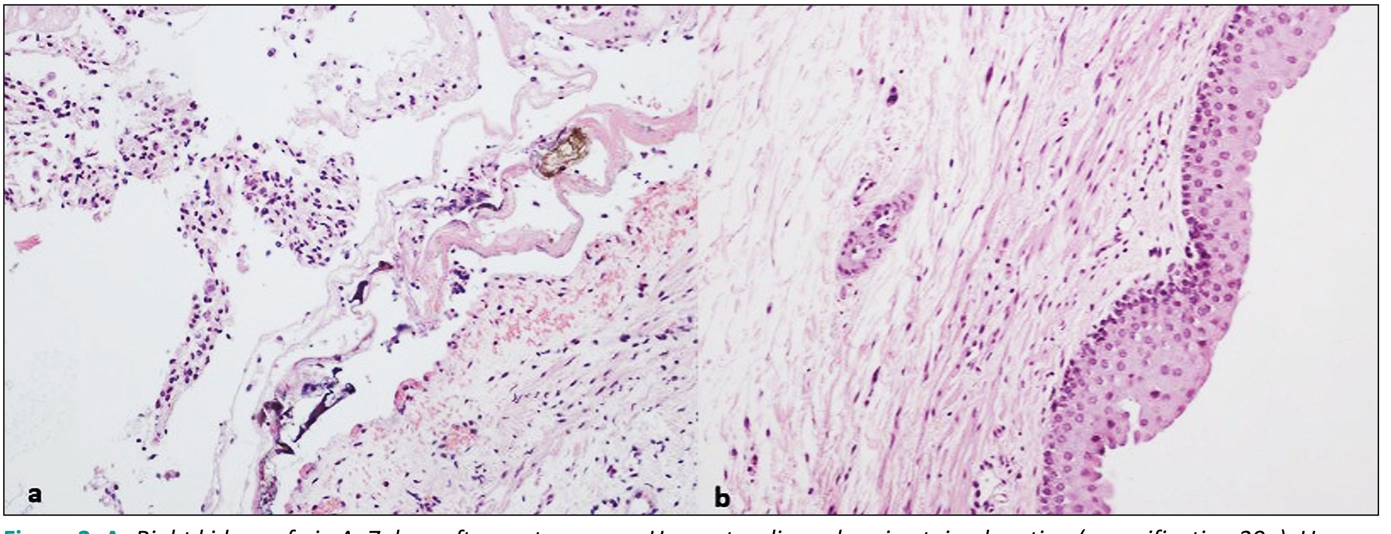

Figure 2. A. *Right kidney of pig A, 7 days after ureteroscopy. Haematoxylin and eosin-stained section (magnification 20×). Urothelial detachment, haemorrhage, fibrin deposition, oedema, and mild inflammation in the lamina propria are demonstrated.*
B. *Right kidney of pig B, 14 days after ureteroscopy. Haematoxylin and eosin-stained section (magnification 20×). Mild oedema in the lamina propria is demonstrated.*

tomy was not significantly different between the 2 kidneys, although the histological report demonstrated more hazardous characteristics on the kidney of pig A in comparison to the kidney of pig B. The histopathological report revealed that the kidney of pig A had severe alterations. The healing process was adequate, and these changes were mild on the second porcine kidney after one week.

The TFL operates between wavelengths 1940 nm and 2013 nm [8]. Thus, the optical penetration depth in water is shorter than that of the Ho:YAG laser. These data confirm that the stone and tissue ablation thresholds are lower for the TFL [9]. The increased efficiency regarding lithotripsy could be hazardous when it comes to tissue. This was also observed during a recent prospective study conducted by Mahajan et al. [10]. The authors reported a reduction of operation time when using the TFL in comparison to the Ho:YAG laser during mini percutaneous nephrolithotomy. However, the TFL was associated with more self-limited haematuria. In contrast to these data, Doizi et al. demonstrated in an experimental ex vivo study that tissue penetration with the Ho:YAG laser was greater in comparison to the TFL [11].

Heat generation is unavoidable during laser activation. Available data demonstrate that denaturation of urinary tract proteins begins at a temperature of 43°C [5]. Nevertheless, 54°C is considered the threshold for the necrosis of coagulative tissue in the porcine kidney [12]. The most efficient and safest combination of laser settings and parameters for laser activation inside the pelvicalyceal system has been investigated in many in vitro and in vivo studies [13, 14]. Regarding the Ho:YAG laser, recent studies have demonstrated that high-power laser lithotripsy can be conducted safely if the irrigation flow is sufficient [6, 15]. Similarly, it has been shown that a decrease in the irrigation flow and the absence of a ureteral access sheath during TFL activation can increase the temperature to levels that possibly cause renal thermal damage [3, 16]. Higher frequency settings are related to ureteral thermal damage, especially when used by inexperienced surgeons [17]. Despite numerous studies conducted in this field, further investigation is needed to clarify the safety of these continuously developing laser devices.

To our knowledge, the current in vivo study is the first to evaluate the effect of prolonged activation of a TFL inside the collecting system on a porcine kidney, maintaining a relatively steady temperature above the protein denaturation threshold for the whole procedure. As with every experimental study, ours is also associated with limitations. The heatsink effect of renal blood flow is present in mechanically ventilated animal under general anaesthesia. In the current experimental study, the setup was identical to the clinical setup. In addition, the instruments used were the same as those used for real cases. Nevertheless, the temperature was measured inside the renal pelvis, and the temperature alterations in different calyces were not evaluated. The laser activation was carried out in the pelvis to avoid direct contact with the laser fiber with the mucosa, but some minor injuries occurred accidentally. Another possible limitation is the absence of stones in the collecting system. Nevertheless, the absence of stones and dust was also an advantage because there were no visibility problems, and the thermocouple tip was visible throughout the operation. In addition, urolithiasis is related to inflammatory reactions inside the pelvicalyceal system, which might increase the vulnerability of the urothelium to possible thermal injury. Despite these limitations, our study provides valuable data about the possible kidney healing processes following intrarenal laser lithotripsy.

CONCLUSIONS

Intrarenal lithotripsy using different laser devices is potentially harmful, causing renal thermal damage. Nevertheless, the results demonstrated by our in vivo study show that 2 weeks after flexible ureteroscopy with temperatures above the protein denaturation threshold, minor alterations were observed in porcine kidneys. The different results demonstrated by the histopathological report reveal that after one week the severe alterations can improve significantly, and 2 weeks can be required for the kidney to return to normal status.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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