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Review

Virus infection and direct-acting antivirals in pregnancy

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Abstract

Objective: Antiviral therapy during pregnancy has always presented difficulties in clinical practice. This review covers the safety and efficacy of the direct use of antivirals during pregnancy. **Mechanism**: We conducted literature research to summarize the available evidence on the use of direct-acting antivirals during pregnancy for infections due to influenza, hepatitis B and C, human immunodeficiency, herpes simplex virus, cytomegalovirus, varicella-zoster virus, Ebola, and Zika viruses, and human coronavirus. **Findings in brief**: To support further the rational use of antivirals during pregnancy, the discussion includes the influence of pregnancy on pharmacokinetics, safety, and transplacental permeability, and the protection of mothers and children from vertical transmission. **Conclusion**: Data on the use of antiviral drugs during pregnancy are currently insufficient. Promoting research on the ethics of drug experimentation, and pharmacokinetics, drug metabolism, and pharmacological effects of pregnancy, is essential to improve the care of pregnant women and even save lives during current and future outbreaks.

Keywords: Antivirus drug; Pregnancy; Pregnancy complications; Coronavirus; Mother-to-child transmission; Direct-acting antivirals

1. Introduction

We currently grapple with the pandemic caused by the 2019 novel coronavirus (2019-nCoV), which is reminiscent of the serious pandemics caused by severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS). As well, infections due to the human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV) remain ongoing. These and other viral infections are challenging to treat during pregnancy and may cause serious sequelae. The Zika virus is a particularly severe danger to pregnant women and their fetuses [1]. Maternal virus infection threatens not only the wellbeing of the woman, but adverse outcomes of the fetus can include intrauterine growth restriction, premature delivery, spontaneous abortion, and perinatal death.

The complex physiological changes of pregnancy cause differences in drug metabolism and pharmacokinetics. The management of antiviral therapy must consider the long course of some, and the safety associated with maternal dosing and mother-to-child transmission (MTCT). This review discusses the influence of viral infection on pregnant women and fetuses, and evaluates some important direct-acting antivirals used to treat viruses during pregnancy. The clinical evidence considered includes therapeutic effects, pregnancy-related pharmacokinetic changes, placental transport, blocking MTCT, and long-term safety.

2. Methods

We conducted a literature search within the Web of Science, PubMed, and Elsevier ScienceDirect databases for all English-language studies published in the recent 10 years. Google Scholar was also searched. The search terms used for the study selection were "pregnan*" associated with virus infection and direct-acting antivirals. Specifically, the terms included the following: "influenza", "hepatitis B", "hepatitis C", "human immunodeficiency", "herpes simplex virus", "cytomegalovirus", "varicella-zoster virus", "Ebola", "Zika viruses", and "human coronavirus", and the direct-acting antivirals included in this review. Relevant literature ranked as Q1 to Q3 by the Journal Citation Indicator were identified manually and were eventually included in the review.

3. Viral infectious during pregnancy

3.1 Human coronavirus

Severe acute respiratory syndrome coronavirus (SARS-CoV) infection is associated with maternal morbidity, mortality, and spontaneous abortion. In a case-control study, 3 of 10 pregnant women with SARS died, although the mortality for 40 infected non-pregnant women was nil [2].

Significant abnormalities have been found in the placenta of some women who recovered from SARS-CoV infection in late pregnancy, including a wide range of fetal thrombotic vasculopathy and vascular malperfusion. Although the placentas of some pregnant women infected with SARS-CoV have been normal with healthy delivery [3], such patients have an increased risk of renal failure and disseminated intravascular coagulation compared with non-pregnant adults.

There is limited data on the prevalence and clinical characteristics of MERS during pregnancy, childbirth and

postpartum. The overall mortality rate of pregnant women with MERS has been very high, and the rate of fetal death is 27%. There have been 11 cases reported of pregnant women with MERS, and 91% had undesirable clinical results [4].

