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Exploring Passive Immunotherapy in the Treatment of COVID-19: Mechanisms, Efficacy, and Clinical Use

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ABSTRACT

The cause of the severe acute respiratory syndrome during the current pandemic was COVID-19 (SARS-CoV-2), which led to thousands of cases and significant death rates in all affected countries. The immune-therapy methods for COVID-19 treatment are the main topic of this review. Administration of interferon, convalescent plasma, intravenous immunoglobulin, monoclonal antibodies, cellular therapies, and immunomodulatory medications are the unique immunotherapeutic approaches. Immunotherapy is recommended in addition to antivirals since the infected patient has immunity against the antigen, and the virus inhibits the activation of interferon to prevent the immune system from attacking it. Interferons are used to treat the infection at specific stages. Worldwide, patients with severe COVID-19 infections are treated with convalescent plasma therapy. Several antibodies neutralise the virus and combat SARS-CoV-2 at various phases of its life cycle. To manage the cytokine storms caused by COVID-19 in its late stages, the immune response is modulated with JAK inhibitors, corticosteroids, and other medications. To combat the virus, patients need to receive freshly updated medication due to changes in the cytokine storm and antibody reactivity against SARS-CoV-2. Investigating the process of development, the immune system's reaction to infection, and viral-mediated reactions aids in the creation of effective therapeutic and preventive drugs.

Keywords: COVID-19, SARS-CoV-2, Immunotherapy, Monoclonal antibody, Interferon, Infection

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Introduction

The novel coronavirus, also known as COVID-19, caused a serious health crisis with far-reaching socioeconomic effects. The initial announcement was made at the end of December 2019 in Wuhan, China [1]. WHO announced a global pandemic on March 11, 2020 [2]. COVID-19 can remain non-indicative or show mild symptoms before developing into a more severe sickness that can be lethal [3]. Its ability to spread efficiently across hosts' respiratory tracts, making it highly contagious and causing Severe Acute Respiratory Syndrome (SARS), is a crucial aspect of the infection [4]. Their diameter ranges from 80 to 120 nm. They are the largest RNA infections that science is aware of, with an average genome size of 26 to 32 kb [5]. According to genomic research, there is a 96% similarity between COVID-19 and a coronavirus that originated in bats [6]. This virus is a member of the Coronavirinae subfamily of the Nidovirales [8] and the *Betacoronavirus* [7] genus, which is a positive-sense, single-stranded RNA enclosed virus. Spike proteins (S), membrane proteins (M), envelope proteins (E), and

nucleocapsid proteins (N) are the five structural proteins found in the genome encoding SARS-CoV-2 [6, 9]. Apart from genes that encode structural proteins, other genes encode nonstructural proteins like coronavirus major protease (3CLpro), both of which are necessary for viral replication, including papain-like protease (PLpro) [10–12]. Because SARS CoV-2 has a greater affinity for the angiotensin-converting enzyme 2 (ACE-2) and neuropilin-1 (NLP1) host cell receptors through the S-spike protein, its infectivity is increased [13–15]. Angiotensin-converting enzyme 2 (ACE2) on the host cell interacts with SARS-CoV-2 and its receptor-binding domain (RBD) to stop the virus from entering the host cells [16]. In any event, even at room temperature, where it can survive for up to nine days, the viral endurance declines with increasing temperatures. It is likely to inactivate on its own when 62–71% ethanol, 0.5% hydrogen peroxide, or 0.1% sodium hypochlorite are applied to the water's surface [17].

The immune-therapy methods for COVID-19 treatment are the main topic of this review.

