Contributions to the study of natural orifice translumenal endoscopic surgery: feasibility, immunological impact, limitations

- THESIS RESUME -

PhD Adviser:
Prof. Univ. Dr. Ion Georgescu

PhD Candidate:
Pătraşcu Ștefan

Craiova
2011
Table of contents

- GENERAL ASPECTS -

1. History .............................................................................................................. 2
   1.1. Nosology ................................................................................................. 2
   1.2. Surgery: initial steps ..................................................................... 2
   1.3. Minimal invasive surgery .............................................................. 4
      A. Laparoscopic surgery .................................................................. 4
      B. Interventional endoscopy ............................................................. 7
      C. Birth of a concept: N.O.T.E.S. ..................................................... 8
      D. N.O.T.E.S. – from experiment to practice ..................................... 9

2. Experimental models in N.O.T.E.S. .......................................................... 12
   2.1. Importance of the experimental setting ....................................... 12
   2.2. Animal models .................................................................................. 12
   2.3. Swine model: particularities .......................................................... 13

3. Prevention of peritoneal contamination .................................................. 16
   3.1. Sterilization or high level disinfection ........................................ 17
   3.2. Preoperative preparation of the access organs ............................. 19

4. Endoscopic platforms used in NOTES: drawbacks and solutions ......... 23
   4.1. Exposure and retraction ................................................................ 23
   4.2. Endoscopic stability ...................................................................... 24
   4.3. Adapted platforms ........................................................................ 25
   4.4. Endoscopic accessories ................................................................ 27
   4.5. Status of translumenal robotic surgery (R-NOTES) ................. 28

5. The transluminal access ............................................................................. 31
   5.1. The transgastric endoscopic access ............................................. 31
5.2. The transvaginal route ................................................................. 34
5.3. The transcolonic and transrectal access ..................................... 35
5.4. Transvesical NOTES ................................................................. 38
5.5. Transesofagian and transtraheal approach ............................... 40
5.6. Other types of natural orifice surgery
   – laparoscopic translumenal surgery ............................................... 41
      A. The transombilical approach .................................................... 41
      B. The laparoscopic transvaginal approach – natural
         orifice laparoscopic surgery ............................................... 41
      C. Hybrid N.O.T.E.S. ................................................................. 42
5.7. N.O.T.E.S. experience on humans .............................................. 43
6. Closure of the translumenal access site ........................................ 44
7. Physiological response in N.O.T.E.S. ............................................. 49

- PERSONAL RESEARCH -

1. Aim and objectives ........................................................................ 52
2. Material .......................................................................................... 55
   2.1. Experimental laboratory in N.O.T.E.S. .................................. 55
   2.2. Study groups .............................................................................. 56
3. Methods .......................................................................................... 58
   3.1. Preoperative training ................................................................. 58
   3.2. Design of the study .................................................................. 58
   3.3. Feasibility .................................................................................. 61
      A. Preoperative settings ............................................................... 61
      B. Anaesthetic control ................................................................. 62
      C. Surgical intervention .............................................................. 63
      D. Postoperative follow-up .......................................................... 72
      E. Necropsia ................................................................................ 72
      F. Gastric resistance testings ......................................................... 74
      G. Histologic protocol ................................................................. 75
3.4. Comparative study of the inflammatory response ........................................ 76
   A. IL 1β assay ........................................................................................................ 77
   B. IL 6 assay ........................................................................................................ 78

3.5. Statistical analisys ...................................................................................... 80
   A. Data collection ................................................................................................... 80
   B. Statistics ............................................................................................................ 81

4. Results ............................................................................................................... 84
   4.1. Feasibility of N.O.T.E.S. ........................................................................ 84
       A. Translumenal access ...................................................................................... 84
       B. Intraoperative data ...................................................................................... 88
       C. Closure of the acces site ............................................................................ 94
       D. Intraoperative cardiorespiratory response .............................................. 95
   4.2. Postoperativ evolution ............................................................................... 97
   4.3. Necropsy results ....................................................................................... 99
   4.4. Evaluation of gastric resistance .............................................................. 104
   4.5. Histopatologic data .................................................................................. 104
   4.6. N.O.T.E.S inflammatory results ............................................................ 106

5. Discutions ......................................................................................................... 111
   5.1. Current challenges .................................................................................. 113
   5.2. Advantages ............................................................................................... 126
   5.3. Acceptability ............................................................................................. 130
   5.4. Perspectives ............................................................................................... 130

6. Conclusions ...................................................................................................... 133

BIBLIOGRAPHY ................................................................................................. 136
Key words: NOTES, natural orifice, endoscopy, laparoscopy, inflammation.

