ADENOSINE DIPHOSPHATE-INDUCED PLATELET AGGREGATION IS ENHANCED IN PLATELET-RICH PLASMA OBTAINED FROM PATIENTS WITH PRIMARY ANTIPHOSPHOLIPID SYNDROME WITH THROMBOSIS

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Introduction: The majority of the studies evaluated the direct effect of antiphospholipid antibodies isolated from APS patients in platelets obtained from healthy volunteers. The literature is scarce about platelet activity obtained from patients with primary antiphospholipid syndrome with thrombosis (t-PAPS). **Aims:** To evaluate platelet function in platelet-rich plasma (PRP) obtained from patients with t-PAPS or healthy volunteers. **Methods:** Forty patients with t-PAPS (62.5% females, mean age: 44 years) and 62 volunteers with no history of thrombosis (64.5% females, mean age: 38 years) were included. Firstly, PRP was obtained and stimulated with adenosine diphosphate (ADP, 3 or 10 μM), collagen (1 μg/mL) or arachidonic acid (AA, 300 μM). Next, PRP was pre-incubated with platelets inhibitors, as nitric oxide donor, sodium nitroprusside (SNP, 3 or 10 μM) or the stable analogue of prostacyclin, iloprost (ILO, 3 or 10 nM), and then stimulated with ADP 3 μM. In another set of experiment, ticagrelor, a P_2Y_{12} receptor antagonist (2 μM) was also incubated in PRP. Second, washed platelet (WP) from t-PAPS patients was obtained for P_2Y_{12} protein and cyclic nucleotides quantification. In another assay, WP from healthy volunteers was incubated with IgG antibodies (500 μg/mL, 30 min) isolated from the serum of healthy volunteers or t-PAPS patients and then stimulated with ADP 30 μM in the absence and in the presence of ticagrelor (2 μM). **Results:** ADP-induced platelet aggregation was significantly higher in t-PAPS group than in controls (ADP 3 μM: 69.3% ±23.8% vs 57.8% ± 24.3%, p = 0.02). No difference in AA- (52% ± 33.2% vs 56% ± 29.1%, P = 0.95) or collagen- (72% ± 19.3% vs 72.4% ± 17.3%, p = 0.51) -induced aggregation was seen between groups. The amplitude of platelet inhibition induced by SNP 3 μM (46.4% ±25.8% vs 34.7% ± 20.9%, p = 0.02) and 10 μM (31.4% ± 23.1% vs 18.8% ±14.9%, p = 0.008) or ILO 3 nM (23.3% ± 23.3% vs 12.1% ± 14%, p = 0.02) was less prominent in platelets from t-PAPS than in control volunteers. The intraplatelet levels of cAMP (6.3 ± 5.1 pmol/10^8 platelets vs 14.6 ± 8.1 pmol/10^8 platelets, p = 0.01) and cGMP (2.3 ± 1.7 pmol/10^8 platelets vs 4.6 ± 1.9 pmol/10^8 platelets, p = 0.01) was significant reduced in platelets from t-PAPS than in healthy volunteers. In platelets from t-PAPS patients the protein expression for the P_2Y_{12} receptor was significantly greater than in platelets from healthy volunteers (0.81 ± 0.23 vs 0.53 ± 0.24, p = 0.01). The IgG antibodies obtained from t-PAPS patients produced greater amplitude of aggregation in ADP-stimulated platelet than in platelets stimulated with IgG antibodies obtained from healthy volunteers (66.2% ± 7.9% vs 52.2% ± 10.6%, P = 0.006). Ticagrelor practically abolished ADP-induced aggregation in both PRP from control and t-PAPS patients (12.9% ±6.7% vs 10.2% ± 6.4%, p = 0.09) and in WP treated with IgG antibodies (0.3% ±0.6% vs 0.0% ±0.0%, p = 0.4). **Discussion:** Platelet activity from t-PAPS patients was enhanced upon ADP stimulation, but not by collagen or AA, mainly due to higher protein expression for P_2Y_{12} receptor subtype and lower intraplatelet levels of cAMP and cGMP. **Conclusions:** Our findings suggest that ADP receptor antagonists can be considered as first-line therapy to treating patients with t-PAPS or in those who have contraindications to receiving aspirin.

https://doi.org/10.1016/j.htct.2021.10.405

ANÁLISE DA ALTERAÇÃO DO D-DÍMERO EM PACIENTES COM COVID-19

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Objetivos: Em março de 2020, foi descrito pelas autoridades de saúde brasileiras os primeiros casos de infecção pelo SARS-CoV-2, vírus responsável pela Covid-19, no Brasil. Desde então, houve uma intensa mobilização científica para descobrir cada vez mais sobre a doença e suas consequências a curto e longo prazo. Sob esse aspecto, levantou-se a hipótese de uma relação entre o aumento de marcadores da coagulação, como o d-dímero, e a severidade da doença. Diante disso, o presente estudo tem como intuito realizar uma revisão literária sobre as alterações da dosagem do d-dímero observadas em pacientes com Covid-19. **Materiais e métodos:** Foi realizado um estudo de revisão bibliográfica a partir da análise de 9 artigos científicos publicados entre os anos de 2020 e 2021. Os materiais foram selecionados utilizando os seguintes critérios de inclusão: abordagem do tema e disponibilidade em acesso aberto. Assim, foram selecionados 3 artigos na base de dados do PubMed, utilizando como termos de pesquisa: “Covid-19” e “Fibrin Fibrinogen Degradation Products”, terminologias de acordo com o sistema de Descritores em Ciências da Saúde (DeCS). **Resultados:** De acordo com a literatura, a Covid-19, hoje reconhecida como uma desordem sistêmica e não mais somente uma síndrome respiratória aguda, pode levar à indução de um estado pró-trombótico. Nesse viés, segundo literatura, foi observado que a dosagem do d-dímero, produto de degradação da fibrina, era maior nos pacientes que não sobreviveram. Assim, pôde-se perceber que os níveis de d-dímero em pacientes hospitalizados com a doença é diretamente proporcional à mortalidade pela infecção, e o risco já se torna significativamente maior quando os níveis de d-dímero estão acima de 1,0 mg/L. Por isso, o d-dímero pode ser considerado um fator preditor independente da morte de pacientes hospitalizados com Covid-