Results and Discussion

Passive immunotherapeutic treatments against SARS-CoV-2

To ensure the patient's recovery, oxygen therapy, mechanical ventilation, antibiotics, and plasma therapies are the primary treatment methods, and antibiotics are used to prevent secondary infections [18]. In an endeavor to manage immunodeficiency, immunotherapy has been depicted as a supportive treatment. But, to limit the possibility of fatality, therapeutic medication has been restricted to extreme cases and in consolidated treatments [19]. For non-clinical and clinical trials, factors such as sex, age, pregnancy, diabetes, hypertension, autoimmune disorders, heart illnesses, malignancy, and heftiness would need to be examined to determine if an infected patient would benefit from the prior treatments [20]. Importantly, certain promising immunotherapies are quite certain when it comes to immunity and pathways, and they are designed to avoid unfavourable situations and be used only to reduce the infection caused by the viral disease. In light of this, immunotherapy strategies are designed to be beneficial regardless of comorbidity [21].

Few drugs are useful in combating COVID-19. Since the WHO announced the pandemic, numerous researchers have started researching the various medications that block SARS-CoV-2 and conducted numerous clinical trials [22, 23]. Inhibitors that targeted the viral infection were the first medications to be examined. Remdesivir, a medication that belongs to the class of adenosine analogues, inhibits the synthesis of viral RNA. Remdesivir's clinical studies for COVID-19 patients have also produced encouraging outcomes. The effectiveness of nucleoside analogues such as ribavirin and favipiravir in treating COVID-19 is not currently being investigated [24]. Viral invasion of antigen-presenting cells (APCs) via the major histocompatibility complex (MHC) initiates the immune response. Innate immunity causes the diseased cell to release interferons, which alert and warn the surrounding cells to fight off the infection [25]. The coronavirus inhibits type I interferons (interferon-alpha and -beta), which evade the innate immune response. Additionally, SARS-CoV-2 alters the immune response between humoral (Th1) and cellular (Th2) responses and suppresses the cytokine pattern. The study, which was based on 20 recovered patients, found that the virus was repressed by the cellular response [26-29]. The virus's capacity to impede APC through inhibition of MHC class I and II molecules prevented T cell-mediated immunity [30]. A cytokine storm is the uncontrollable release of provocative cytokines. The decrease in the number of lymphocytes during the second stage of infection is what starts it. Among the inflammatory cytokines are TNF-α, TGF-s, GM-CSF, G-CSF, IL-1s, IL-6, IL-12, IL-18, IL-33, IFN-α, and IFN-γ. Inflammatory cytokines also contain chemokines, which can include CCL2, CCL3, CCL5, CXCL8, CXCL9, and CXCL10. The cytokine levels are also restored while the patient recovers from the infection. The cytokine storm triggers ARDS (acute respiratory distress syndrome), which results in lung damage and other organ failures. Given all of these effects, people with serious infections have weakened immunity. Given the function of immunity and the state of the immune system at various phases of infection in the sick patient, immune modulation is a crucial treatment to cure SARS-CoV-2 [31]. For COVID-19, a variety of approaches can be used as immunotherapeutic medications.

Interferon-based immunotherapy

Type I IFNs

The immunological response of a host depends on interferons as a defence mechanism against several illnesses. COVID-19 inhibits IFN-1 secretion by interfering with the IFN-signaling pathways. STAT-1 (signal transducer and activator of transcription 1) and STAT-2 (signal transducer and activator of transcription 2) are crucial intracellular pathways for generating IFNs since the virus suppresses IRF-3 (interferon regulatory factor 3) [32]. Different people have different amounts of production of IFN depending on their age; however, SARS-CoV-2 still triggers IFN-based immune responses. Children's low IFN secretion range leads to early IFN initiation and infection suppression, resulting in low mortality, while older adults' high IFN secretion limit causes an inadequate immune response and slow down IFN production. Inadequate IFN secretion and obstruction of the IFN-secreting pathway are two of the major challenges for immunisation against SARS-CoV-2 [25]. Since COVID-19 is more vulnerable to IFN-α and β, treating it with these interferons has proven to be more successful [33]. The combination of IFN-β1b, lopinavir, and ritonavir suppresses SARS-CoV-2 more effectively than lopinavir and ritonavir alone. It has also been demonstrated that early triple treatment reduces the risk of infection developing into serious problems [34]. Because type I IFNs are effective against SARS-CoV-2 in in vitro settings, IFN-based immunotherapy is approved for use in clinical trials of infected individuals [35]. To determine the effectiveness of the treatment, several clinical trials using IFN-α1β, IFN-β, recombinant human IFN-α, IFN-β1a, and IFN-β1b were conducted in different countries. According to recent research on COVID-19, the peripheral immune responses have only been investigated transcriptomically in a single cell, and monocytes and lymphocytes have not been shown to express any cytokines. However, in a small number of COVID-19 patients, the immune cells can express the genes that are activated by interferon. The mechanism for viral entry and further protein metabolism will be provided by these genes.

