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Review Article

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Considerations in the Management of Covid-19 in Patients with Chronic Kidney Disease

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Abstract

The purpose of this review is to synthesize the existing evidence on the management of Covid-19 in patients with chronic kidney disease and acute kidney injury. The evidence reviewed is a summary of relevant scientific publications, expert opinions, and current practice guidelines in regard to prevention, inpatient, and outpatient management as it relates to treating Covid-19; summation of management of other diseases in conjunction with Covid-19 have not been detailed. This review does not include a formal systemic review of evidence.

Introduction

The severity of SARS-CoV-2 is increased by both comorbidities and age [1,2]. Six of the seven most common underlying medical conditions in a sample of 4,899,447 adults hospitalized for Covid in the US were associated with CKD [2]. These include essential hypertension, disorders of lipid metabolism, obesity, diabetes with complication, coronary artery disease, and CKD. In adults with 2-5 comorbidities the risk ratio for death was 2.55 and the risk ratio for invasive mechanical ventilation was 2.91. Per the CDC patients aged 65 and older are the group most likely to have CKD and are also the age range where the risk of death due to covid-19 begins to escalate [3]. With such great risk posed in this population, comprehensive understanding of Covid treatments in relation to kidney health is quite important.

Methods

This article does not follow a formal systemic review but instead aims to synthesize the current best practices from a variety of expert opinions, clinical research, meta-analyses, and randomized control trials. The focus is on the treatment of patients with COVID-19 and adjustments necessitated by chronic kidney disease and acute kidney injury.

Covid Treatments

Vaccines

Per CDC recommendation staying up to date on vaccines is critical for all people with health conditions; this includes covid 19 vaccination [4]. Renal insufficiency leads to multifactorial decrease in host defenses which is further exacerbated by renal replacement therapies [5,6]. Decreased ability of the kidneys to clear toxins, nutritional deficiencies, and administration of immunosuppressives lead to alterations in immune function early in CKD [5].

There are currently four vaccines approved either through full FDA approval or emergency use authorization. These include Pfizer-BioNTech, Moderna, Janssen (commonly referred to as Johnson & Johnson), and Novavax. Both Tozinameran (Pfizer) and Spikevax (Moderna) are mRNA vaccines, Janssen is an adenovirus vector vaccine, and Novavax is an adjuvanted recombinant protein vaccine.

Tozinameran (brand name: Comirnaty) (Previously marketed as Pfizer-BioNTech COVID-19 vaccine)- Approved by the FDA for persons aged 12 years and older and is available under EUA for children 6 months to 11 years of age. This vaccine is delivered via lipid nanoparticles to express a full-length spike protein [7]. Large scale randomized trials assessing the efficacy of Tozinameran have found 95% reduction in infection for individuals 16 years and older at 2 months, 90% at 2-4 months, and 84% at 4-6 months [8,9]. In adults over the age of 65 who had other comorbidities the vaccine was 91% effective. Observational data from a variety of countries have been reported following vaccine implementation and found a very similar effectiveness at 90% [10-21]. Primary side effects include injection site reactions, fatigue, headache, myalgias, fever, and chills. Serious adverse effects include myocarditis and pericarditis. Incidence rates of the serious adverse effects were found to be very rare at 1

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in 10,000 people, this is only slightly higher than the baseline incidence rate of 6.1 per 100,000 men and 4.4 per 100,000 women for myocarditis and 3.3 per 100,000 for pericarditis [7]. It is important to note that the baseline incident rates for these two disorders is poorly defined due to lack of sensitive and specific non-invasive testing [22].

