Objective: to analyze immediate organic modifications and complications subsequent to orthotopic liver transplantation in pigs. Method: fourteen female pigs, specie Sus domesticus, were utilized in this study, with body mass between 5 and 8 Kg, considering that we evaluated the main immediate intra and post-surgery complications of the liver transplantation. Results: in the donor, we highlighted as the main complication the occurrence of bleedings, considering that this was observed in all procedures. In addition, such situation occurred during surgery involving the receptor, in which the bleeding was also perceived as the most frequent complication. However, it is valid to highlight that the hemodynamic instability was present in 5 procedures involving the receptor. Conclusion: among transplant surgery complications we may cite: difficulty of oro-tracheal intubation, intra surgery hemorrhages, hemodynamic and respiratory instability and anesthetic complications. In the immediate post-surgery, thus, we observed as the most frequent complications: hemodynamic instability and small anastomotic bleedings.

KEYWORDS: Liver transplantation, Pigs, Complications

INTRODUCTION
Liver transplantation is a surgery that consists of removing the sick liver from a person who suffers from chronic or acute liver disease for replacing, in the same place, a healthy liver donated by someone with encephalic death or for replacing part of a liver from an alive donor. These days, it has been an effective treatment for chronic liver diseases and it has presented a global rate of survival of about 80% in three years. It is, however, an alternative of treatment indicated to terminal cases, where the mortality with conservative treatments may reach even 70% by the end of twelve months.

In general, liver transplantation is indicated to the advanced and irreversible chronic liver disease, when the perspective of survival, resulting from the liver disease, is less than one year, without clinical or surgical alternatives of treatment which is not the transplantation, when the disease may greatly interfere in the individual’s capacity of working or in his quality of life, and the progression of the disease results in life expectation smaller than the one resulting from the transplantation.

Brazil is the country that has provided the best public program of transplantations in the entire world, having accomplished, in 2008, 5373 transplantations of organs. In relation to liver transplantation, we may observe an increasing in the procedure from 1998 to 2008. For ten years, Brazil had realized only 288 liver transplantations, while, currently, this number has reached 1174 realized transplantations.

Liver transplantation and immune-suppressors have highly increased the survival of bearers of terminal and irreversible chronic liver diseases, but the death resulting from transplantation has been still a constant concern. Brazil has been offering the procedure free by SUS.
being the second country in the world in realized transplantations a year by the public system (93%), making possible to investigate the effect of socio-economical inequalities on the transplantation result. The Ophir Loyola Hospital, in Belém, has had the service of collecting livers since 2007 and has maintained the authorization for the realization of grafts. The causes of death include, mainly, infectious (38%), followed by cardiovascular (18%) and surgical ones (12%). In pediatric liver transplantations, 50% of the listed deaths occurred in the first 354 days after the inscription, being this time inferior to the average of waiting time until the transplantation of the group with chronic liver diseases of 492 days. This finding has emphasized the importance of reducing the time of the waiting list, through a greater awareness related to the importance of donating and collecting organs, as well as through the implementation of surgical techniques, as split and inter-alive transplantation, which such procedures have already been applied in other countries.

The proposal of new surgical procedures likely to be simulated in animals has been frequent in surgery. Studies may, then, not only evaluate the feasibility of the procedure itself, but also its physiopathological consequences and therapeutic effectiveness.

The training of anesthetic-surgical teams through experimental surgeries in animals has been considered a fundamental step before its clinical application because of the technical complexity involved in liver transplantation.

Currently, similarities of pigs to humans, considering their anatomy, physiology and physiopathology, have been widely established in the literature. Tumbleson and col. complemented that a pig is an useful model for studies in biomedical researches, once it presents similarities to humans in structure and functions, including size, food pattern, digestive physiology, dietetic habits, structure and functions of kidney, vascular structure of lungs, distribution of coronary artery, tendency to obesity, respiratory rate and social behavior.

The scarceness of papers describing liver transplantation in pigs and the analysis of the anatomical configuration have justified the realization of this research, which aims to analyze the organic modifications and immediate complications after graft liver transplantation in pigs, in order to corroborate to the training and improvement of the technique aiming not only to extend the anatomical knowledge and the experience, but also decreasing, this way, the incidence of surgery complications.

METHODS

The Committee of Ethics and Research from the Center of Biological Sciences and Health at Pará State University approved the pre-project of this research. It is an experimental study, observational and comparative, realized in the Laboratory of Experimental Surgery (LCE) at Pará State University (UEPA), Belém – PA.

