Animal ethics in laparoscopic urology training

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ABSTRACT

Laparoscopic urologic operating techniques are in widespread use throughout the world and because of various advantages, over the years they have virtually become a gold standard surgical intervention method. As laparoscopy is a painstaking technique to learn, the training consists of different stages. Within these stages of training, wet laboratory training where animals are used, is the most sensitive stage. The widespread use of experimental animals in medical research necessitated standardization and the establishment of certain regulations. This standardization and organization of laws and regulations started to be discussed in Europe approximately a century ago and have been established on a certain foundation. In this review article, we discuss some important points and ethic rules about laparoscopic urologic training practiced on live animals.

Keywords: Animal ethic; laparoscopy; urology; wet laboratory training.

Introduction

Laparoscopic surgery has been increasingly used worldwide since the 1980s due to advantages such as shorter hospital stay, better cosmetic results, rapid healing and less formation of post-operative adhesions compared to open surgery.^[1]

Laparoscopic operating techniques are widely used as minimally invasive urological surgeries. Over time, in some operations this method has virtually become the gold standard method of surgical intervention.

Importance of training

Manipulations are made on a 2-dimensional screen in laparoscopic urologic surgery. This causes a restriction in the perception of depth and difficulties in eye-hand coordination, especially for those physicians just starting to perform laparoscopic interventions. Therefore, training is necessary to acquire the skills needed before starting laparoscopic interventions. Briefly, this training consists of 3 stages;

1. Theoretical education,
2. Dry laboratory training with Pelvitrainer,
3. Wet laboratory training on live animals.

Recently, cadaver training and simulator training have been added to these.^[2] Training made on live animals in the 3rd stage of laparoscopic urologic surgery raises the subject of animal ethics.

History of using animals in experimental applications and surgical trainings

In history, the first experimental applications can be said to have been those by Galen, who removed various organs from the bodies of pigs, monkeys and dogs in an attempt to understand their functions. Those experiments on live animals were the first physiological studies.^[3]

Many animal species, from simple vertebrates to developed mammals are currently used as experimental subjects. Some species of mammals are the most preferred experimental ani-

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mals. The most frequently used experimental animals are rats, mice, rabbits and fish, followed by pigs, guinea-pigs, hamsters and monkeys. Pigs are more generally used as human models because of many similarities for human skin, skeleton, gastrointestinal and cardiovascular systems, pancreas, and kidneys.^[4]

Many life-saving treatment methods in current use have been learned from experimental studies made on animals. For example, discovery of anthrax, rabies and polio vaccinations, functions of insulin, anticoagulants, monoclonal antibodies and neurons, leprosy treatment, laparoscopic surgery, applications of pacemakers, organ transplantations and many more procedures have been learnt from animal experiments.

Basic principles related to the use of experimental animals

The widespread use of experimental animals in medical research necessitated standardization and the establishment of certain regulations. Standardization and organisation of relevant laws and regulations were started to be discussed in Europe approximately a century ago and have been established on a certain foundation.

The zoologist, William Russell, and the microbiologist, Rex L. Burch, described the rule of the 3 Rs.^[5] These are Reduction, Refinement and Replacement which define some basic principles related to the use of experimental animals.

Reduction: The principle of reaching the best result using the lowest number of animals possible in the research.

Refinement: This can be summarised as the methods needed to take precautions to provide the least pain possible and welfare in all the processes used from birth to the termination of the experiment.

Replacement: This item of the 3Rs refers to the replacement of one thing with another. According to this item, the use of other substances rather than vertebrates should be preferred as far as possible in research and biological tests. These basic rules, which have been established in relation to animal ethics, are also valid in the use of animals in experimental applications and surgical trainings.^[5]

The stages of laparoscopy training

Theoretical education

Using the lowest number of animals in training is an essential point regarding the reduction principle which is the most important rule of 3Rs. Furthermore, training will be more cost-effective which can provide an advantage to trainees. The first step in theoretical education related to laparoscopy before starting laparoscopic training to be taken by the physician is to use fewer animals in training. Then, this should be consolidated in a

dry laboratory with pelvitrainer, laparoscopic training boxes or computer-assisted laparoscopic operation simulators.

During theoretical education, knowledge of the normal anatomy should be reinforced with topographic anatomy training. In this way it will be easier to combine the operation applied in a 3-D environment with the image on a 2-D screen. In the theoretical part of training, sufficient information must be given to the participants on the endoscopic hardware used in laparoscopy, insufflators, trochars, laparoscopic scissors, dissectors, hooks, forceps, needle holders and devices providing coagulation. Information should be given on how these devices can be used more ergonomically, holding techniques and technical information about the instruments.