Spikevax (Previously known as Moderna COVID-19 vaccine)- FDA-approved vaccine for persons 18 years of age and older. The mechanism underlying this vaccine utilizes mRNA delivered via lipid nanoparticles to express a complete spike protein similar to Tozinameran [23]. Available under EUA for a third primary series dose to individuals 18 years of age and older who are immunocompromised, single booster for individuals who have finished primary series with Moderna COVID-19 vaccine, and a single booster to individuals who have completed primary vaccination with another authorized COVID-19 vaccine. In randomized control trials at two months Spikevax was found to prevent Covid in 94.1% of cases and in adults aged 65 and older it prevents 86.4% of cases [24]. In large scale observational studies Spikevax has been associated with 90% prevention rate [21,25-30]. Side effects are similar between Spikevax and Tozinameran with injection site reactions, fatigue, headache, myalgias, fever and chills being the most common and myocarditis and pericarditis being the more serious concerns [24].

Novavax- Authorized for use under EUA as a two dose primary series for individuals 18 years of age and older. Novavax is a recombinant protein subunit vaccine that contains trimeric spike glycoproteins and a potent Matrix-M1 adjuvant [31]. In phase III efficacy trials Novavax was shown to have 90.4% efficacy in preventing Covid in patients 18 years and older [32,33]. The side effects for Novavax are similar to those of the mRNA vaccines with systemic side effects being the most common and myocarditis and pericarditis being the more serious adverse events. There are also some limited reports of uveitis, thrombosis, cholecystitis, and cardiomyopathy but data is limited [32,33].

Janssen- Authorized for use under EUA in individuals 18 years of age and older for whom other vaccines are no accessible, clinically appropriate, or individuals who elect to receive Janssen due to preference. Janssen functions via a replication-incompetent adenovirus 26 vector that encodes a stabilized spike protein [34]. In a large-scale randomized control trial Janssen was shown to reduce the incidence of Covid-19 by 67% two weeks after administration [35]. Vaccine efficacy was higher against severe covid-19 at 76.7% prevention by two weeks up to 85% by 28 days [7]. Efficacy after four months was found to be 56.3% for moderate Covid and 74.6% for severe covid [36]. Observational data has been associated with 67-75% efficacy for preventing hospitalization and 83% efficacy for prevention of death [21,37,38]. The most common side effects associated with Janssen are systemic in nature with some anxiety related effects such as tachycardia, hyperventilation, light-headedness, and syncope [39,40]. Serious adverse events including thromboembolic events, tinnitus, and seizures were reported but the causal association has yet to be proven and the reported incidence rate did not exceed the expected basal rate of the population in a report of over 400,000 healthcare workers [35,41].

Per current NIH recommendation the available mRNA vaccines and Novavax are preferred over the Janssen vaccine due to slightly better efficacy and slightly lower risk profile [42]. Data assessing vaccine response in CKD does not report efficacy across the population but instead looks at serum markers, Tozinameran was found to show lower anti-spike antibody levels for dialysis patients compared to healthy controls [43]. Spikevax was found to have 97% seroconversion after 2 doses when separated by a 28-day interval [43]. Patients with CKD 3-5 currently using immunosuppressive agents have been demonstrated to show decreased development of neutralizing antibodies [44]. This is consistent with previous data developed regarding treatment of Hepatitis B [45]. Current recommendations do not exclude patients with chronic use of glucocorticoids but future studies looking at following treatment recommendations similar to that of Hepatitis B where vaccination is performed after steroid discontinuation or in conjunction with low dose steroids would be beneficial. There is also concern that in patients with primary glomerulonephritis that vaccination may induce relapse [46-48]. Efficacy of Tozinameran was assessed in patients on dialysis by measuring IgG after completion of 2 doses. 96% of patients had a humoral response but antibody titer levels were lower, a greater association was noted in older patients and those with relative lymphopenia [49]. Similar results were found in a study of Spikevax in peritoneal dialysis patients [49]. Current data regarding vaccination in solid organ transplant patients is limited but shows similar immune responses; further studies looking to obtain a comprehensive understanding for different organ types and levels of immune suppression need to be performed [50].