Type III IFNs

The antiviral response against SARS-CoV-2 includes type III IFNs, often known as IFN-λ (lambda). Janus kinase (JAK)-STAT activation triggers the production of IFN-related genes and activates the IFN-λ signalling pathway [36]. IFN-λ therapy produces a potent immune response against COVID-19. In a clinical experiment, researchers are employing type III IFN to treat an infection via peginterferon IFN. In the early stages of COVID-19, the IFNs are essential for generating a sufficient immune response to the infection [37]. During the most severe phases of the infection, granulocytes, lymphocytes, monocytes, and macrophages trigger the immunological response against SARS-CoV-2. Because of the overabundance of monocytes and macrophages, more proinflammatory cytokines are released. The phase of infection must be identified to choose the best IFN-based treatment. IFN can be used to start a strong immune response against SARS-CoV-2 in the early stages of infection. Injecting IFN triggers hyperactivated immune responses, but in severe cases, it exacerbates the cytokine storm. As a result, patients with severe infections are not candidates for immunotherapy or the immunomodulatory approach to decrease the uncontrollable immune response [25].

Convalescent plasma therapy

Convalescent plasma therapy is an ancient medical practice that includes infusing an infected patient's serum after they have fully recovered from their illness. The antibodies in the convalescent plasma destroy the antigens after injection. Convalescent plasma therapy is beneficial for SARS-CoV-2 patients; it was mentioned in the most recent study. Three patients were fully cured of the virus and released, two patients were observed for 37 days for adverse effects, and five severely infected SARS-CoV-2 patients received convalescent plasma [38]. There are several hazards associated with this treatment. Convalescent plasma therapy increases the risk of immune-related infections and serum-associated illnesses. Furthermore, the antibodies generated by other viral strains against a recognised COVID strain increase the likelihood of infection transmission during convalescent plasma therapy. The potential for infection transmission from other virus strains is one of the risks associated with the treatment [39]. Every trial that used convalescent plasma to assess the therapy's efficacy lacked a negative control group. Furthermore, to prevent COVID-19, human monoclonal antibodies for an antigenic determinant or epitope of SARS-CoV-2 must be identified.

By adhering to the virus and blocking its entry into the host cells, antibodies in the convalescent plasma (CP) can neutralise the blood virus and limit its spread [40, 41]. The effectiveness of CPT varies according to the kind of microorganism, pathophysiology, and treatment practices [42]. Early CP transfer can speed up recovery and is likely effective for patients with severe infections, such as those with SARS-CoV, MERS, and other coronaviruses that are already being researched concerning plasma therapy. Similar to other viral infections, the amount of virus

in the blood increases during the first week of the infection [41, 43]. It might not work for patients who are nearing the end of their lives. Given the severity of their infections, CPT is undoubtedly unable to significantly reduce the death rate among end-stage patients. Patients with fewer infections, however, do not require CPT because they can heal on their own [44]. The amount of COVID-19 neutralising antibodies in the CP increases the effectiveness of CPT. Although antibody levels are not known before plasma transfer, several studies have shown that IgG levels rise approximately three weeks following the onset of side effects and peak at week twelve. Therefore, 12 weeks following the onset of the illness, the donors provide the effective CP [45, 46].

