BRAZILIAN JOURNAL OF IMPLANTOLOGY AND HEALTH SCIENCES

ISSN 2674-8169

Drug Candidates for COVID-19 Treatment in Brazil: Updated Review and New Therapeutic Approaches

Marvin Gonçalves Duarte, Gracielle Radja Rodrigues de Lima, Juliana Perez Leyva Ataíde, Letícia Almeida Guedes de Lima, Ana Carolina Bastos do Rêgo, Rodolfo Scavuzzi Carneiro da Cunha, Eudoro de Queiroz Marques Filho, Rosana Maria Coelho Travassos, Ailton Coelho de Ataíde Filho, Luciano Barreto Silva

https://doi.org/10.36557/2674-8169.2025v7n4p617-628
Artigo recebido em 03 de Março e publicado em 13 de Abril de 2025

LITERATURE REVIEW

ABSTRACT

Background: The COVID-19 pandemic has evolved rapidly, causing significant global mortality and straining healthcare systems. While new therapeutic strategies are continually emerging, several repurposed drugs have been evaluated for their potential efficacy against SARS-CoV-2. Recent advancements in treatment protocols and the emergence of new variants necessitate an updated analysis of therapeutic options. **Objective:** This review critically analyzes the role of repurposed drugs, including chloroquine, ivermectin, and nitazoxanide, as well as corticosteroids, immunomodulators, and novel antiviral strategies for the treatment of COVID-19 in Brazil. The discussion incorporates emerging evidence from clinical trials and the latest research on treatment responses to new variants of the virus. **Methodology:** This study synthesizes evidence from clinical trials, systematic reviews, and meta-analyses available in databases such as PUBMED, BVS/BIREME, Web of Science, Science Direct, CAPES Portal, Cochrane Library, and PROSPERO. Studies evaluating the efficacy and safety of repurposed drugs and novel interventions in different phases of the disease were included. **Results:** While chloroquine, ivermectin, and nitazoxanide initially showed in vitro antiviral activity, randomized controlled trials have not demonstrated significant clinical benefits. However, dexamethasone and other corticosteroids remain the cornerstone for managing severe COVID-19 cases with respiratory failure. Additionally, monoclonal antibodies, antiviral drugs like remdesivir and molnupiravir, and immunomodulatory therapies, such as tocilizumab and baricitinib, have emerged as effective options, particularly against severe disease forms caused by new variants. **Conclusion:** Although initial enthusiasm for repurposed antiparasitic drugs has waned due to lack of robust evidence, corticosteroids, targeted antiviral therapies, and immunomodulators have demonstrated efficacy, especially in severe cases. Ongoing research is essential to refine treatment protocols and optimize therapeutic strategies for emerging SARS-CoV-2 variants.

Keywords: COVID-19; Therapeutics; Adrenal Cortex Hormones; Antiviral Agent; Monoclonal Antibodies; Immunologic Factors.

Candidatos a fármacos para tratamento da COVID-19 no Brasil: revisão atualizada e novas abordagens terapêuticas

RESUMO

Contexto: A pandemia da COVID-19 evoluiu rapidamente, causando mortalidade global significativa e sobrecarregando os sistemas de saúde. Enquanto novas estratégias terapêuticas surgem continuamente, vários medicamentos reaproveitados foram avaliados quanto à sua eficácia potencial contra o SARS-CoV-2. Avanços recentes nos protocolos de tratamento e o surgimento de novas variantes exigem uma análise atualizada das opções terapêuticas. **Objetivo:** Esta revisão analisa criticamente o papel dos medicamentos reaproveitados, incluindo cloroquina, ivermectina e nitazoxanida, bem como corticosteroides, imunomoduladores e novas estratégias antivirais para o tratamento da COVID-19 no Brasil. A discussão incorpora evidências emergentes de ensaios clínicos e as pesquisas mais recentes sobre respostas ao tratamento de novas variantes do vírus. **Metodologia:** Este estudo sintetiza evidências de ensaios clínicos, revisões sistemáticas e meta-análises disponíveis em bancos de dados como PUBMED, BVS/BIREME, Web of Science, Science Direct, Portal CAPES, Biblioteca Cochrane e PROSPERO. Estudos avaliando a eficácia e a segurança de medicamentos reaproveitados e novas intervenções em diferentes fases da doença foram incluídos. **Resultados:** Embora cloroquina, ivermectina e nitazoxanida tenham mostrado inicialmente atividade antiviral in vitro, ensaios clínicos randomizados não demonstraram benefícios clínicos significativos. No entanto, dexametasona e outros corticosteroides continuam sendo a pedra angular para o tratamento de casos graves de COVID-19 com insuficiência respiratória. Além disso, anticorpos monoclonais, medicamentos antivirais como remdesivir e molnupiravir e terapias imunomoduladoras, como tocilizumabe e baricitinibe, surgiram como opções eficazes, principalmente contra formas graves da doença causadas por novas variantes. **Conclusão:** Embora o entusiasmo inicial por medicamentos antiparasitários reaproveitados tenha diminuído devido à falta de evidências robustas, corticosteroides, terapias antivirais direcionadas e imunomoduladores demonstraram eficácia, especialmente em casos graves. Pesquisas em andamento são essenciais para refinar protocolos de tratamento e otimizar estratégias terapêuticas para variantes emergentes do SARS-CoV-2.