Tixagevimab-Cilgavimab

In patients with decreased immunity Tixagevimab 300 mg plus cilgavimab 300 mg has been recommended a pre-exposure prophylaxis (PrEP) by the NIH with repeat dosing every 6 months [42]. In randomized control trials Tix/Cil showed a 76.7% relative risk reduction compared to placebo [51]. Tixagevimab and cilgavimab are not eliminated intact in the urine therefore patients with renal impairment likely do not need dose adjustment; similarly, dialysis is not expected to have an impact, but further clinical data is needed to make a stronger recommendation [52,53]. A retrospective study done in France with 430 patients showed significant reduction in symptomatic Covid and Covid hospitalizations for kidney transplant patients [54]. Patients with advanced CKD and ESKD in renal replacement therapy, should be considered for pre-exposure prophylaxis. This is even worth considering in patients receiving in center dialysis where the risk of exposure is relatively higher.

Dexamethasone

Dexamethasone is a synthetic corticosteroid that is often used to treat autoimmune conditions and to relive inflammation. It is metabolized hepatically and less than 10% is excreted renally. Median time to peak concentration is 1 hour and mean half-life is 4 hours. Dexamethasone is a

generally well tolerated drug with its most reported adverse effect being insomnia following use [55].

Per NIH recommendation Dexamethasone is advised to be given for patients who are hospitalized and are requiring conventional oxygen or more invasive methods of ventilation [56]. Multiple meta-analyses have demonstrated moderate decreases in all-cause mortality at 28 days for hospitalized patients receiving systemic glucocorticoids [57,58] and more recently published Cochrane meta-analyses demonstrate with moderate-certainty that inhaled and systemic steroids reduce the risk of both admission and death [59,60]. Of less certainty is if inhaled steroids are decreasing duration of mild symptoms [59]. There is low-certainty evidence that inhaled corticosteroids offer little to no difference in outpatient management of mild disease severity [59]. Due to lack of sufficient patient population receiving alternative corticosteroids dexamethasone is the primary intervention discussed in the literature but according to NIH guidelines if dexamethasone is not available, an equivalent dose of another corticosteroid may be used [56].

Data regarding optimal starting dose is less robust. Current NIH guidelines suggest 6 mg once daily for up to 10 days or until supplemental oxygen is discontinued [61]. There have been some smaller studies that showed inconclusive evidence of high dose vs. low dose therapy in the improvement of ventilator free days or all-cause mortality [62-64]. In patients with altered kidney function there are no recommendations for adjusted dose [55,65,66].

Baricitinib

Baricitinib is a Janus Kinase inhibitor typically used in the treatment of rheumatoid arthritis, it was predicted through use of artificial intelligence algorithms to be useful for Covid-19 management. The proposed mechanism was a combination of anti-cytokine effect and inhibition of host cell viral propagation [67]. Baricitinib is primarily cleared renally with 75% being excreted in the urine. Median time to peak concentration is 1.5 hours after dosing with a half-life of roughly 8 hours [68]. Baricitinib comes with a black box warning for risk of serious infection, most patients who developed these infections were taking other immunosuppressive drugs such as methotrexate or corticosteroids [69]. If serious infections do occur interruption of treatment with baricitinib is recommended [69]. Per NIH and FDA guidelines starting baricitinib is recommended for patients who are within the 24-48-hour window of onset of ICU level care and within 96 hours of hospitalization or who are receiving dexamethasone and have rapidly increasing oxygen needs with systemic inflammation [56].

Per FDA package insert Baricitinib dose is eGFR dependent with a maximum duration of therapy up to 14 days or discharge, whichever is sooner. For patients with an eGFR between 60 - < 90 mL/min/1.73 m^2 a dose of 4 mg once daily is recommended, for eGFR between 30 - < 60 mL/min/1.73 m^2 a dose of 2 mg once daily is recommended, for eGFR between 15 - < 30 mL/min/1.73 m^2 a dose of 1 mg once daily is recommended, for eGFR of < 15 mL/min/1.73 m^2 treatment with Baricitinib is not recommended [69].