All animals from the present research were cared according to the norms of the Brazilian School of Animal Experimentation (COBEA) and the national legislation for the current animal vivisection (Federal Law 11.794, October 9th, 2008).

Fourteen female pigs specie Sus domesticus were utilized for studying the technique of liver transplantation, with body mass between 5 and 8 Kg. The animals were allocated in appropriate Biotery with individual fences measuring 150cm x 150cm, cemented floor, water ad libitum, being offered 500g of ration daily, environmental temperature and natural light. Besides, a technician in biotery carried out the sanitization of the cages daily. There was pre-surgery fasting of 24 h.

The preparation of the procedure was initiated in the eve, conferring and testing the utilized equipments in anesthesia, in the surgical procedure of collection, “back-table” and graft, as it was also necessary to verify the size and weight of the animals destined to the procedure in order to calculate the drugs doses to be administrated, evaluate its health conditions and initiate the fasting to avoid complications as bronco-aspiration or surgical difficulties, due to the gastric...
fullness, as well as choose which would be the donor and the receptor animal, once the receptor animal must be larger than the donor so that a relatively small liver may be implanted in a cavity a little larger than its size, facilitating the manufacturing of vascular anastomoses.

All utilized techniques for collecting the graft, back-table and its implantation, were carried out according to the description by Brito and col. 12,13,14,15

After collecting histological and biochemical material, the euthanasia was carried out with an injection of 50 ml of Kcl 10% EV. The carcass was discarded in biological trash involved in a hospital plastic bag, according to the norms of COBEA.

The statistic study of the obtained results was realized in the Bio-statistic Department of UEPA. According to the nature of variables, the comparative statistic analysis was applied and utilized Anova non-parametrical tests with Bonferroni’s correction. In all tests, the rate of hypothesis rejection of nullity was fixed in 0,05 or 5% (α ≤ 5%).

RESULTS

TABLE I – Surgical complications of donor animals in liver transplantations in pigs realized in the LCE 2009.

<table>
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<tr>
<th>Complications</th>
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<td>Transpl. Bleedings</td>
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<td>Lacer. branches pancreat.</td>
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<td>Anatonic variation</td>
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<td>Superf. Anest.</td>
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<td>Hemod. Instability</td>
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<td>Heart Failure</td>
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Source: Research protocols

Transpl. : Transplantation
Lacer. branches pancreat. : Laceration of branches from the pancreatic artery
Superf. Anest. : Superficialization of anesthesia
Hemod. Instability : Hemodynamic instability
TABLE II – Surgical complications of receptor animals in liver transplantations in pigs realized in the LCE 2009.

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Source: Research protocols

DISCUSSION

By leaving the details referring to the utilized techniques, some commentaries are necessary on some key points in the surgery. Noticeably, the most delicate part of the whole procedure is the graft implantation. From the difficulties found during the research, we may mention technical problems referring to the available physical structure for the realization of transplantations. We had only the respirator model Takaoka (“little onion”), which is inadequate to a procedure of such a size; the monitoring was damaged due to not having all adequate parameters available to the hemodynamic control of animals, as the central venous pressure and diuresis control.

Related to the occurrence of trans-surgical complications, intra-surgical bleedings were the main complications, being present in all procedures, however, all of them minor, due to the rupture of small collaterals and controlled with relative facility. In addition, anatomical variations in some animals made the procedure difficult, delaying some surgical times. One frequent complication, occurring in three transplantations, was the laceration of small pancreatic branches during the dissection of the portal vein, all connected without difficulties.

The hemodynamic instability is the most marked aspect of the procedure. According to Leite and col. in the pre-anhepatic stage, the inadequate reposition of fluids in responding to a rapid blood lost and surgical manipulation, which always alters the pre-load of heart, are factors responsible for the instability, and, in the anhepatic stage, beyond the previously indicated factors, the occlusion of the cava inferior vein leads to a fall of the venous return from the inferior members and splanchnic territory around 50%, conducting to the accumulation of acid metabolites in the congest lay. Subsequently, these metabolites have intensified the hypotensive situation. The post-reperfusion syndrome may occur, which is constituted in the highest degree of hemodynamic instability and it is characterized by a bradycardyarrhythmia, the decrease of arterial medial pressure and the reduction of peripheral vascular resistance.

