centros; volume coletado, os quimioterápicos e o corticóide utilizados variaram entre os centros e foram de acordo com protocolo de tratamento utilizado. Da amostra/análise: o tempo de processamento de amostras foi de até 1 hora em 12/20 centros respondedores e entre 2-3h em 3 centros (utilização de conservante); 85,7% dos centros fazem análise citomorfológica independente da contagem de células sendo 52,4% realizada por bioquímico; 11/21 tem avaliação liquorica por ICF disponível, e na maioria dos centros é realizada ao diagnóstico ou na suspeita de recaída. O guia de recomendações gerado a seguir contemplou 4 partes: I- Punção lombar e coleta de LCR, II- Quimioterapia intratecal, III- Processamento do LCR, IV- Análise Imunofenotípica de LCR. Conclusão: O questionário permitiu identificar uma variabilidade nas etapas de coleta, manuseio de quimioterapia intratecal e análise de LCR no cenário brasileiro, com possibilidade de impacto direto no sucesso terapêutico dos pacientes pediátricos. Esses achados justificaram a criação de um guia de boas práticas em punção e análise de LCR, baseado em literatura e experiência dos centros participantes, com o objetivo de equalizar a rotina do oncologista/hematologista pediátrico, obter reprodutibilidade dos processos e o benefício final dos pacientes pediátricos.

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PEDIATRIC CEREBRAL SINUS VENOUS THROMBOSIS (CSVT) IN A BRAZILIAN SINGLE-CENTER: A 3-YEAR RETROSPECTIVE ANALYSIS OF A MULTIDISCIPLINARY EXPERIENCE

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Objectives: CSVT is rare in pediatric patients but is related to considerable morbidity and mortality. Its etiology is multifactorial: infections, head trauma, cancer and some chronic inflamatory diseases are some of the risk factors. Clinical manifestations are variable and non specific: headache, seizure, focal neurologic deficit and impaired consciouness. Pathogenesis involves venous obstructive ouflow which results in impaired drainage of cerebrospinal fluid and increased intracranial pressure. Diagnosis involves a high suspicious index and an adequade neuroimaging. Management consists of suportive care, anticoagulation and treatment of the neurologic complications. This sudy has the purpose of describing a cohort of pediatric CSVT. **Materials and methods:** Patients under 18 years diagnosed with CSVT between august 2021 to august 2024 were retrospectively included. Demographic informations, signs and symptoms, laboratory parameters, management information, venous recanalization rate, chronic complications and follow-up were evaluated. **Results:** 22 patients were included, 72.7% male and 27.2% female. Median age at diagnosis was 9.8 years (0.16–17). Headache was the most common clinical manifestation (72.2%). In 90.9% of patients at least one risk factor for CSVT was present and infections were the most common (40.9%). 63.6% had more than one sinus affected and 22.7% had cerebral venous infarct. Median values of aPTT, PT, fibrinogen and platelet count were normal and median D-dimer was 3.598ng/mL (275-21373). Complete treatment and follow-up data were available in 17 patiens. Treatment included anticoagulation with enoxaparin in all patients and 2 completed antithrombotic therapy with rivaroxaban. Acetazolamide and lumbar puncture were necessary in 35.2% for high intracranial pressure control. One patient (5%) needed surgical thrombectomy. Median time of anticoagulation was 5.4 months (2.6-13.5) with 62.5% of patients with complete venous recanalization. There was no death related to CSVT but 11.7% had chonic motor sequelae. Median time of follow-up was 1.4 years (0.3-2.3) with 5.8% of recurrence thrombosis. **Discussion:** This is the first brazilian cohort of pediatric CVST. Infections were the most common risk factor. There were no clear correlation between number of sinuses affected and acute and chronic neurologic complications. Despite a small number of patients, some patients were treated with direct oral anticoagulants. The cooperation of hematology, neuroradiology, neurology and neurosurgery was essential. This cohort has limitations and some similar findings of other studies, but it highlights the role of pediatric hematologists in the approach of thromboembolic events, and also emphasizes the need of multidisciplinarity from diagnosis to acute and chronic management of pediatric thrombosis. **Conclusion:** CVST as other pediatric thrombosis needs a multiciplinary team for adequate acute and long term treatment. Multicentric studies are needed to establish more concrete data about CVST in pediatric population in Brazil.

