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Expression of Procoagulant Activity by Lysophosphatidic Acid in Human Platelets

Seung Min Chung, Ok Nam Bae and Jin Ho Chung
College of Pharmacy, Seoul National University

Lysophosphatidic acid (LPA), an important mediator in blood clotting and wounds healing, has been recently reported to induce influx of extracellular calcium into erythrocytes (RBC). This elevation in intracellular calcium level may cause destruction of membrane asymmetry and microvesicle formation, resulting in procoagulant activity of RBC. Thus, we investigated if LPA could induce phosphatidylserine (PS) exposure and microvesicle formation as a result of extracellular calcium influx in human RBC. Treatment with LPA to RBC resulted in microvesicle generation in a time-, and concentration- dependent manner. Consistent with these findings, scanning electron microscopy studies revealed that LPA treatment changed normal discocytic shape into echinocyte followed by spherocyte. Both microvesicles and remnant erythrocytes expressed procoagulant PS on their surface membrane in a concentration-dependent manner. Chelation of extracellular calcium with EGTA did not affect vesiculation and PS exposure, suggesting that calcium influx into RBC was not responsible for these events. Suramin that can block the interaction of LPA with its receptor did not inhibit microvesicle formation, indicating that this LPA-induced response in RBC might not be mediated by the known receptor but simply due to the amphiphilic character of LPA itself. LPA-exposed RBC potentiated the generation of thrombin by human recombinant thromboplastin in plasma. These results suggest that LPA-exposed erythrocytes can express procoagulant activity in RBC mediated by microvesicle formation and PS exposure, possibly leading to clot formation or thrombosis.
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