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SHORT COMMUNICATION

Head transplant - the newest reports and concerns on planned procedure

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ABSTRACT

Transplantation, one of the most intensively developing fields of medicine, is giving patients hope for the chance of "second life" and health. The 21st century medical achievements heralded to achieve more difficult challenges, such as face transplant or lower extremity transplant. Among the futuristic dreams of the scientists, one of the projects - the Head to Body Transplant, stands out as one of the most controversial surgeries of the century. The aim of this study was to present the current state of art in medical aspect on cephalic anastomosis, as well as ethical implications. Among articles in PubMed Medline database related to human cephalic anastomosis, head transplant, head to body transplant keywords, 15 articles were selected for further analysis. Reviewed research presents significant development in conduction of the human cephalic anastomosis project. Most of the crucial parts of the surgery, such as deep profound hypothermia, spinal cord anastomosis - the detachment and fusion with the fusiogenes particles, have been practiced on animal models. The more newest revelations are revealed to the public, the more ethical and technical concerns are raised, primarily in terms of one-center study approach, infavourable benefit-cost ratio and futuristic apprehensions of infertility, transsexual or even unnatural life prolongation reasons for performing this type of surgery.

Keywords: human cephalic anastomosis, head to body transplant, head transplant

1. BACKGROUND

1. 1. Challenges of modern transplantation

"Materialized dream of a miracle", which is the science of transplantation, brings with itself the hope for innovative, incomprehensible so far for the human reasoning therapeutic options, in order to help patients with diseases impossible to defeat for centuries. The true Enlightenment Era of Transplantation started in the turn of the 19th and 20th centuries, with the first successful grafts - in 1837 corneal transplantation by Edward Zim, in 1883 thyroid transplantation by Theodor Kocher. [1,2]

These achievements heralded a new era of treatment for patients in the last stages of organ failure. As a result, the 21st century medicine strives to achieve even more difficult medical challenges in the field of transplantology - in 2010 the first whole face transplant was performed, in 2011 - a transplant of both lower extremities, and in 2014 - the first transplant in a newborn patient. [3,4] One of the unrealized plans of transplantology is a futuristic vision of a head transplant, in patients with progressive genetic, metabolic diseases, and muscular dystrophies.

1. 2. History of the head anastomosis

The first attempts and plans on head transplant started in the beginning of 20th century. Alexis Carrel was one of the pioneers in transplantation due to invention of a modern method of triangular anastomosis, called the "Carrel maneuver" after its inventor, anastomosis type which enables fast and stable stitching, also prevents postoperative bleeding and clots formation. His second achievement - perfusion pump, allowed further research on the development of heart-lung machine - consequently contributed to development of cardiac surgery and transplant surgery. [5] Carrel was involved in less popularized research project, canine head anastomosis.

Team Carrel-Guthrie conducted the procedure in 1908, during the experiment the anastomoses remained without a blood circulation for 20 minutes, and despite demonstration of positive response by the animals to the given stimuli immediately after the transplant, their condition deteriorated rapidly, and they were anesthetized several hours after the procedure. [6] Next daredevil of cephalic anastomosis in 1950s, Vladimir Demikhov, improved the overall survival of the dog patients (29 days) and better stimuli response. [6] However, the main inspiration for recent head transplant fascination, comes as a result of the research of American neurosurgeon Robert White in 1970s, who performed successful head and brain transplants in monkeys and dogs.

His most important contribution was the creation of the "auto-perfusion" mechanism by means of vascular loops, while despite the already available immunosuppressive therapy, its high doses were one of the main reasons for the fail of the experiments and deaths of animals 9 days after surgery. [7,8]

Starting from 2013, whole world is also observing with simultaneous fright and admiration plans of the project HEAVEN, started by an Italian neurosurgeon Sergio Canavero from Turin Neuromodulation Group, and Chinese transplantation specialist, participant of the first hand transplant, Xiao Ping Ren. It has been 5 years since the research project plan has been revealed to the world, and every now and then, new pieces of information has been published on achieved steps of the procedure.

2. AIM OF THE STUDY

The aim of this study is to present the state of art about cephalic anastomosis research and the concerns of scientific and ethical matter.

3. METHODS

Substantial articles on cephalic anastomosis, head transplant, have been analyzed. Among articles in PubMed Medline database from years 2013-2018, 15 articles were selected for analysis, according to keywords: cephalic anastomosis, head transplant, body transplant, head transplantation, Body To Head Transplant, BTH transplant.

4. RESULTS

4. 1. Description of the procedure

Project HEAVEN / GEMINI project consists of two procedures: HEAVEN-the HEad Anastomosis VENTure- the transplant procedure of the deceased donor's body to the living recipient's head combined with GEMINI- subsequent spinal cord graft. [9]

There are several inclusion criteria which could, or should be applied if such procedure would come into practice. Theoretically, the recipients of the transplant could be patients suffering from tetraplegia, multi-organ failure, progressive and destructive muscular dystrophies, genetic and metabolic progressive disease syndromes, also possibly cancer patients with multiple metastases without brain metastases. The donor of the body is a patient with confirmed brain death, of a similar immunotype, height and body type to the recipient, with absence of an active systemic disorder and brain diseases. [10]

