(GraphPad Prism 8 software). All animal procedures were carried out with approval of the local Commission for Ethics in Animal Experimentation (University of Campinas; protocols 5790-1/6078-1). Different areas of the ventral region of mice were chosen for the analysis due to variations in vascularity and skin thickness when compared to the dorsum. Analyses of the entire images (total shaved area) of the mice demonstrated a significant reduction in the perfusion of the skin microvasculature after TNF-α (88 $\pm$ 5 units) administration, when compared with saline-treated mice (110 $\pm$15 units) ($p < 0.035$). The comparison of each region in the Saline- or TNF-α-treated mice suggested that Region 5 (abdomen and pelvis) was the only region that demonstrated decreased blood perfusion (Saline: 128 $\pm$8 units, TNF-α: 104 $\pm$ 5 units, $p < 0.0335$); the other regions presented reduced blood perfusion, but there was no statistical significance. Results suggest that the total area of the abdomen and pelvis is the best region to detect the variation in blood perfusion in the skin microvasculature using the LSCI technique in the Townes SCD mice model. Furthermore, the administration of a potent inflammatory molecule, known to induce vaso-occlusive-like processes in SCD mice, significantly decreased skin perfusion, confirming this method as suitable for analyzing and visualizing microcirculatory skin vaso-occlusion.

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INTRAVASCULAR HEMOLYSIS ACCELERATES NEOVASCULARIZATION AND ANGIOGENIC PROCESSES IN VIVO THAT ARE AMELIORATED BY HYDROXYUREA ADMINISTRATION

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Several diseases and pathological events incur intravascular hemolysis (IVH), a pathophysiological mechanism characterized by the destruction of red blood cells and the release of hemoglobin (Hb) and heme into the circulation. Hemolytic diseases, such as sickle cell disease (SCD), result in chronic inflammation and vascular damage due to the accumulation of plasma Hb and heme, which overload the homeostatic defense system. Hemolytic disorders are often associated with dysregulated angiogenic processes, contributing to complications that include proliferative retinopathy, pulmonary hypertension, leg ulcers and neovascularization of ischemic tissues. However, the role of hemolytic events in generating angiogenic factors and mechanisms is unclear. Therefore, the aim of this study was to investigate the effects of hemolysis on neovascularization and angiogenic parameters in an *in vivo* experimental model of IVH. C57BL/6J mice were subjected to chronic IVH, induced by the administration of low doses of phenylhydrazine (LDPHZ; 10 mg/kg.day i.p twice a week) for 4 weeks, while control mice (CON) received saline at the same frequency and during the same experimental period. Blood samples were collected 48 hours and plasma separated after the last induction. Matrigel® plugs pre-inoculated with 50 μL plasma from mice subjected to hemolysis, or not, were injected subcutaneously in mice for evaluation of neovascularization. Chronic IVH significantly increased plasma vascular endothelial growth factor (VEGF) levels ($p = 0.04$; $n = 5$) and liver VEGF expression ($p = 0.02$; $n = 4$) compared to saline mice. No significant differences were found in other angiogenic factors evaluated. Furthermore, factors present in the plasma of mice subjected to chronic IVH stimulated neovascularization and accelerated the formation of new vessels, as demonstrated by a significant increase in Hb levels quantified in the plug ($p = 0.04$; $n = 5$), compared to control plugs. Concurrently with hemolysis induction, an experimental group received treatment with hydroxyurea (LDPHZ+HU; 50 mg/kg.day i.p. five times a week) during the 4 weeks. LDPHZ+HU mice presented a trend towards increased VEGF protein expression in the liver ($p = 0.06$; $n = 4$) and the plasma factors of these HU treated mice reduced (although not significantly) Matrigel-plug neovascularization, when compared to neovascularization induced by LDPHZ plasma ($p = 0.06$; $n = 5$). An *in vivo* wound healing assay was also performed on the dorsal skin of mice subjected to IVH and treated or not with HU ($n = 2$). Preliminary results showed that wound healing was slower in the LDPHZ group when compared to the CON group, while treatment with HU improved the wound-healing process. Therefore, this study provides important perspectives for understanding the angiogenic mechanisms associated with IVH and may contribute to the development of therapies aimed at modulating neovascularization and minimizing complications associated with dysregulated angiogenic processes in patients with clinical complications of hemolytic diseases. **Funding:** FAPESP.

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APLICAÇÃO DO GEL DE ARNICA DURANTE A REALIZAÇÃO DO ULTRASSOM, PARA REDUÇÃO DA DOR AGUDA E LOCALIZADA NA DOENÇA FALCIFORME: UM ESTUDO PROSPECTIVO

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Introdução: O ultrassom é um método que tem a vantagem de não requerer ingestão ou injeção de medicamentos. O alívio da dor ocorre exclusivamente em consequência dos estímulos ultrassônicos aplicados sobre a pele, à utilização do gel de arnica será um somatório neste efeito analgésico, será feita uma única aplicação durante a dor aguda, com duração de 10 minutos. Quando o ultrassom penetra no corpo, o efeito das vibrações move todas as partículas internas e estimula a reabsorção do líquido inflamatório, no momento da crise vaso oclusiva existe um processo inflamatório na membrana do endotélio vascular. A ultrassonografia transmite energia ao tecido que atravessa produzindo calor. Outro efeito é o aumento da permeabilidade da membrana celular que