Role of Quality Control Measures in Ensuring Production of Safe Autologous Platelet - Extracellular Vesicles (P-EV)

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INTRODUCTION:

Cell and Tissue Transplantation Laboratory, UM is a cGMP accredited facility, produces intraarticular P-EV injections for patients. P-EV has a high concentration of growth factors, helpful in treating musculoskeletal injuries involving tendon, cartilage and bone[1,2]. Quality control (QC) measures are essential throughout processing stages of P-EV. A retrospective analysis on the P-EV production over 6 years (2018-2023) was reviewed.

MATERIALS & METHODS:

Patients were pre-screened according to exclusion criteria before they gave consent for blood sample for serology test and initial platelet count. Only patients with negative serological results having 150-400 x (10^9/L) platelet count were included in P-EV treatment. P-EV was prepared by double-spin technique of the patient's 24-32 ml blood in ACD-A tubes. After the first spin, a small aliquot of red blood cells was cultured into T25 flask containing DMEM for pre-culture test. After the second spin isolating P-EV for 70-90 minutes, a small aliquot of P-EV sample was cultured into T25 flask for post-culture test. A small amount (0.5-1ml) of P-EV was transferred into an EDTA tube before aspirating the remaining P-EV into a 5ml syringe. All culture flasks were placed in CO_2 incubator for growth test and EDTA tube was for final platelet concentration. The P-EV was packed into sterile double layer polyethylene bag and sealed before sending to clinic for injection.

RESULTS:

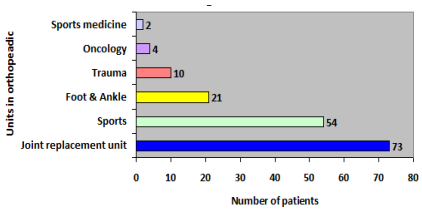

Figure 1: P-EV injections received by patients (2018-2023).

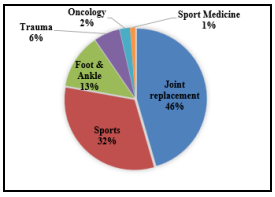

Figure 2: P-EV injections according to sub-specialties.

A total of 164 P-EVs were administered to 103 (62.8%) female and 61 (37.2%) male patients (Figure 1) with the mean age of 59.33 ± 12.81 years old, ranging from 22 to 86. Patients with single and bilateral knee osteoarthritis (OA) received the most injections, 81 (49.40%) and 48 (29.30%) respectively followed by 11 (6.7%) patients with medial meniscus injuries (Figure 2). Mean of initial and final platelet concentrations were 282.42±61.67 x (10^9/L) and 995.84±273.40 x (10^9/L) respectively with 4-fold increments.

DISCUSSION:

No motility of microorganisms was observed in the pre-post culture flasks elucidating that P-EV was processed in a sterile manner. A significant increase in platelet concentration ($p<0.05$) showed high staff competency in EV isolation techniques. No complaints received from patients and surgeons.

CONCLUSION:

Processing P-EV in a cGMP facility with controlled environment is perquisite. Stringent QC measures during P-EV production must be implemented to ensure CTTL produces safe and high-quality P-EV for patients.

REFERENCES:

1. Kikuchi N et al. Journal of Clinical Medicine. 2021; 10(21):5121.
2. Otero L et al. British Journal of Oral and Maxillofacial Surgery. 2017; 55(7):697-702.