After induction of anesthesia with barbitural/propofol and obtaining Burst Supression Pattern, recipients head undergoes deep profound hypothermia, and the donors body receives spinal cord hypothermia. Next step is to separate anatomical structures of patients, in particular cervical and spinal vessels, which can be achieved with anterior approach firstly one incision around the basis of the neck and three incisions along the sternocleidomastoideus muscle, later turned in second phase to posterior approach, in order to start to GEMINI procedure. Following these steps, the spinal cord anastomosis and vessel anastomosis is performed, suturing of the dura and anastomosis of trachea, esophagus, ligation of the nerves as a last items of the procedure. After the surgery, minimum 3 days of sedation of the recipient is required. [9]

4. 2. Crucial novel steps in cephalic anastomosis - deep profound hypothermia and spinal cord anastomosis

The head transplant procedure contains two of the most controversial and complicated elements, such as the profound hypothermia protocol and the anastomosis of the spinal cord. Within HEAVEN procedure, the most crucial aspect is to preserve the neurological functions of the recipients CNS and to prevent tetraplegia in spinal cord of the donor. Profound Hypotermia (PH) is an essential element to counteract ischemia and gives time to surgeons to perform the cephalic anastomosis without brain damage. Used in cardiac surgery or surgical

clipping of aneurysms during complete cardiac arrest, it provides up to 45 minutes of no visible neurological damage after surgery. In HEAVEN, the recipient's head will undergo hypothermia up to 10⁰C, while in the case of the donor partial hypothermia will be used only in the spinal cord to prevent damage to other organs. [10] Within the GEMINI part, the most important part of the anastomosis of the spinal cord, is construction of the GEMINotome - a tool with extremely sharp nanometer edges and micro-connections with negative pressure, ensuring the circulation of fusiogens [9,11] The most accurate and least scarifying cut is extremely important to ensure the least altered surface for axon fusion and reconstruction after iatrogenic damage. The bonding of damaged axons is possible thanks to a mixture of chitosan-PEG glue, compounds known as "fusiogens". Fusiogens have been known in science since 1986, but their contribution in neuronal regeneration has been reviewed from 2005. [12] Polyethylene glycol (PEG) has a rehydratative effect in a dehydrating, disorganizing environment, which allows polar molecules to reorganize cell membranes, while the its hydrophobic side chains fill the site of a given damage by additionally sealing it. [13] Chitosan also acts neuroprotectively and repairs the cell membrane, creating phospholipid aggregates with dipalmitophosphatidylcholine. [14] In animal studies, fusiogens showed high efficacy - 100% electrophysiological efficacy and 93% in behavioral recovery in canine experiments. Nevertheless, science is lacking the data regarding fusiogens testing in human spinal cord, as well as the magnitude of the successfully treated lesions so far is proportionately lower than that caused during a head transplant. [6,11]

4. 3. Current achievements and progression in research

In 2016, Canavero and Ren reported successful completion of GEMINI procedure with use of "nano-enhanced" Texas PEG, which led to recovery of somatosensory evoked potentials in 24 hours post-operatively in animal study. [15] In June 2017, Li et al. Developed a cross-circulated, bicephalic model in rats, which enabled proper blood supply of donor brain with peristaltic pump application, with no ischemic reperfusion events in EEG after surgery. [8] In November 2017, Ren et al. announced the first successful cephalosomatic anastomosis in human cadavers. The 18-hours long surgery resulted in optimizing the crucial steps, such as vertebral stabilization, and also preserving the peripheral nerves in order to reduce the time of the procedure (vagi nerves, phrenic nerves, laryngeal nerves and cervical plexus). In the future plans, heart-beating brain dead organ donors replication of the surgery is considered, before the actual first live patient head transplant. [16]

4. 4. Scientific and ethical concerns

Numerous scientific and ethical concerns have been raised regarding the conduction of the head transplant procedure. The most crucial possible complication is the damaging of intersection of the core-thalamic pathway during the anastomosis of the spinal cord, which can result in permanent pain sensations in the patient after transplantation. Current research on resolution of this medical condition is still in the experimental phase. [6,10] Plenty of ethical dilemmas are raised regarding this procedure - starting from the postoperative reproductive health of the patient, who might want to become parents in the future, which would mean the subsequent use of the gametes of the body of the donor. As reproductive health is one of the main factors for wellbeing of human mental and physical health - if the procedure proves to become a success and will be introduced into the general medical

practice, future regulations should contain important limitations regarding fertility of donors and recipients, preventing the use of head transplant surgery in infertility treatment. [17] Significant possibility of a desire to perform intersexual transplants, creates a risk of using this type of surgery as a method of changing gender. The balance between saving a prematurely ending live and the urge to obtain immortality should be found within the future regulations, in order to prevent unnatural extension of life of recipients at the expense of the lives of donors. [17-19]

European Association of Neurosurgical Societies published its statement on unethicity of the proposed treatment, stating, among many reasons, unfavourable risk-benefit ratio, no evidence of scientific validity - long term positive results in animal studies, as well as need for independent review. [20] Project is supposed to take place in China, country known for obtaining over 90% of transplants until 2010 from prisoners, and despite the 2014 legislative changes in this matter, no data proving improvements in the human rights violations in transplantation, has been published so far. [21]

5. CONCLUSIONS

Transplantation is both a miracle and a failure of modern medicine that can not cope with the reversal of disease processes. Despite the fact that head transplant procedure was planned for the year 2017 and the news about improvements of each step of the procedure are published, the development methods are still case reports/several animal subjects studies, rather than realistic achievements or long-term stable results.

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