Dry laboratory training with Pelvitrainer

There is no single model recommended or accepted by all for laparoscopic simulation used in dry laboratories. There are many models on the market from simple training boxes to computer-based virtual reality models. While simple simulators are sufficient for the development of basic skills, virtual reality simulators can be more effective in the acquisition of complex skills.^[6,7]

Laparoscopy training boxes are cheap and provide the facility of simulation for several skills. The training box, which was once developed at home with a laptop, a simple web camera, a cardboard box and a table lamp, is now produced commercially and studies have shown that it provides the possibility of laparoscopic training in the same way as a video pelvitrainer.^[8]

Virtual reality simulators simulate an environment resembling the real working environment through a program loaded on a computer. This system gives a response to the manipulations of the operator which are close to reality. The accuracy of the movements of the operator can be evaluated objectively with these systems. Currently, there are virtual reality simulators available such as the MIST-VR® (Mentice-Sweden), Lap-Sim® (SurgicalScience, Sweden), and Lap-Mentor® (Simbionix-Israel). Various studies have reported that training using virtual reality simulators has significantly increased skills in laparoscopic urology under real-life conditions.^[9,10]

Wet laboratory training on live animals

The stages in the process of selecting an animal model can be summarised as;

1. Identify the basic problem,
2. Decide what the basic element should be,
3. Define which animal species has this key element,
4. Determine which of the animal species with the basic element would be more advantageous and to which the least discomfort could be given,

5. Determine the importance of the factors in the application such as procurement, sheltering, caring, and managing animals, equipment, experience, and literature information
6. Select an animal model appropriate to the scientific application and ethics.^[11]

Some basic principles must be followed when working with experimental animals in laparoscopy training. These include:

1. The animals to be used for training must be obtained from a legal supplier and the animals must have been bred for experimental purposes,
2. The animals obtained must be quarantined for 7-15 days, depending on the animal species, in the unit where the training is to be undertaken,
3. The animals to be used in training must be free of any disease contagious to humans,
4. If the experimental animals are to be used for research or a course, there must be good selection of the animal species. Incorrect model selection can lead to future problems,
5. The team dealing with the experimental animals must be experienced and should have been working on this subject for at least one year.^[11,12]

Wet laboratories, as the place where training is given on live animals, should be accepted as operating rooms. The dimensions of these rooms, the organisation, structure and quality of the equipment used are extremely important. The rules of asepsis prevalent in normal operating theatres must be considered to have the same validity in these rooms. There must be no difference in principle between a laboratory designed for animal surgery and a normal operating theatre.^[13]

To prevent unnecessary loss of animals in training, the instructor and technical team must be highly knowledgeable on the subject of the methods applied to the animals. These individuals should certainly have taken a certified course on this subject with national or international validity. Uncertified personnel should not work in training programs, not even just in the care of the animals. In the training team there must certainly be a veterinary or an anesthetist experienced in the field of anesthesia of these types of animals.

The Turkurolap is a research group which employs highly experienced and certified trainers working in our country (www.turkurolap.com). The Turkurolap group has organised approximately 40 courses, both in Turkey and abroad, and in all of these courses the subject of ethics in animal experiments has been considered.

The animals used in laparoscopy training must not be kept in haphazard places or under haphazard conditions. The conditions of the cages or rooms where animals are kept are also important and

the management of these conditions has been defined.^[14,15] These conditions have been defined according to the requirements of the species. The room temperature, humidity, intensity of light and aeration of the room are included in these conditions, and if conditions are not complied with, the health of the animals will suffer.

Not with standing the attention that is required within the Ethics Rules related to the living conditions of the animals, the technicians involved in their care must also be informed, knowledgeable and animal-loving. Otherwise, the animals can be harmed during care or transport. Therefore, the technicians must also undergo continuous training and observation.

In addition to the provision of comfort for the animals in their shelter, they must not be hurt while being used for training. From an ethical perspective, this must be prevented or at least reduced to a minimum level. To achieve this, the team who will transport the animals to the operating area must be trained and the anesthetist who will administer the anesthesia must be experienced and certified in the subject of animal anesthesia.

Principles of anaesthesia for experimental animals

General anesthesia for experimental animals is administered via injection or inhalation, in other words by inhalation of anesthetic gases.

The conditions of correct selection applied in consideration of both the features of the animal and the experiment to be applied will conform to the Ethics Rules. Injection of anesthetic agents to animals is a simple method as it does not require additional instruments or equipment, but with this route, in case of overdose, it is not possible to recover the animal. To recall the Reduction rule, there is a requirement that an animal should not be lost unnecessarily in these studies (Figure 1).

However, as a result of small inattentions, a significant number of animals are known to be lost during anesthesia applied with injection. Thus it is necessary to calculate the dose very well according to the actual weight of the animal. Although the application of anesthesia via the inhalation route is more challenging due to the need for special equipment, there is a stronger possibility of resuscitating the animal in case of an overdose.^[3]

The procedures of Euthanasia

After completing the surgical procedures performed for training purposes, euthanasia must be applied to the animals. This procedure is perhaps the stage requiring the most compliance to the Ethics Rules. An incorrect method selected at this stage can cause unnecessary pain to the animal.