Current data suggests with moderate-certainty that baricitinib decreases all-cause mortality in patients with moderate to severe covid, there is currently no evidence on the use of JAK inhibitors for outpatient management [70]. There is also moderate-certainty evidence that JAK inhibitors make little to no difference in improvement of clinical status, decrease the risk of worsening of clinical status and decrease the occurrence of serious adverse events [70]. The RECOVERY trial in combination with previous trials found a 20% reduction in mortality for patients with moderate-severe Covid without showing significant excess in death due to other safety concerns [67,71-75].

Tocilizumab

Tocilizumab is an IL-6 pathway inhibitor used in several inflammatory diseases including cytokine release syndrome, giant cell arteritis, rheumatoid arthritis, and scleroderma. As elevated inflammatory and pro-inflammatory markers are associated with increased mortality in severe Covid, and cytokine mechanisms were initially theorized to be involved in the systemic presentation of Covid, use of Tocilizumab was suggested for intervention [76]. Tocilizumab's half-life is 4 days, the exact route of elimination of monoclonal antibodies is not currently known [77]. Dosing for Tocilizumab is reported in the FDA package insert as 8 mg/kg as a single IV dose [77] with a second dose give 8 hours after the first if the patient fails to improve per NIH guidelines [56]. Per NIH and FDA guidelines Tocilizumab is recommended to be added in addition to Dexamethasone in mild cases if the patient has elevated inflammatory markers, was hospitalized within 96 hours and, their oxygen requirements are increasing, described as more than 6 ml/min increases within 24 hours, more than 10 ml/min requirement, or if more invasive methods than nasal cannula are required [56]. Tocilizumab is also recommended in patients with moderate or severe Covid if they are within 24-48 hours of onset of ICU-level care and within 96 hours of hospitalization [56]. There are no currently available guidelines on dosing adjustment in the context of severe renal impairment, but no dose adjustment is required in patients with mild or moderate impairment [77].

Two large multi-institute meta-analyses looking at Tocilizumab in hospitalized patients found moderate-certainty evidence that tocilizumab likely reduced all-cause mortality at day 28 compared to placebo but that its effect on other outcomes is less certain [78,79]. Very low certainty evidence was obtained on the effects of tocilizumab in relation to adverse events [78,79]. As the medication has been reserved for more acutely ill patients no data for preventing admission has been generated. Odds ratio reports for worsening clinical course leading to mechanical ventilation or death compared to placebo showed .74 for Tocilizumab [78]. In one randomized control trial in the U.K. where 82% of participants were receiving both Tocilizumab and Dexamethasone separate subgroup analysis was obtained that showed patients were more likely to benefit from combined treatment than those who received only glucocorticoids [80].

Remdesivir

Remdesivir is a novel nucleotide analog that was originally developed for the treatment of Hepatitis C and RSV but treatment for both of these infections was unsuccessful [81]. It was later demonstrated to be safe in patients during trails as a treatment for Ebola which it was also unsuccessful in treating [81]. Remdesivir showed promise early in the pandemic in animal models and was shortly after introduced for use in clinical trials where it was found to show clinical improvement at day 15 when compared to placebo [82,83]. Remdesivir is detectable at peak concentrations following 30-minute infusion [84]. Nonclinical evaluation supports hepatic metabolization with the main metabolite primarily being eliminated renally; half-life is reported at 1 hour [84]. The pharmacokinetics of Remdesivir have not been evaluated in patients with kidney impairment but due to the presence of sulfobutylether-β-cyclodextrin (SBECD) in the formulation treatment is not recommended in patients with an eGFR less than 30 [85]. In a small scale observational report of 157 patients with either AKI or CKD with 46 receiving remdesivir no renal function abnormalities were attributable to remdesivir and the drug was overall well tolerated [86]. The authors of this study report several limitations most notably that most of their patients were receiving hemodialysis [86]. The pharmacokinetics and clinical implications of SBECD in kidney failure comes primarily from studies on voriconazole which utilizes SBECD as a carrier in the intravenous formulation [87]. Renal clearance of SBECD in patients with renal failure was found to be 2.6 ml/min without dialysis and 48 ml/min during dialysis when receiving the standard dose of voriconazole [88]. In the standard voriconazole dose patients received approximately 528 mg/kg across the 5 days of treatment [88]. Remdesivir in powder formulation contains 3g of SBECD and in the liquid formula contains 6g of SBECD; both of these concentrations are for 100 mg of remdesivir [85]. Following the NIH Covid treatment guidelines for remdesivir a 200 mg IV loading dose then 100 mg IV infusion for 4 days means that patients would receive between 18 to 36 grams total of SBECD across 5 days of treatment depending on which formulation was used. This means that an adult patient weighing more than 149 lbs or 68 kg would receive a higher dose of SBECD from voriconazole treatment than they would from the liquid formulation of Remdesivir. In animal models toxic effects of SBECD were found at doses approaching 3000 mg/kg, this is 5000 times higher than the highest dose received by patients treated with liquid remdesivir [89]. While monitoring creatinine during treatment and use of the powder formulation is advisable avoidance of remdesivir is unnecessary.