Palavras-chave: COVID-19; Terapêutica; Corticosteroides; Antivirais; Anticorpos Monoclonais; Fatores Imunológicos.

Autor correspondente: Marvin Gonçalves Duarte - marvingduartee@gmail.com

INTRODUCTION

Throughout history, pandemics have significantly impacted human civilization. The 1918 influenza pandemic, caused by the H1N1 virus, infected an estimated 500 million people in a pre-antibiotic and pre-antiviral era, leading to catastrophic mortality (Johnson & Mueller, 2002). Similarly, the emergence of SARS-CoV-2 in late 2019 has challenged global healthcare systems.

SARS-CoV-2, a betacoronavirus closely related to SARS-CoV-1, rapidly spread worldwide, prompting an urgent search for effective treatments. The scientific community initially focused on repurposed drugs, particularly those with known antiviral properties. However, as the virus evolved, new variants emerged with different pathogenic characteristics, necessitating continuous updates in treatment strategies (Gandhi, 2022).

Brazil, one of the most affected countries, adopted various therapeutic approaches, some of which were controversial. This review aims to analyze current drug candidates for COVID-19 treatment in Brazil, with an emphasis on updated clinical evidence, emerging therapeutic options, and their efficacy against recent SARS-CoV-2 variants.

COVID-19 Classification and Treatment Approaches in Brazil

Hospitals in Recife were among the first in Brazil to implement structured treatment protocols based on international experiences, particularly from Spain. The disease has been classified into three stages, guiding therapeutic decisions:

- Stage 1 - Viral Replication Phase: Initial symptoms include fever, malaise, sore throat, anosmia, and gastrointestinal disturbances. Antiviral treatments, including remdesivir, molnupiravir, and paxlovid, have been explored for early intervention (Gottlieb, 2021).

- Stage 2 - Inflammatory Phase:

- Phase 2A: Mild lung involvement without hypoxia. Supportive care, anti-inflammatory agents, and selective antiviral treatments may be considered.
- Phase 2B: Progressive lung inflammation with hypoxia. Dexamethasone, tocilizumab, and baricitinib are now preferred for managing hyperinflammation (RECOVERY Trial, 2020).

- Stage 3 - Hyperinflammatory and Life-Threatening Phase: Characterized by cytokine storm, multi-organ failure, and high mortality. IL-6 inhibitors (tocilizumab), JAK inhibitors (baricitinib), and corticosteroids play crucial roles.

Updated Therapeutic Approaches

Drug Class	Examples	Mechanism of Action	Current Evidence
Antivirals	Remdesivir, Molnupiravir and Paxlovid	Inhibits viral replication	Reduces hospitalization risk in high-risk patients (Beigel, 2020)
Monoclonal Antibodies	Casirivimab/Imdevimab, Sotrovimab	Neutralizes viral spike protein	Effective against early-stage COVID-19 (Weinreich, 2021)
Corticosteroids	Dexamethasone, Methylprednisolone	Reduces inflammation and cytokine storm	Reduces mortality in severe cases (RECOVERY Trial, 2020)

Immunomodulators	Tocilizumab, Baricitinib	Blocks IL-6 and JAK pathways	Reduces progression to mechanical ventilation (Marconi, 2021)
Anticoagulants	Enoxaparin, Rivaroxaban	Prevents thrombotic complications	Reduces COVID-19-associated coagulopathy (TICOVID, 2021)
Adjunctive Therapies	Vitamin D, Zinc	Supports immune function	Limited evidence (Martineau, 2021)

MATERIALS AND METHODS

During the development of this narrative review article, it was essential to

establish a methodological strategy to ensure the inclusion of the most current, relevant, and scientifically validated information on the topic, providing robust and well-supported content. Searches were conducted across multiple databases, including DeCs, BVS/BIREME, PROSPERO, SciELO, PubMed Central, ScienceDirect, Web of Science, and The Cochrane Library, in conjunction with Google Scholar. Additionally, gray literature was utilized to provide supplementary and relevant insights, which proved crucial for a comprehensive exploration of the subject matter. To refine the scope and relevance of the searches, the following descriptors were employed: COVID-19; Therapeutics; Adrenal Cortex Hormones; Antiviral Agent; Monoclonal Antibodies and Immunologic Factors. Given the narrative review format, it was necessary to adopt a framework that defines the structure, essential elements, and exclusions pertinent to this type of study. Consequently, Rother's (2007) work served as a methodological guide throughout the preparation of this article, ensuring consistency and adherence to the standards of narrative literature reviews.