Monoclonal antibody therapy

Monoclonal antibodies (mAbs) are produced by a specific type of B-cell that produces a set of antibodies against a specific epitope. mAbs are used to treat a variety of infections and cancers [47]. By preventing the ACE receptors from binding to the appropriate host cell, several monoclonal antibodies developed expressly against the S1 region of SARS-CoV have demonstrated the ability to eradicate virulent illnesses. Among these antibodies are S230.15 and m396 80 R [48]. The monoclonal antibody CR3014 eliminated SARS-CoV by preventing the virus from replicating and spreading. Similar to how the immune response itself functions, this immune response inhibits SARS-CoV by lowering SARS-CoV's affinity for attaching to the ACE receptor and host cells [49]. Since the receptor-binding domains of SARS-CoV-2 and SARS-CoV vary, monoclonal antibodies (such as CR3014 and m396) that target the S1 domain of SARS-CoV are ineffective. According to a recent study, the SARS virus and its variation are killed by the human monoclonal antibody-like CR3022. Considering all of this, studies have shown that CR3022, either by itself or in combination with other drugs, is highly effective for suppressing COVID-19 [50]. Additionally, the human monoclonal antibody 47D11 suppresses SARS-CoV-2 by blocking the conserved regions on the receptor-binding domain of the S1B protein. In uninfected people, these antibodies can prevent the spread of viral diseases. To create monoclonal antibodies capable of controlling or stopping SARS-CoV-2, it is best to focus on the receptor-binding domain. In addition, further research will reveal that in severely infected patients, COVID-19-specific monoclonal neutralizing antibodies can be used to suppress the virus.

Inhibition of cytokine pathways

Inter-leukin 1 inhibition

A pro-inflammatory cytokine called IL-1β is essential for the development of respiratory infections in several viral illnesses. As a result of alveolar inflammation, macrophages release IL-1β, which causes fever and respiratory fibrosis. IL-1β levels are higher in patients with severe infection. Therefore, the inhibition of IL-1β in severe SARS-CoV-2 phases can control ARDS and cytokine discharge disorder and is a practical solution to reduce the development. The recombinant IL-1 receptor antagonist Anakinra (NCT04341584) has been approved by SARS-CoV-2 clinical studies. Canakinumab has been proposed as a potential monoclonal antibody against IL-1β in SARS-CoV-2 clinical trials [37].

Inter-leukin 6 inhibition

The injury to the lung's air sac as a result of ARDS brought on by excessive IL-6 release is what caused the lung haemorrhage. Finally, these consequences result in the induction of pneumonic fibrosis. Serum IL-6 levels rise with a serious SARS-CoV-2 infection. As a result, suppressing IL-6 reverses the inflammatory responses, reducing the severity of SARS-CoV-2. Tocilizumab (ACTEMRA), an anti-IL-6 monoclonal antibody, can block the proinflammatory pathway that is initiated by IL-6. Tocilizumab treatment has been effective in some infected patients. An indirect antiviral effect against COVID-19 is provided by tocilizumab. COVID-19's detrimental effects on the lungs are inhibited by tocilizumab. Among the negative effects of excessive tocilizumab use are an increase in hepatic chemicals, hypercholesterolaemia, skin allergies, and fungal infections. Sarilumab (KEVZARA) is an antibody that blocks interleukin-6 (IL-6) signalling, which in turn blocks IL-6 receptor signalling. Tocilizumab and Sarilumab, two IL-6 mAbs, will be used to treat the infected individuals in a stage III clinical trial approved by the FDA.

TNF inhibition

Thalidomide (*-N-[phthalimido] glutarimide) suppresses NF-κB, which in turn inhibits proinflammatory cytokines like IL-8 and TNF-α. TNF-α is secreted by innate immunity in response to COVID-19. TNF-α, one of

the main cytokines released by innate immunity, has been shown to have a significant role in initiating immunological defence against SARS-CoV-2. Based on the role of TNF-α in the development of the cytokine storm, inhibiting TNF-α can decrease hyper-inflammatory responses in serious SARS-CoV-2 infections. XPro1595 is a soluble TNF-α-neutralizing protein that inhibits the interaction between soluble TNF-α and its receptor. XPro1595 is being tested in a clinical trial against SARS-CoV-2 (NCT04370236) [37]. A COVID-19 pneumonia patient's clinical condition improved within 8 days of thalidomide treatment with methylprednisolone (glucocorticoid) in a mixture with low-portion methylprednisolone (glucocorticoids), including an improvement in oxygen levels, reducing nausea, easing tension to decrease oxygen utilisation, and lung exudation. Cytokine levels, including IL-6, IL-10, and IFN-γ, returned to normal after 5 days of treatment, and lymphocyte counts, D4+ T cells, CD8+ T cells, NK cells, and B cells also significantly increased.