The injury of ischemia and reperfusion has been associated with the increase of acute rejection. Several strategies have been described for preventing this injury in solid organs transplantations. Among them, we have had the utilization of buffers that work as the first line of the organism defense against variations in the concentration of hydrogen ions, being, the bicarbonate, the most important buffer in the extra cellular means.

Another way of decreasing the effects has been by utilizing the named Ischemia pre-conditioning, which is utilized
after the finalization of the overcast and with the realized anastomoses of the supra cava and the portal vein, lacking the anastomosis of the infra liver cava vein and liver artery, loosing the “clamp” of the portal vein for 10 seconds at each first five minutes, and allowing the blood flow occur towards inside the graft. This scaled reflux has been realized in order to provide time for the neutralizing enzymes from the free radicals, as the superoxide dismutase being released inside the liver and, with it, neutralizing great part of the free radicals produced during the ischemia stage, finalizing the time of cold ischemia.

In transplantations numbers 1 to 4 we utilized blood transfusion for the volemic reposition, and two intra surgery receptors’ deaths occurred in transplantation #3 and # 4. Due to this elevated rate of mortality in transplantations numbers 5 to 7, we utilized Ringer Lactate and hypertonic solution of sodium chloride at 7,5% for maintenance, and the fact of not occurring deaths has indicated the possibility of acute hemolytic transfusion reaction even by utilizing animals from the same herd, once, in pigs, 16 systems of blood groups are internationally recognized (A, B, C, D, E, F, G, H, I, J, K, L, M, N, O, P).

In the immediate post-surgery stage we observed the hemodynamic instability and small anastomotic bleedings as the most frequent complications, which were easily controlled by local compression.

As in the technique by Torres and col. the utilization of two animals by transplantation, the donor and the receptor, provided a greater technical learning in comparison with other models that use only one animal.

An alteration that would help increase the survival of the pig during surgery would be a venovenous “by-pass” between the inferior cava vein and the jugular vein. This “by-pass” would make the blood of the territory, drained by the inferior cava vein, to circulate, decreasing, this way, the process of metabolic acidosis and, consequently, the mortality of the animal. This “by-pass” could be carried out with the help of a “pump”, which would provide the blood circulation.

Another update would be a wide dissection of the splenic vein in its discharging in the portal vein, and posterior catheterization of it, without a catheterization of the arterial system. This would save time, avoiding this vein to be dissected twice: the first one for its repair together with the portal vein and the second one for its catheterization together with the spleen. With this modification we would have the disadvantage of not catheterizing the arterial system, what could be compensated with its irrigation in the “back-table”. This change would facilitate carrying out the surgical procedure, minimizing the surgical time from 30 minutes to one hour, what would contribute for decreasing morbidity and surgical mortality.

We have suggested, therefore, the correction of some points during surgery, as supra-cited procedures, in order to optimize the surgical time and minimize trans and post-surgical complications, improving liver transplantation as a whole and encouraging new studies in the field.

CONCLUSION

Related to the occurrence of trans surgical complications we may cite: difficulty of oro-tracheal intubation, intra-surgical hemorrhages, hemodynamic and respiratory instability and anesthetic complications. In the immediate post-surgical stage we observed as the most frequent complications: hemodynamic instability and small anastomotic bleedings.
Objetivo: analisar as modificações orgânicas e complicações imediatas subseqüentes ao transplante hepático ortotópico em suínos. **Método:** foram utilizados no estudo, 14 porcos fêmeas espécie Sus domesticus, com massa corporal entre 5 e 8 Kg, sendo que avaliou-se as principais complicações intra e pós-operatórias imediatas no transplante hepático. **Resultados:** no doador, destacou-se a ocorrência de sangramentos como principal complicação, tendo em vista que esta foi observada em todos os procedimentos. Tal situação também ocorreu no ato cirúrgico envolvendo o receptor, no qual se percebeu o sangramento como a complicação, também, mais frequente. Entretanto é válido destacar a instabilidade hemodinâmica, que esteve presente em 5 procedimentos envolvendo o receptor. **Conclusão:** dentre as complicações trans-operatórias podem ser citadas: dificuldade de intubação oro-traqueal, hemorragias intra-operatórias, instabilidade hemodinâmica e respiratória e complicações anestésicas. Já no pós-operatório imediato observamos como complicações mais frequentes: instabilidade hemodinâmica e pequenos sangramentos anastomóticos.

**DESCRITORES:** Transplante de fígado, Suínos, Complicações

**REFERENCES**


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Recebido em 19.02.09 – Aprovado em 27.08.09