8th International Meeting of the Portuguese Society for Stem Cells and Cell Therapies

In vivo evaluation of the potencial of mesenchymal stem cells (MSCs) from wharton jelly (WJ) to improve the biocompatibility of poly(vinyl) alcohol hydrogel (PVA) membranes in animal model (sheep).

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Introdução

The biocompatibility is a key aspect that can influence the performance of medical devices, for that reason inflammatory and foreign body reaction must be evaluated in pre-clinical studies. MSCs can modify the interaction of biomaterials with tissues by several mechanisms through the immunomodulatory effects of these cells allowing a faster biointegration avoiding an exuberant local inflammatory reaction (Martino et al).These immunomodulatory changes are linked to the suppression of inflammatory cytokines and to the induction of T cells with regulatory or suppressive phenotypes. For this reason, we have decided to evaluate the association of MSCs isolated from the umbilical cord WJ with PVA membranes in order to use this biomaterial in future as a scaffold for vascular reconstruction.

Materials and methods

PVA membranes were produced by a freeze/thawed method with a diameter of 15 mm and 3 mm thickness. In order to coat PVA membranes with MSCs they were seeded with a cell density of 10^4cells/cm^2 for 4 days. For the in vivo evaluation, 24 adult female sheep were divided in 4 groups of 6 animals each. In group 1, were used membranes of PVA and in group 2 PVA membranes coated with MSCs. The third group was referred as the sham surgery group. In the control group (group 4), expanded polytetrafluoroethylene membranes were implanted. General anesthesia was induced and 5 membranes of each material were implanted subcutaneously in each animal of the experimental groups. The samples (membranes and the surrounding tissue) were collected at 1, 2, 4, 8, 16 and 32 week's post-implantation (one animal per time point). The International standard (ISO 10993-6) for biological evaluation of medical devices was employed for assessment of the local effects after implantation of the different membranes with (or without) association with MSCs. The local effects were evaluated by a comparison of the tissue response caused by the tested implant to that caused by the control.

Conclusions

According to the present work it was possible to demonstrate that MSCs can decrease the inflammatory/foreign body reaction when associated to a synthetic biomaterial used in a wide range of biomedical applications.

References

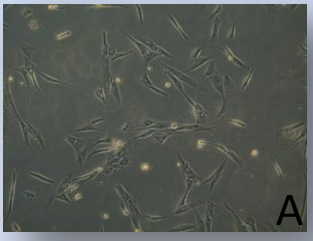
Martino, Sabata, et al. "Stem cell-biomaterial interactions for regenerative medicine." Biotechnology Advances 30.1 (2012): 338-51.

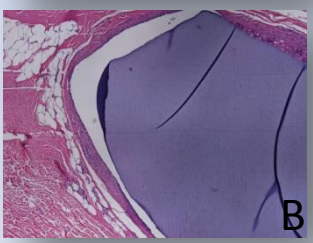
Results and discussion

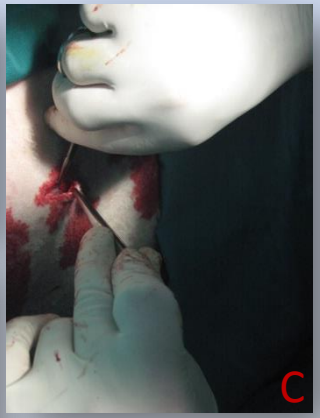
The highest values for the inflammatory parameter were observed up to week four. After this period the values showed a tendency to decrease (16 and 32 weeks). The PVA plus MSCs group (group 2) showed the lowest average value (3.166) for inflammatory response, which according to the ISO standard was considered slightly irritant (3 up to 8.9). The group 1, PVA membranes without MSCs, was also considered slightly irritant (average value of 5.466) to the surrounding tissues. Comparing group 1 and 2 at week 4 and 8, the average scoring value for inflammation was statistically considerable higher for group 1 (P<0.05; T-Student test). For the placebo group, the achieved scoring value (1.3) for inflammation despite being considered non-irritant confirms that the surgical procedure also has a role in the inflammation process of biomaterial implantation.

Table 1 – Scoring values for inflammation

Group	Weeks						
	1	2	4	8	16	32	Mean ±SD
1 PVA	(20,8 -20,4) **0,4**	(20-20) **0**	(21,6-11) **10,6**	(20,2-7,8) **12,4**	(21,8-12,4) **9,4**	(13-17) **0**	**5,46±5,40**
2 PVA plus MSCs	(18,6-20,4) **0**	(20,2-20) **0,2**	(20,6-11) **9,6**	(17-7,8) **9,2**	(10,6-12,4) **0**	(14,2-17) **0**	**3,16±4,40**
3 ePTFE	**20,4**	**20**	**11**	**7,8**	**12,4**	**17**	**14,76±26,19**
4 Sham surgery	(15,4-20,4) **0**	(11,2-20) **0**	(12-11) **1**	(14,6-7,8) **6,8**	(6-12,4) **0**	(5,8-17) **0**	**1,3±11,75**







A- MSCs culture, B- Tissue – PVA interface at 32 weeks post-surgery, C- Implantation procedure of PVA membranes.