Complement system inhibition

Complements are inert proteins found in serum that are a component of innate immunity. After activation, it triggers neutrophil initiation and supports the immune system's antiviral function. Although they play the same roles as cytokines, some system components are not cytokines. The complement system plays an important role in these activities during the infection's progression. Complement activation may be the cause of COVID-19's pathophysiological traits, which include acute kidney injury and thrombotic microangiopathy (TMA). The complement system is composed of two components: C3 and C5. The approved C5 blockers ravulizumab, zilucoplan, and avdoralimab, as well as the approved C3 blocker AMY-101, are used in clinical trials to prevent the transmission of SARS-CoV-2 [37]. The presence of C5b-9 complement in the renal tubules of six COVID-19 patients showed evidence of complement activation in their kidneys. Eculizumab, a monoclonal antibody, prevents complement activation and disrupts the development of C5b.

Cell Therapy

Mesenchymal stem cell therapy

Mesenchymal stem cells (MSCs) are a type of stem cell that has strong immunomodulatory effects. Because of their immunomodulatory effects, MSCs are employed to treat a variety of chronic inflammatory diseases. Growth factors that have rejuvenating effects on target tissues are secreted by MSCs, including keratinocyte growth factor (KGF), glial cell line-derived neurotrophic factor, hepatocyte growth factor (HGF), and vascular endothelial growth factor (VEGF). MSCs' immunomodulatory actions cause T cells and M2 macrophages to respond, suppress T cell overexpression, and limit the release of proinflammatory cytokines. MSC is suggested for managing acute respiratory damage in serious SARS-CoV-2-infected patients due to the immunomodulatory effects and recently revealed information on the efficiency and safety of MSC treatment. Transfer of ACE2-negative MSC was performed in 7 SARS-CoV-2-pneumonia patients, comprehending the harmful effects of the cytokine storm and excessive immune response. Cytokine storm and its damaging impact on the lungs are suppressed by hindering proinflammatory cytokines and immune cells. Alveolar fibrosis and growth factor, and IL-10 secretion can improve lung quality. The patients were monitored for 14 days following the transplant. The patients' symptoms and aspiratory capacity were completely improved two days after the transfer. One patient with a severe SARS-CoV-2 infection showed significant recovery and was released after ten days of infusion. Furthermore, following transplantation, there was an increase in peripheral lymphocytes, a drop in inflammatory cytokine-producing cells, and a rise in inflammatory markers in the blood. Transplanting MSCs that are ACE2-negative seems to be a secure and efficient way to treat SARS-CoV-2. Another MSC therapeutic strategy is the use of secretomes produced from MSCs. MSC secretes extracellular components (Secretome) into the cell culture media through the use of vesicles and exosomes that are external to the cell. MSCs are the source of these secretome constituents. The MSC-derived secretome exhibits favourable immunomodulatory, reproductive, and anti-inflammatory effects, just like MSCs of other origins. As with other MSC techniques, the MSC-derived secretome is suggested as a potential therapy method against SARS-CoV-2. There are two ways to control the secretome: inhalers and intravenous treatments. To assess the secretome approach's efficacy and dependability against COVID-19, clinical trials are carried out.