Remdesivir has been studied in both non-ICU and ICU levels of hospitalized patients. In a Cochrane meta-analysis published in August 2021 that contained 5 randomized control trials they found with moderate certainty evidence that remdesivir makes little to no difference to all-cause mortality up to 28 days, conflicting evidence on the benefit for patients receiving low-flow oxygen, conflicting evidence on decreases in the amount of time patients receive supplemental oxygen, conflicting evidence of changes to clinical worsening, and very low certainty evidence in regards to increases or decreases to adverse events of any severity [90]. A more recent update contained 1 new randomized control trial and 1 new subtrial and showed similar results to the previous meta-analysis [91]. These findings were again correlated by a large multinational study performed by the world health organization that included 454 hospitals across 35 countries with 14,221 patients total, where the study authors concluded that Remdesivir has no significant effect on outcomes for patients who are already ventilated and only a small effect against death or worsening in other hospitalized patients [92]. In a smaller study funded by Gilead Remdesivir was found to decrease risk of hospitalization by 87% for unvaccinated patients [93].

Remdesivir has also been recommended by the NIH a treatment option for outpatient management of patients with risk of severe covid. This treatment regimen is the same as inpatient with patients receiving 200 mg via IV infusion on day 1 followed by up to 4 days of 100mg infusions [94]. This has been a more viable option for patients in long term care facilities given the 30-120-minute administration time with a minimum of 1 hour of observation being recommended.

Nirmatrelvir-ritonavir (Paxlovid)

Nirmatrelvir is a 3C-like protease inhibitor that prevents release of non-structural proteins from corona virus [95]. Ritonavir was originally developed as an antiviral agent but was later found to function as a booster of other protease inhibitors and is now included as a booster in several medications [96]. Nirmatrelvir is eliminated primarily in the kidneys with ritonavir being primarily eliminated by the liver [97]. When given together Nirmatrelvir reaches its peak concentration after 3 hours and has a half-life of 6 hours [97]. With current evidence the NIH is recommending a decreased dose of Paxlovid in patients with moderate renal impairment and is not recommending in patients with severe renal impairment until further data is available [98,99]. Expert opinion on dosing for patients with severe CKD does not agree with the NIH's assessment instead recommending 300 mg of Nirmatrelvir and 100 mg of Ritonavir on the first day followed by 150 mg of Nirmatrelvir and 100 mg of Ritonavir for the next 5 days; this is similar dosing for patients on dialysis with the only change being the treatment should be given following dialysis on days they receive it [97]. Dosing for treatment is simple to follow for patients with medication divided into 5 daily-dose blister packs containing either the standard 300 mg nirmatrelvir with 100 mg of ritonavir or 150 mg nirmatrelvir with 100 mg of ritonavir for the moderate renal impairment dose; each dose pack contains both morning and night dosages [99].