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INTERACTION BETWEEN HAPLOTYPES OF BCL11A AND HBS1L-MYB, MAJOR QUANTITATIVE TRAIT LOCI FOR FETAL HEMOGLOBIN (HBF) LEVELS, AND INCIDENCE OF CLINICAL PHENOTYPES IN CHILDREN WITH SICKLE CELL ANEMIA

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Sickle cell anemia (SCA) is a monogenic disease characterized by HbSS genotype with a complex pathophysiology. Fetal hemoglobin(HbF) is the major modifier of clinical phenotypes, and increased HbF levels inhibit polymerization of HbS and ameliorate clinical severity of SCA. GWAS have identified the BCL11A gene and HBS1L-MYB intergenic region as major quantitative trait loci for regulation of HbF expression. We identified functional SNPs of BCL11A and HBS1L-MYB

associated with increased HbF concentration and milder clinical phenotypes in children with SCA. Moreover, we found HbF-boosting haplotypes formed by these SNPs to be associated with reduced rate of clinical outcomes in children with SCA: BCL11A haplotype with the minor alleles of rs1427407, rs766432, and rs4671393 ("TCA") was associated with higher HbF, total hemoglobin, and lower reticulocyte count compared to reference haplotype "GAG"; the HBS1L-MYBhaplotype with the minor alleles of rs9399137, rs4895441, and rs9494145 ("CGC") was associated with higher HbF and total hemoglobin compared to reference haplotype "TAT". We further found that these HbF-boosting haplotypes may interact to regulate HbF levels. However, no previous study has examined their interaction and association with risks of vaso-occlusive and hemolytic complications of SCA. Objective: We examined whether the interaction of HbF-boosting haplotypes of BCL11A and HBS1L-MYB modifies their individual effect on the rate of transfusion, acute chest syndrome (ACS), pain crisis, infection and acute splenic sequestration (ASS). Methods: We analyzed a retrospective cohort of 220 unrelated children with SCA recruited from the Center of Hematology and Hemotherapy of Minas Gerais State. Haplotype frequencies were estimated using Haplo.stats. Reference and minor haplotypes combined wild-type and minor SNP alleles for BCL11A (GAG or TCA) and HBS1L-MYB (TAT or CGC), respectively. We grouped children who carry ("TCA+"or "CGC+") or not carry ("TCA-"or "CGC-") the "TCA"and "CGC"minor haplotypes, respectively. Incidence of clinical outcomes was reported by relative rates to 10 patient-years, with 95% confidence intervals. Incidence Rate Ratio of clinical outcomes was compared between haplotype combinations using OpenEpi online software. Cumulative incidence of ASS was estimated using Kaplan –Meier and logrank test to compare the incidence between haplotypes using SPSS. Results: Non-carriers of both HbF-boosting haplotypes (TCA-/CGC-) had a significantly higher need for transfusion than children carrying only the HbF-boosting haplotype of BCL11A (TCA+) or those carrying both HbF-boosting haplotypes (TCA+/CGC+). Regarding ACS and infection, non-carriers of both HbF-boosting haplotypes (TCA-/CGC-) had a significantly higher risk of events than children carrying only the BCL11A (TCA+) or HBS1L-MYB (CGC+) haplotypes. Carriers of both HbF-boosting haplotypes (TCA+/CGC+) did not show significant lower rate of ACS and infection. Cumulative incidence of ASS was marginally significant lower (P = 0.051) in children carrying only the HbF-boosting haplotype of BCL11A (TCA +/CGC-) than the HBS1L-MYB (TCA-/CGC+) or non-carriers of both haplotypes (TCA-/CGC-). Discussion: Our findings showed that the presence of the HbF-boosting haplotypes don't make a difference in rate of ACS, ASS and infection. On the other hand, our data support that the presence of, at least, one of the HbF-boosting haplotypes are related to lower rates of transfusion. Conclusion: Therefore, our novel findings contribute to understand multilocus interactions underlying molecular basis of major clinical events of SCA.