Natural killing cell therapy

NK cells are a subset of lymphocytes and an aspect of innate immunity that plays a role in the main immune response against viruses or malignancies. An antigen may not be necessary for a cancer cell's immunological response to NK cells. In an increasing number of clinical trials, NK cell-based immunotherapy has demonstrated encouraging outcomes in the treatment of tumours. NK cells stimulate type I IFNs and macrophage-associated cytokines to combat the infected cells. MHC independence and speed are two crucial aspects of NK-inferred immunity. Following the outbreak, medical professionals proposed that NK cells could be a useful treatment for SARS-CoV-2. Since then, China has accepted NK cell-based therapy for enhancing immunity against COVID-19 infection and antiviral defence [37]. Three binding groups are present in a synthetic molecule known as an antibody recruiting molecule (ARMTM): a linker, a spike protein, and an antibody binding region. Through FC*R, ARM attaches itself to the virus and lymphocytes, triggering the destruction of the virus by NK cells and macrophages. ARM prevents COVID from connecting with host cell ACE2 receptors by binding the spike protein to the virus's surface. It supplies cells that deliver antigens with viral proteins, which can trigger persistent immunity. Additionally, research has demonstrated that vaccination is the most effective means of stopping the transmission of COVID-19 [50].

Immunomodulators

JAK inhibitors

JAK is a component of the intracellular cytokine signalling process known as the JAK-STAT pathway. The activation of JAK results in the release of proinflammatory cytokines, which interfere with the phosphorylation of STAT. Many pro-inflammatory cytokines are secreted due to the phosphorylation of the STAT. After infection, SARS-CoV-2 patients typically have a cytokine storm because of a reduction in proinflammatory cytokines released as a result of this agent's inhibition of JAK. Baricitinib, Fedratinib, and Ruxolitinib are among the JAK-inhibitors that effectively reduce SARS-CoV-2 infection and have anti-inflammatory effects in a variety of disorders, including myelofibrosis and rheumatoid arthritis. According to the most recent trial, baricitinib, a JAK blocker, is an effective treatment for acute pneumonia in SARS-CoV-2 patients. Baricitinib inhibits the adapter-linked protein kinase 1 receptor, which limits the virus's ability to infiltrate host cells and reduces infection by inhibiting JAK. Baricitinib has gained more attention than other medications for four reasons:

- Anti-incendiary properties
- The increased interest in NAKs
- The capacity to improve interferonopathies' persistent aggravation associated
- Because the chemical has little effect on plasma proteins and little interaction with cytochrome P medications, it has a lot of potential as a mixed treatment.
- Since Th17 cells, including the cytokines they produce, play a major role in determining cytokine storms and the pathology of coronaviruses, baricitinib is recommended in conjunction with antiviral drugs such as lopinavir, ritonavir, and ramsudavir to reduce the host infection and the likelihood of the virus reemerging. Fedratinib (JAK2 inhibitor) may be used to reduce COVID-19 death because this cell relies on the JAK signalling pathway for separation and to function as an effector system [48].

Antimetabolites

The genome of SARS-CoV-2 is deubiquitinated and replicated by an enzyme called papain-like protease (PLpro). PLpro is the primary target of the viral class inhibitor medications. However, because of its therapeutic action, PLpro is susceptible to antimetabolites. Among the key SARS-CoVPLpro inhibitors are 6-thioguanine (6TG) and 6-mercaptopurine (6MP). An immunosuppressant called mycophenolate mofetil is efficient in inhibiting the PLpro of SARS-CoV and MERS-CoV in both in vitro and in vivo settings. More therapy research is needed to determine the effectiveness. There is no solid evidence to support the antimetabolites' efficacy.

Calcineurin inhibitors

Because calcineurin inhibits T-cell activation, tacrolimus (a calcineurin inhibitor) effectively combats COVID-19. Usually, organ transplantation operations employ it. When compared to a patient who did not receive tacrolimus during the procedure, it was demonstrated to be effective against MERS in renal transplant patients. Tacrolimus is effective against SARS-CoV in cell line studies. More research is undoubtedly needed to determine

the effectiveness against COVID-19. There is no solid evidence to support the effectiveness of cyclosporine or calcineurin inhibitors.

