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

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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, 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.

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

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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:

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• 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 Current Evidence

Action

Antivirals Remdesivir, Molnupiravir Inhibits viral Reduces

and Paxlovid replication hospitalization risk in

high-risk patients

(Beigel, 2020)

Monoclonal Casirivimab/Imdevimab, Neutralizes viral Effective against

Antibodies Sotrovimab spike protein early-stage COVID-

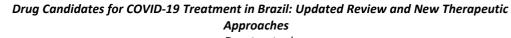
19 (Weinreich, 2021)

Corticosteroids Dexamethasone, Reduces Reduces mortality in

Methylprednisolone inflammation and severe cases

cytokine storm (RECOVERY Trial,

2020)



Immunomodulators Tocilizumab, Baricitinib Blocks IL-6 and Reduces progression

JAK pathways to mechanical

ventilation (Marconi,

2021)

Anticoagulants Enoxaparin, Rivaroxaban Prevents Reduces COVID-19-

thrombotic associated

complications coagulopathy

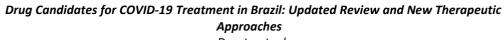
(TICOVID, 2021)

Adjunctive Vitamin D, Zinc Supports immune Limited evidence

Therapies function (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

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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

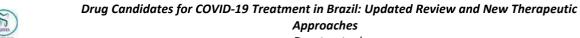
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international guidelines.

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.

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