

da mutação em JAK2, 27% não tinham acesso a exames para pesquisa de CALR e MPL, enquanto 47% possuíam apenas no ambiente privado. O sequenciamento de nova geração (NGS) não estava disponível para 60% dos profissionais. Apesar de quase todos possuírem acesso ao exame de cariótipo, quase 30% não o solicitam no diagnóstico. Apenas 12,5% usam o escore MPN SAF para avaliar a carga de sintomas de seus pacientes. Em relação a MF secundária, a minoria (22%) utiliza o escore MYSEC para estratificação de risco. Quando questionados acerca do manejo de trombose venosa profunda em pacientes com Ph- NMPs, houve grande discordância entre as respostas, com a maioria preferindo anticoagulação contínua (30%) ou mudando a conduta de acordo com a estratificação de risco (30%). Para o tratamento da MF, os inibidores de JAK2 estão disponíveis quase exclusivamente em ambientes privados (67%). Para pacientes com MF de alto risco, 79% dos entrevistados consideraram o transplante alogênico de medula óssea como uma opção de tratamento. Em relação aos desafios no manejo das Ph- NMPs, 82% citaram a solicitação de exames moleculares e genéticos como a principal dificuldade, enquanto 71% identificaram o acesso a terapias mais recentes. **Discussão e conclusão:** Este é o primeiro levantamento brasileiro sobre o manejo de pacientes com Ph- NMPs. Ele destaca dificuldades no acesso a diagnóstico e tratamento, particularmente no sistema público de saúde. Além disso, destaca a subutilização de questionários de sintomas na avaliação dos pacientes, assim como discordância de condutas em alguns cenários clínicos, como por exemplo na anticoagulação de pacientes com Ph- NMPs. Os dados ainda estão sendo coletados, com a expectativa de números mais robustos para análises futuras. Essas informações podem nos ajudar a compreender não apenas nossas práticas como médicos brasileiros, mas também possíveis lacunas de conhecimento e os principais problemas de acesso.

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BCR-ABL1 KNOCKDOWN IN LEUKEMIC CELLS USING A HYBRID NANOPARTICLE-BASED siRNA DELIVERY STRATEGY

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Introduction: Chronic myeloid leukemia (CML) is a myeloproliferative neoplasm characterized by the presence of the mutant BCR-ABL1 gene, which encodes a constitutively active tyrosine kinase that drives uncontrolled cell proliferation. Despite the efficacy of tyrosine kinase inhibitors (TKI), the development of resistance remains a major therapeutic challenge. Therefore, there is a growing interest in alternative strategies to enhance treatment success in CML. In this context, small interfering RNA (siRNA) have garnered attention due to their ability to induce gene knockdown selectively.

However, efficient delivery systems are essential to ensure that siRNA reach target cells intact. Considering these factors, hybrid nanoparticles (HNP) emerge as a potential platform for siRNA encapsulation and delivery, given their high biocompatibility and versatility. **Objectives:** This study aimed to induce knockdown of the BCR-ABL1 gene in K562 cells using nanoencapsulated siRNA, and to evaluate both the delivery efficiency to target cells and the safety profile of the HNP used as delivery vehicle. **Material and methods:** HNP were synthesized via self-assembly from the stoichiometric mixing of two buffer solutions containing CaCl₂, TRIS-HCl (pH 7.4), HEPES (pH 7.4), Na₃PO₄, polyethylene glycol, and siRNA. Particle morphology was assessed by dynamic light scattering (DLS) and transmission electron microscopy (TEM). siRNA delivery was evaluated by fluorescence microscopy in K562 (CML), HS-5 (bone marrow stroma), and HUVEC (vascular endothelium) cell lines using the BLOCK-iT™ Alexa Fluor® Red Fluorescent Control kit. The cytotoxicity of empty nanoparticles (Mock HNP) was assessed in the same cell lines using the CellTiter 96® Aqueous One Solution Cell Proliferation Assay after 24, 48, and 72 hours of incubation. Additionally, a novel siRNA sequence targeting BCR-ABL1 was designed and encapsulated, and its gene silencing efficacy was evaluated in K562 cells via RT-qPCR after 24 and 48 hours of incubation. **Results:** The synthesized HNP had an average diameter of 54.4 nm and appeared spherical under TEM. Fluorescence microscopy confirmed that HNP successfully delivered the nucleotides into target cells. Mock HNP exhibited low cytotoxicity, with a decrease in cell viability observed only at higher concentrations, above 1200 nM, after 48 and 72 hours in HUVEC and HS-5 cells. In K562 cells, no significant reduction in viability was observed at any concentration or time point tested. Finally, RT-qPCR analysis showed that the designed siRNA, at a concentration of 200 nM, reduced BCR-ABL1 expression by 48% after 24 hours and by 56% after 48 hours of incubation. **Discussion and conclusion:** The results demonstrate that the synthesized HNPs exhibit suitable morphology, low cytotoxicity, and efficient siRNA delivery to target cells, including those relevant to the CML microenvironment. Moreover, the novel siRNA sequence effectively silenced the target gene in leukemic cells that comprise a liquid tumor type. These findings support the conclusion that the synthesized HNP proved to be a safe and effective system for delivering siRNA targeting BCR-ABL1, leading to significant gene silencing in CML cells. These results highlight the potential of this approach for RNA-based therapies, especially in overcoming resistance to TKI.

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BICITOPENIA E COMPLICAÇÕES HEMORRÁGICAS EM LEUCEMIA MIELOIDE CRÔNICA (LMC) E TRAUMATISMO CRANIOENCEFÁLICO

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