Introduction

For more than two decades the surgical world is finding itself in a continuous change. As a notable example natural orifice translumenal endoscopic surgery appears to be a new and innovative approach, combining interventional endoscopy and laparoscopy in order to annulate the abdominal parietal trauma. As a more recent concept, natural orifice translumenal endoscopic surgery came with the revolutionary idea of accessing closed cavities of the body (peritoneal or thoracic) through natural orifices.

As in laparoscopy, the field of NOTES rapidly expanded, in just a few years, from simple peritoneoscopy to more complex operations like splenectomy, sigmoidectomy etc. Despite the early success, the translumenal endoscopic surgery comes with several problems that need to be solved before effective clinical implementation. An effective closure, maintaining spatial orientation, multitasking platforms and training were identified as potential barriers by the NOSCAR group since 2005.

PERSONAL CONTRIBUTION

Aim of the study

This work aims to investigate the feasibility of the endoscopic access through natural orifices - transgastric and transvaginal for different surgical procedures with various degrees of difficulty, as well as the efficiency of a novel endoscopic closure device. We have also assessed the perioperative immuno-inflammatory response in N.O.T.E.S. and compared it with laparoscopy.

Methods

1. Preoperative care

Our study included a total of 28 subjects. This experimental research was conducted in accordance to the European and national legislation for animal use (directive 86/609/EEC) and the protocol had the approval of the local Ethics Committee. Five days
before the planned procedure the animals were placed in quarantine in special rooms, with adequate space and controlled temperature and light cycles, in our University’s new Animal Facility. The pigs were removed from woodchip bedding 3 days later in order to avoid gastric fitobezoars, and placed into separate cages, with access to a liquid diet. 24 hours before surgery animals were fasted with a 6 hours restriction from water.

For the transvaginal group food and water was provided ad libitum, the only precaution taken was total alimentary restriction 12 hours before the surgical intervention. For an adequate decontamination of the access site, repeated vaginal irrigation with diluted 10% Polyiodine solution (Polyiodine, Hexi Pharma Co., Bucuresti, Romania) was performed preoperatively.

2. Intraoperative protocol

Every animal was monitored daily for signs of distress by qualified personnel. The surgical interventions were performed by a mix group of surgeons, endoscopists, veterinary technicians and anesthetists. Ten pigs had transgastric endoscopic surgery performed, another ten were operated by laparoscopy and four animals underwent transvaginal endoscopic operations with laparoscopic support (hybrid translumenal-laparoscopic procedures). The need for a hybrid approach was due to the lack of advanced technological devices, adapted for similarly complex procedures as in laparoscopic surgery. The transgastric NOTES procedures started with a normal esogastroscopy to evaluate the integrity of the stomach and to find an adequate puncture site. The translumenal access consisted in creating, after local gastric lavage with sterile saline solution, of a 2-3mm long incision in the anterior gastric wall with the needle knife. The guidewire was inserted and, finally, the endoscopic balloon was inflated in order to obtain an orifice large enough to allow the passage of the endoscope into the peritoneal cavity. The peritoneoscopy evaluated both supra and submezocolic floor, the exposure being granted by the endoscopic forceps and by placing the operating table at different angles, in Trendelemburg/anti-Trendelemburg position with a left-right tilt.

The actual intervention in the transgastric group was unilateral or bilateral adnexectomy with oophorectomy, achieved with the help of a polipectomy snare. Local haemostasis was ensured by endoscopic monopolar diathermy. The specimen was
extracted translumenally, after which the gastric access site was either closed with an OTSC™ clip or left open.