Initial studies on the effectiveness of Nirmatrelvir/ritonavir have shown significant reduction in risk of hospitalization in unvaccinated patients [100,101]. A population-based study in Israel used data from the largest healthcare provider to identify 4,737 adults who were treated with Nirmatrelvir/ritonavir and found that treatment seems more effective in older, immune-compromised patients [100]. A phase 2-3 double blind RCT with 2,246 patients funded by Pfizer found

Table 1: Covid treatments.

Treatment	Tixagevimab-cilgavimab	Dexamethasone	Baricitinib	Tocilizumab	Remdesivir	Nirmatrelvir	Monoclonal Antibodies (Bebtelovimab)
Standard regimen	300 mg + 300 mg Cil	6 mg once daily for 14 days or hospital discharge	4 mg once daily for 14 days or hospital discharge	8 mg/kg once, second dose in 8 hours if no improvement	200 mg IV on day 1 followed by 100 mg once daily for 5 days	Nirmatrelvir 300 mg with ritonavir 100 mg administered together, twice daily for 5 days	175 mg as a single dose within 7 days of symptom onset.
CKD - without dialysis	No changes	No changes	2 mg for GFR 30-60; 1 mg for GFR 15-30	No changes	No changes	Nirmatrelvir 300 mg with ritonavir 100 mg on day 1 followed by Nirmatrelvir 150 mg and ritonavir 100 mg for the next four days when GFR < 30 [114]	No changes
CKD with dialysis	No changes	No changes	Use not recommended	No current recommendations. Some case studies have been reported with favorable outcomes [111,112]	No changes	Same dose as without dialysis but given on dialysis days following dialysis	No changes
Important drug interactions	Covid-19 vaccine, Efgartigimod alfa	Antibacterials and antifungals, calcineurin inhibitors, and desmopressin. More complete lists of medications can be found on CDC website.	Synergistic immune suppression is seen with other immune suppressive therapies	Synergistic immune suppression is seen with other immune suppressive therapies	Chloroquine, Hydroxychloroquine	Ritonavir is a potent CYP3A4 inhibito. Important drugs to consider are statins, calcineurin inhibitors, estradiol contraceptives, and HIV treatments. Refer to Paxlovid FDA sheet for a more comprehensive list.	No known significant interactions

Transplant considerations	Given immune compromised state use of Tix/ Cil in transplant patients is advisable especially in patients who were unable to receive a vaccine or those who did not mount an adequate immune response.	Earlier initiation of treatment in patients with Covid-19 is advised, transplant team should be notified and brought on for management following confirmation of infection	Benefit of treatment in immune compromised patients needs to be heavily weighed against risks as significant immune suppression can result.	Benefit of treatment in immune compromised patients needs to be heavily weighed against risks as significant immune suppression can result.	Earlier initiation of treatment in patients with Covid-19 is advised, transplant team should be notified and brought on for management as early as possible following confirmation of infection.	Treatment should only be considered if remdesivir is unavailable per the American society of transplantation.	Some small studies have shown monoclonal antibodies to be effective in transplant patients. Earlier initiation of treatment in patients with Covid-19 is advised, transplant team should be notified and brought on for management as early as possible following confirmation of infection.
Adverse effects	Dizziness, fatigue, headache, insomnia, anaphylaxis (< 1%)	Adverse reactions to systemic steroids are extensive, an in depth analysis of side effects are available on the FDA insert	Elevated ALT and AST, Deep vein thrombosis, pulmonary embolis, septic shock, UTI, Thrombocythemia, Pneumonia, Tuberculosis	Elevated cholesterol, Constipation, neutropenia, increase ALT and AST, injection site reaction, infusion related reaction. Incidents that happened < 10% of the time can be found on the FDA package insert.	Increased serum glucose, Decreased creatinine clearance, increased serum creatinine	Hypertension, Diarrhea, Dysgeusia, Myalgia	Rash, Pruitus, Nausea, vomiting
Further considerations					Use of powder formulation to minimize concentration of SBECD is advised. Short overall duration of therapy is unlikely to lead to significant adverse outcomes, risks of clinical worsening should be weighed against benefits of treatment.	A clinical trial is currently underway evaluating use in patients on dialysis. Clinicaltrials. gov Identifier is NCT05366192. At the time this article was submitted for publication the report had not been published yet.	As new strains develop efficacy will need to be reevaluated. Treatment should be reserved for only those who are most at risk and most likely to benefit. Other more well documented treatments should be used when available for patients who are not immune compromised.