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RESPOSTA À TERAPIA IMUNOSSUPRESSORA EM CRIANÇAS COM ANEMIA APLÁSTICA E HEMOGLOBINÚRIA PAROXÍSTICA NOTURNA

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Objetivos: Avaliar a presença de clone de Hemoglobinúria Paroxística Noturna (HPN) em crianças com Anemia Aplástica grave (AAG) e sua correlação como fator preditor de resposta à terapia imunossupressora (TI). **Materiais e métodos:** Estudo retrospectivo, baseado em coleta de dados de prontuários de pacientes pediátricos com AAG, tratados no Hospital Infantil Darcy Vargas de 2003 a 2021 e que receberam terapia imunossupressora com timoglobulina de cavalo ou de coelho associada a ciclosporina. Todos os pacientes incluídos realizaram citometria de fluxo para HPN ao diagnóstico ou em algum momento durante o seguimento. Considerado clone HPN positivo se > 0,15% em neutrófilos ou monócitos, e a resposta terapêutica foi avaliada aos 6 e 12 meses do início da TI. Para verificar a correlação da presença de clone HPN como fator preditor de resposta à TI realizado teste exato de Fisher. **Resultados:** Participaram do estudo 35 pacientes, de 2 a 17 anos, com média de 10 anos (±3,81), sendo 80% do sexo masculino. Todos os pacientes tinham DEB teste negativo e citogenética de medula óssea normal. Clone HPN foi encontrado em 53,1% dos pacientes. Dos 35 pacientes que participaram do estudo, ocorreram três óbitos precoces, assim, 32 pacientes tiveram resposta à imunossupressão avaliada 6 meses após início do tratamento e em 30 pacientes foi avaliada a resposta aos 12 meses, pois um paciente perdeu seguimento e outro realizou transplante de medula óssea. O tempo de seguimento variou de 7 meses a 13 anos, com média de 6,1 anos (±3,53). O clone permaneceu estável em 58,8% dos casos, aumentou em 17,7% e diminuiu ou desapareceu em 23,5%, nenhum paciente com ausência de clone HPN ao diagnóstico positivou durante o acompanhamento. Dos 32 pacientes avaliados aos 6 meses, 13 (40,6%) tiveram resposta parcial à TI e nenhum resposta completa. Aos 12 meses, 15 (50%) pacientes responderam, sendo, 11 com resposta parcial e 4 com resposta completa. Aos 6 meses houve resposta à TI em 10 (58.8%) dos 17 pacientes com clone HPN e apenas em 3 (20%) dos 15 pacientes sem clone HPN (p = 0,036) e aos 12 meses, houve resposta em 11 (68.8%) dos 16 pacientes com clone HPN e em 4 (28,6%) dos 14 sem clone (p = 0,065). **Discussão:** A HPN clássica é rara na pediatria, porém sua associação com AA é semelhante a encontrada em adultos. Existem poucos estudos em crianças que avaliaram a presença de clone HPN na AAG e sua relação com resposta à TI. Outro ponto importante é a definição do tamanho do clone HPN, pois a falta de padronização nos estudos em definir o tamanho do clone a ser considerado, pode se tornar um viés na correlação com a resposta terapêutica. Nesse estudo, encontramos clone HPN em 53,1% dos pacientes com AAG, semelhante ao encontrado na literatura exclusivamente pediátrica, com variação de 39-73%. Em adultos diversos estudos correlacionam a presença do clone a melhor resposta à TI, entretanto na pediatria esta boa correlação permanece discutível, uma vez que os poucos estudos diferem entre si, sendo o nosso estudo mais um a verificar que a presença de clone HPN pode ser um preditor de