In the transvaginal NOTES group the animal was placed in a 30 ° Trendelemburg position and a 1.5 cm long posterior colpotomy was created. The endoscope was advanced through the transvaginal incision into the peritoneal cavity and a thorough examination of the intraabdominal organs was performed in the same manner as in the transgastric group. The gallbladder was identified and the Callot’s triangle was exposed with the help of a laparoscopic trocar. After endoscopic dissection, the cystic artery and duct were clipped using a laparoscopic multiple clip applicer and cut. The gallbladder was separated from the liver bed using the needle-knife and the polipectomy snare, and extracted transvaginally. At the end of the intervention the colpotomy was closed with interrupted 3-0 monofilament polydioxanone (Marisorb violett, Catgut GmbH, Germany).

3. Postoperative follow-up and main parameters followed

Specific procedural time and pathological variations of biologic parameters (arterial blood pressure, heart rate, O2 saturation) were recorded. The immune response was assessed in the transgastric group by successive determinations of IL1β and IL6 preoperatively, one hour from the initiations of surgery and at the end of the procedure. The values were compared to those taken in a similar group operated by laparoscopy. Swine were euthanized 14 days after procedure. According to the predetermined biopsy protocol, the abdominal organs were grossly examined to determine the presence or absence of abscesses, intraperitoneal adhesions or any other sign of inflammation. The stomachs were removed and a pressure test for leakage was performed in every case.

Excisional biopsies were obtained based on the gross aspect of the specimen during the necropsy protocol. The specimens were processed and analyzed using hematoxylin and eosin and examined at 4X and 10 X magnifications by an investigator who was blinded to the type of specimen and time of harvest.
4. Inflammatory response

For all animals in the transgastric and laparoscopic groups preoperative, intraprocedural and postoperative samples (5ml) of IL1b and IL6 were obtained following a predetermined protocol. They were compared to each other and to a non-surgical control group consisting of four animals which underwent only general anesthesia. Data were expressed as percentage, average and standard deviation. The groups were compared by considering $t$-student test is significant if $p$ value $<$0.05.

Results

All 24 procedures were successfully performed as planned, with no major intraoperative incidents. Three types of transgastric access were tested: a direct technique, balloon dilation and short tunneling access, all conducted without major incidents. There was no major vascular or visceral lesion during the peritoneal access. We noted two hemorrhagic accidents, both in the moment of the direct incision of the gastric wall, managed successfully, but with some degree of difficulty, by monopolar coagulation. Transvaginal access was performed by endoscopic or open posterior colpotomy. We successfully performed uni or bilateral transgastric oophorectomy and transvaginal cholecystectomy.

Transgastric endoscopic peritoneoscopy: small bowell mobilization using an endoscopic biopsy forceps
The gastroscopy closure using the OTSC™ system in six animals proved efficient. From the 4 animal cases with unclosed gastric orifice, 2 were sacrificed at the end of the intervention and the other 2 died in the first 48 hours postoperatively progressively developing fever and altered general status. In the first 2 cases we noted the minimal contamination of the peritoneal cavity. For the other two cases that died afterwards, the cause of death was sepsis due to generalized peritonitis. When the gastric breach was closed with the OTSCs, the animals survived for 14 days and were sacrificed afterwards. We registered one postoperative complication consisting in perigastric abscesses and acute gastric ulcerus, which were histopathologically confirmed. For the rest of the animals necropsy registered minimal adherences around the gastroscopy orifice. At the gastric air test we noted the resistance of the closure up to a level of bursting pressure.

Evaluation of IL1β showed no difference in the preoperative ($p=0.446$) and intraoperative determination ($p=0.298$), but a statistically significant increase in the laparoscopic group when compared to either the NOTES ($p=0.028$) or the control group ($p=0.011$) for the postoperative prelevations. Determination of IL6 followed similar dynamics for the postoperative period.
Conclusions

Natural orifice transluminal endoscopic surgery (N.O.T.E.S.) was feasible for both transgastric and transvaginal approaches.

The choice for the access route is largely dependent on the type of intervention planned, due to the technical characteristics of current endoscopic equipment.

N.O.T.E.S. comes with a lower postsurgical inflammatory response and inferior immunological impact compared to laparoscopy.

OTSC clip offers a safe and efficient endoscopic closure solution for the transgastric access site.

Leaving gastrotomy site open is potentially dangerous and totally inadvisable.

Working as a multidisciplinary surgeon-endoscopist team is essential in the early phase of development of N.O.T.E.S.

The limitations of this method are related to the introduction of stable, multitasking endoscopic platforms and appropriate endoscopic accessories.
Bibliography