RESULTS AND DISCUSSION

The COVID-19 pandemic has posed unprecedented challenges to the scientific community, driving research into various therapeutic approaches. The analysed study highlights the evolution of treatments used in Brazil, emphasising the transition from repurposed therapies to more targeted strategies against SARS-CoV-2.

At the onset of the pandemic, there was considerable enthusiasm regarding the use of previously approved drugs, such as chloroquine, ivermectin, and nitazoxanide, owing to their in vitro antiviral activity. However, most randomised clinical trials have failed to demonstrate significant clinical benefits for COVID-19 patients. The study corroborates the findings of the WHO Solidarity Trial (2021), which ruled out the efficacy of these drugs in reducing mortality.

As the pandemic evolved and the pathophysiology of COVID-19 became better understood, new treatments were incorporated into the therapeutic arsenal. Corticosteroids, particularly dexamethasone, demonstrated a significant reduction in mortality in patients with respiratory failure, as evidenced by the RECOVERY Trial (2020).

Furthermore, immunomodulatory therapies, such as tocilizumab and baricitinib, have proven effective in controlling hyperinflammation and reducing the need for mechanical ventilation. The positive results of these medications highlight the importance of targeted therapies addressing specific mechanisms of the disease.

Antivirals such as remdesivir, molnupiravir, and paxlovid have also shown promising reductions in hospitalisation risk in the early stages of the disease, emphasising the necessity of early diagnosis and intervention.

The emergence of new variants of SARS-CoV-2 has altered the therapeutic response of some initial treatments. The study highlights that certain lost monoclonal antibody therapies are effective against newer variants, requiring ongoing adaptation of treatment protocols.

However, research into new antivirals and immunomodulators remains crucial to the development of more effective therapies. The study highlights the need for continued clinical trials and the integration of emerging evidence into national and

international guidelines.

CONCLUSION

The review highlights the significance of an evidence-based approach to COVID-19 treatment, pointing out that corticosteroids, antivirals, and immunomodulators are currently the most effective therapies. The gradual discontinuation of repurposed therapies without proven benefits represents progress in clinical practice. The pandemic has reinforced the necessity for continuous scientific updates and the adaptation of treatments in response to emerging variants, ensuring improved patient outcomes. The study emphasises the pivotal role of clinical research and the dissemination of evidence-based information in effectively combating COVID-19.

REFERENCES

Beigel JH, Tomashek KM, Dodd LE, et al. Remdesivir para o tratamento da Covid-19 —

Relatório final. N Engl J Med. 2020;383(19):1813-1826.

Gandhi RT. O desafio multidimensional do tratamento da COVID-19: Remdesivir, corticosteroides e além. Clin Infect Dis. 2022;74(3):469-471.

Gottlieb RL, Vaca CE, Paredes R, et al. Remdesivir precoce para prevenir a progressão para Covid-19 grave em pacientes ambulatoriais. N Engl J Med. 2021;386(4):305-315.

Johnson NP, Mueller J. Atualizando as contas: mortalidade global da pandemia de gripe "espanhola" de 1918-1920. Bull Hist Med. 2002;76(1):105-115.

Marconi VC, Ramanan AV, de Bono S, et al. Eficácia e segurança do baricitinibe para o tratamento de adultos hospitalizados com COVID-19 (COV-BARRIER): um estudo randomizado, duplo-cego e controlado por placebo. Lancet Respir Med. 2021;9(12):1407-1418.

Martineau AR, Forouhi NG. Vitamina D para COVID-19: um caso a ser respondido? Lancet Diabetes Endocrinol. 2021;9(2):81-83.

RECOVERY Collaborative Group. Dexametasona em pacientes hospitalizados com Covid-19. N Engl J Med. 2020;384(8):693-704.

Consórcio de Ensaios Solidários da OMS. Medicamentos antivirais reaproveitados para Covid-19 — Resultados provisórios do ensaio de solidariedade da OMS. N Engl J Med.

2021;384(6):497-511