an 89% decrease in the progression to severe Covid when compared with placebo in unvaccinated, Covid naïve patients [101]. There are some initial reports showing rebound symptoms in high-risk patients with patients in some cases testing positive on direct viral testing before becoming positive again shortly after, but analysis done by the FDA did not show increased occurrence of hospitalization, death, or development of drug resistance [102,103].

Given that high risk patients are likely to be taking other medications it is imperative that the significant drug interactions of ritonavir are taken into consideration prior to therapy initiation. Of primary concern would be medications that are either cleared by or induce CYP3A. Any medication that is harmful at elevated levels is a contraindication to starting nirmatrelvir-ritonavir, if these medications can be held for a time or have an acceptable alternative treatment with Paxlovid may still be beneficial. Current FDA recommendations support holding medications for 3 days following completion with the 5-day course or longer if there is a very narrow therapeutic window [99]. A full list of known and suspected significant drug interactions can be found on the FDA package insert [99]. In kidney transplant patients a very important consideration is tacrolimus. Paxlovid may increase the serum concentration of tacrolimus and as such the American society of Transplantation is recommending the use of alternative therapies [104].

Monoclonal antibodies and convalescent plasma

Current infectious diseases society of America and NIH recommend use of monoclonal antibodies for treatment of Covid-19 when compared to no treatment [94,105]. Two randomized control trials published in 2021 and 2022 were both halted due to futility analysis [106,107]. Problems highlighted in use of antibodies for treatment include the ever-evolving nature of variants which leads to difficulty staying up to date. Currently the NIH recommends use with bebtelovimab 175 only and recommends against the use of bamlanivimab plus etesevimab, casirivimab plus imdevimab, or sotrovimab; this is based on invitro studies [94]. Both organizations call for further research into the use of antibodies for both inpatient and outpatient management. The use of monoclonal antibodies was found to be effective in kidney transplant recipients who had mild Covid-19 symptoms in a small retrospective study [108].

The NIH and IDSA give similar recommendations against the use of convalescent plasma citing lack of evidence of efficacy and uncertain evidence of significant adverse events [94,105]. In hospitalized patients there was moderate certainty of evidence that convalescent plasma had no effect on mortality and low certainty evidence that it may have increased the need of mechanical ventilation [105]. For outpatient management they found moderate certainty evidence that convalescent plasma reduced hospitalization rates and low certainty evidence showed a reduction of progression to severe respiratory disease [105]. There have been no published studies at this time exploring the use of convalescent plasma in CKD or AKI, given the lack of evidence of efficacy its use in patients with CKD should only be considered when other options are unavailable.

Vitamins

Vitamin deficiencies were thought to be a possible contributing factor to worse outcomes early in the pandemic [109]. At the time of writing there is one living cochrane meta-analysis assessing effectiveness of vitamin D supplementation in patients with Covid that has been unable to find significant benefits or harm association [110]. There is currently a double blind clinical trial looking at the effectiveness of vitamin B3 (Niacinamide) on the outcomes of Covid-19 in AKI that is estimated to be completed by March 2023. Current data from observational studies shows that vitamin B3 lowers the risk of needing renal replacement therapy or death [111]. Currently neither the FDA or NIH recommend treatment with any supplements for Covid-19 [112,113]. As vitamins are not currently recommended by any regulatory bodies or professional organizations and vitamin use in CKD is explored extensively in other locations further inquiry should be sought there [24,114-117] (Table 1).

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