Metal-based agents

Some metal-based treatments for SARS-CoV-2 patients include gold, ruthenium, and bismuth. Auranofin (Ridaura®), a gold compound approved by the FDA, is mainly advised for the treatment of rheumatoid arthritis. Although its exact mechanism is still unknown, this chemical is classified as an anti-inflammatory and immune-modulating drug. Auranofin has gained greater attention in the treatment of HIV and other viral disorders. Because of HIV, hydroxychloroquinewas was found to be less effective than auranofin in limiting viral replication, inertness, and viral renascence. It was hypothesised that auranofin inhibits IL-6 signalling, which suppresses the JAK1 and STAT3 pathways. The micromolar dosage of auranofin was found to diminish the inhibition of COVID-19 viral replication and cytokine expression caused by viral stimulation in human cells.

Corticosteroids

Dexamethasone and other oral/IV corticosteroids were the first drugs prescribed for cytokine storm in a severe SARS-CoV-2 infection because of their immunomodulatory effects. The antiviral properties of corticosteroids inhibit the expression of pro-inflammatory transcription factors in nuclei [47]. While it is not required for mediocre patients, the infusion of corticosteroids can lower the infection and ARDS in critical patients with SARS-CoV-2 hyperinflammation. Numerous clinical trials are conducted to evaluate the efficacy of drug-induced treatment against severe SARS-CoV-2 infection. Among the side effects of corticosteroids (immunosuppressant medications) are vascular necrosis and hyperglycemia. The approach can be quite stress-inducing and humane based on the immune therapy. According to statistical analysis studies, the only way to prevent and stop the spread of COVID-19 is to alter the public environment [46].

Conclusion

Despite the scientific competition to create a therapy, there is currently no viable cure for COVID-19. Integrated treatments oversaw the immunotherapies discussed here. When used as immunotherapy to prevent viral transmission or passing, monoclonal antibodies are superior to serum treatment and intravenous immunoglobulins because of their purity, selectivity, reduced risk of blood-borne infection, and increased protection. By recognising different epitopes on the viral surface, monoclonal antibody combinations improve the effectiveness of virus suppression. There is currently no commercially available monoclonal antibody for COVID-19, despite recent developments in monoclonal antibody development, such as passive immunotherapy. The challenge, expense, and laborious nature of large-scale production limit the use of monoclonal antibodies in therapeutic settings. The development of improved protein production is necessary to enable the provision of antibodies at a reasonable cost. During the early stages of the infection, a passive immunotherapeutic strategy is used to stimulate the patient's immunity and aid in their recovery from the suppression of COVID-19. The effectiveness of CPT is evaluated with possible results in several nations. In severely infected patients, cytokine storm may be triggered by immune system malfunction during the latter stage of SARS-CoV-2. Immunosuppressive pharmaceuticals, including corticosteroids, TNF-α blockers, JAK inhibitors, and other immunosuppressive antiviral medications, are the most successful therapeutic options for patients in these circumstances. Numerous medications in these groups are being investigated for their benefits, drawbacks, efficacy, and detrimental effects to stop the undesired immune suppression that aids in viral multiplication in the host. It was found that patients who received a smaller dose of dexamethasone had greater survival advantages. In severe situations, the inflammatory response is used to induce acute respiratory distress syndrome (ARDS), which is a crucial component. Blocking the control of the type-1-IFN-associated pathway by targeting the virus is an example of suppressing the coronavirus. To lessen the strong antiviral reaction, the immunomodulatory method developed for the administration of the inflammatory reaction is employed. When Tocilizumab is used to treat patients with severe COVID-19 infection, clinical indications and research findings, such as white blood cell (WBC) count, CRP, and lymphocyte count, return to normal. Additionally, Thalidomide is well-known for its ability to lessen aspiratory fibrosis and lung injury by preventing inflammation, preventing cell growth, and generating T cells. Tocilizumab, sarilumab, tocilizumab, IL-6 inhibitors, and baricitinib, a JAK inhibitor, are used to treat SARS-CoV-2 patients. These treatments may be

more effective than the standard anti-inflammatory medications. We conclude this review that immunotherapy is a successful COVID-19 treatment.

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