Euthanasia can be applied as either chemical or physical euthanasia. In chemical euthanasia, the procedure can be applied with a high dose of anesthetic agent.

Figure 1. Preparation for general anesthesia

Injectable or inhalation anesthetics can be used in this chemical euthanasia method, CO or CO₂ gases can be used in the ventilation method. A reason for the choice of these gases is that they are inexpensive and odourless.

Physical euthanasia methods permitted by the Ethics Rules.^[3]

- Cervical dislocation (separation of the neck from the spine with a single, sudden action),
- Decapitation (instant cutting of the neck of the animal with a guillotine),
- Freezing in liquid nitrogen (can only be applied to small animal species as the procedure send the animal instantly to -196°C),
- Microwave (a microwave system developed specifically for neurological research which is applied to the brain and enzymes are fixed),
- Cutting of the carotid artery in large animals,
- Firearms (very occasionally applied to large animals),
- Electrocution (this method is very rarely applied).

Ethics and legal regulations for experimental animals in Europe and Turkey

The European Union (EU) regulated the protection of animals in agriculture and research by means of 9 directives and one decision in 1986. The agricultural regulations concern the protection of slaughter animals, protection of animals during transport and the protection of animals kept for farming purposes as they also cover the protection of laying hens in battery cages and minimum standards for the protection of calves and pigs in intensive farming systems. The protection of animals used for experimental and other scientific purposes is covered by a Directive that approximates the laws, regulations and administrative provisions of the Member States. The legal texts are presented and where necessary commented on.^[16]

On 8th September 2010 the long process of revising the EU Directive for the protection of laboratory animals was concluded. The new Directive acknowledges that animals, includ-

ing nonhuman primates, are still needed for scientific purposes today. Importantly, animals have an intrinsic value, which must be respected. There are some major advances for animal welfare, many of which had however already been common practice in the more developed Member States. The new Directive prohibits new, more progressive legislation if not already in place and thus harmonizes but also freezes the 27 Member States at a relatively high level. The revision was an important opportunity for the European Commission, on one side to demonstrate its commitment to improve human health and safety by enabling animal testing and on the other side to improve animal health and welfare by setting minimum standards. It also represents a formal implementation of the 3Rs principle.^[17]

This European Directive was adapted one by one by the legislators in our country. The first serious laws and regulations in this area started to be made in 2004 and the first Experimental Animal Center Ethics Committee and Local Ethics Committees defined in law were established in July 2007. The legal regulations have been updated and are in current use.

The experimental animal units in Turkey and the research conducted must conform to the relevant regulations of the Ministry of Agriculture and Rural Affairs and the Ministry of the Environment and Forestry.

One of the most important legal regulations related to the ethics of animal experiments is the 'Regulation on Working Procedures and Principles of Ethics Committees of Animal Experiments'. This regulation was issued by the Ministry of Forestry and Water Works. The aim of this regulation was to define acceptable ethical standards related to the methods and materials used on experimental animals in the basic activities, such as scientific research, testing, training and teaching, to establish an experimental animal center ethics committee and experimental animals local ethics committees, to present the planned procedures of studies, to examine and give permission for the recommended research and studies, to observe the applications, to record all the procedures made on experimental animals, to be able to follow up these procedures immediately or retrospectively, to provide inspection of all the procedures and to define the basis for terminating procedures when necessary.^[18]

Another regulation related to the Ethics Rules concerning animal experiments, of which physicians must be aware of is the 'Regulation for the Protection and Welfare of Animals used for Experimental and Other Scientific Purposes'. The aim of this regulation is to provide welfare and safety for animals bred, and procured for use in procedures by defining the principles to be followed by breeders, suppliers and institutions authorised for use and research, in the work and procedures of the origin, breeding marking, care and shelter of the animals, when necessary to

evaluate projects with the use of animals in procedures, to authorize procedures and to ensure the qualifications of the personnel, that records are kept, and of species which must be bred in authorized institutions for use in procedures and of the animal species used.^[19]

In conclusion, laparoscopic urologic operating techniques are in widespread use throughout the world and because of their various advantages, and over the years they virtually become a gold standard surgical intervention method. As laparoscopy is a painstaking technique to learn, the training process consists of different stages. Within these stages of training, wet laboratory training where animals are used, is the most sensitive stage. In this stage, another living organism is used to improve human health. Therefore, ethical issues related to this method have been regulated with national and international laws and regulations. During this training made on live animals, the rearing, care and transport of the animals used and the preparation for surgery with the appropriate anesthesia must be applied by trained personnel in compliance with the defined protocols.

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