

Stem cells procedure can modernize cleft palate repair

Current surgical techniques are long, complicated and ineffective

A constant problem in humans and animals, the cleft palate occurs when there is an opening in the palate – roof of the mouth. It can happen in different intensities, ranging from a small opening in the soft palate to the almost complete separation of the roof of the mouth. Since there is a risk of aspiration of food into the respiratory tract, the flaw should be corrected surgically. Currently, the techniques used for its repair are not satisfactory. Priscilla Domingues Mörschbacher, in her doctoral dissertation, defended at the end of March in UFRGS' Graduate Program in Veterinary Sciences, evaluated the use of polypropylene mesh, along with mesenchymal stem cells and fibrin sealant, for repairing the cleft palate in pigs.

This physical constitution problem may arise from congenital, traumatic, mechanical, hormonal, nutritional factors – deficiency of riboflavin, folic acid or vitamin A –, chronic infections and dental extractions. The defect can cause problems such as aspiration pneumonia, fat loss, rhinitis, nasal discharge, among other pathogens. It can be classified as primary, if it occurs in the lip and in the alveolus, or as primary and secondary, when it occurs in the lip and in the secondary palate, or even as secondary, when it occurs only in the secondary palate. The primary one is easily diagnosed because there is an abnormal opening in the upper lip. The secondary one is only diagnosed when some clinical signs appear, such as flow of milk through the nostrils, coughing, choking or sneezing during feeding.

According to Priscilla's research, the problem is between the 3rd and 4th most common congenital deformity in humans. Current methods for its repair present several problems. It is necessary that the child complete one or two years of life to perform the repair. Depending on the severity of the flaw, surgery can be delayed until the child reaches five to seven years, in order to avoid structural problems. In many cases, multiple procedures may be required. A plastic surgeon and/or

oral-maxillofacial surgeon perform corrective surgery on the face, while a dental surgeon, general surgeon, otolaryngologist and/or orthodontist make devices to correct other defects. Surgeons still face a shortage of material to correct the flaw.

The researcher uses tissue engineering to solve some of these limitations and considers the use of polypropylene mesh with mesenchymal stem cells (MSC) and fibrin sealant. "In the current techniques, many surgeries are necessary. The correction with stem cells comes precisely to avoid the great amount of procedures and the removal of pieces of the skin, as well as to preserve the patient from a possible rejection," says Priscilla. The development of the new technique for cleft palates reconstruction has taken into account the evaluation of the healing of the mucosal and bone tissues of the hard palate.

Materials

Stem cells are good candidates for cellular tissue engineering therapies as they are recruited by the body for the repair of injured tissues. Mesenchymal cells have the capacity to proliferate and originate another group of cells. In addition, they can easily differentiate themselves from other types of tissue. MSC is a term often applied to cells with high plasticity, adherent and that can be acquired from both bone marrow and adipose tissue. In the experiment, MSC derived from adipose tissue are used, since it presents better accessibility, safety of harvest and abundance of subcutaneous fat. In addition, it is easy to acquire – through liposuction – and it has low morbidity rates and high yield.



Cleft palate is among the four most frequent congenital deformities in humans – Photo: Senior Airman Peter Reft/U.S. Pacific Fleet

Polypropylene is the most used material in hernia restoration surgeries because it is low cost, non-biodegradable and has extensive tissue incorporation. Fibrin sealant improves and speeds up local healing.

Methodology

To verify the effectiveness of the new repair technique, 13 female pigs were used, with 34 to 36 days of life. One of the animals had its abdominal fat collected for the acquisition of stem cells. The other 12 were used for preparation and repair of cleft palate.

The study was developed in two stages: one *in vitro* and one *in vivo*. The *in vitro* research analyzed two techniques of stem cell cultivation in different culture plates using two types of polypropylene mesh – macroporous and microporous – during a period of 15 days. The goal was to identify the best interaction conditions between the mesh and the cells. In all forms of culture there were adherence of the cells, however, the best result was obtained with the microporous mesh in the period of seven days. For the *in vivo* study, the 12 pigs were divided into four groups and submitted to treatment with the following materials:

Group A - polypropylene mesh;

Group B - polypropylene mesh associated with adipose stem cell and fibrin sealant;

Group C - polypropylene mesh and adipose stem cell;

Group D - polypropylene mesh and fibrin sealant.

Results and possible applications

The pigs were examined for 15 days for evaluation of inflammation, healing and opening of sutures in the palate implant. In all cases there was complete scarring of the oral mucosa. It was observed that group D presented a higher degree of inflammation compared to the other groups.

The polypropylene mesh associated with stem cells (Group C) was the one that presented better performance, as it provided complete healing of the oral and nasal mucosa, as well as bone healing, proving to be a safe and effective technique. According to the researcher, this happens because the stem cells help to decrease the inflammation.

Priscilla says that the technique has the potential to be applied in humans and hopes that the work has a good reach between doctors and veterinarians. "I hope my research will help to correct the cleft palate in humans and animals."

Translated by Camila Wisnieski Heck, under the supervision and translation revision of Professor Elizamari R. Becker (PhD/UFRGS).

Dissertation

Title: Correção de fenda palatina com revestimento de tela de polipropileno associada a células-tronco mesenquimais de tecido adiposo e selante de fibrina em suínos: estudo *in vitro* e *in vivo*

Author: [Priscilla Domingues Mörschbacher](#)

Advisor: [Emerson Antonio Contesini](#)

Department: Graduate Program in Veterinary Sciences

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Universidade Federal do Rio Grande do Sul

Av. Paulo Gama, 110 - Bairro Farroupilha - Porto Alegre - Rio Grande do Sul

CEP: 90040-060 - Fone: +55 51 33086000

Directions