SARS-CoV, MERS-CoV, and 2019-nCoV have similar pathogenicity. Pregnant women are at increased risk of viral infection, which may lead to serious adverse consequences for the mother and during the perinatal period [5]. There has been no case reported of vertical transmission of SARS-CoV or MERS-CoV. This may indicate that MTCT of coronavirus is relatively rare [6].

A recent publication provides reasonable evidence of transplacental transmission of Coronavirus Disease 2019 (COVID-19). Viremia and neurological damage were observed in a newborn whose mother was infected with 2019-nCoV. The viral load of 2019-nCoV in placental tissue is much higher than the viral load in amniotic fluid or maternal blood. Other transmission routes have not been confirmed [7]. Immunoglobulin M (IgM) antibody from a neonate whose mother was infected with 2019-nCoV was elevated, which indicates vertical transmission [8].

There have been several reports of serious infection and perinatal deaths of pregnant women caused by COVID-19 [9]. Women with COVID-19 infection in the third trimester have presented with fever (68%), cough (34%), lymphocytopenia (59%), and elevated C-reactive protein (70%), 91% elected cesarean section [10].

3.2 Influenza virus

Pregnancy and postpartum status are the highest risk factors of serious complications and death from seasonal and pandemic influenza. The potential adverse effects of influenza on pregnant women are particularly serious, especially for those with additional health complications. All pregnant women with suspected or confirmed influenza must be given antiviral treatment (oseltamivir or zanamivir) within 48 hours of symptom onset, regardless of vaccination status [11]. Currently, oseltamivir is the first choice for pregnant women. Pregnant women in close contact with a person with confirmed, possible, or suspected influenza A or influenza B virus infection should receive preventive treatment with oseltamivir or zanamivir [12].

3.3 HBV

HBV in pregnant women is an independent risk factor of gastrointestinal disease in offspring [13]. In areas endemic to chronic hepatitis B, perinatal transmission occurs in 70% to 90% of children born to $HBeAg^+$ mothers. There is a linear correlation between vertical transmission and maternal $\log_{10}$ HBV load [14]. The probability of MTCT is significantly lower if maternal HBV DNA is less than 200,000 IU/mL at delivery. For mothers whose HBV DNA levels exceed 6^{10} IU/mL, MTCT can be reduced by antiviral treatment.

Six nucleotide analogues have been approved by the United States Food and Drug Administration for antiviral treatment of chronic hepatitis B, which can be classified as either nucleoside or nucleotide analogues. The three nucleoside analogues are lamivudine, telbivudine, and entecavir. The nucleotide analogues comprise adefovir dipivoxil, tenofovir alafenamide, and tenofovir disoproxil fumarate (TDF) [15]. Adefovir and entecavir are not recommended in pregnancy. Women with a high viral load should be treated, and the preferred agent is TDF, because of its lower association with resistance, and greater efficacy and safety in pregnancy.

3.4 HCV

Studies have shown that HCV is associated with elevated risks of low gestational weight, preterm birth, gestational hypertension, and diabetes [16]. HCV status in pregnant women is an independent risk factor for gastrointestinal disease in their offspring [17]. HCV infection can spread vertically in pregnant women, with a transmission rate of about 5.8%, especially in women with high HCV load [17]. Viremia is the only absolute risk factor for MTCT of HCV, so if the pregnant woman's HCV infection is cured, transmission to the baby will be averted [18]. Direct-acting antivirals for HCV can achieve a high cure rate (>95%), however the guidelines recommend deferring these during pregnancy [19].

3.5 HIV

HIV infection during pregnancy can lead to vertical transmission. The exact mechanism of MTCT of HIV remains unclear, but may occur during intrauterine life, delivery, or breastfeeding. The greatest risk of transmission is in the late stage of acquired immune deficiency syndrome (AIDS). Without treatment, the risk of MTCT is as high as 25%; while antiretroviral therapy during pregnancy reduces the risk to less than 1% [20]. Pregnant women with HIV should undergo antiretroviral therapy for their own health, and reduce the possibility of HIV transmission to infants. During pregnancy, the use of the integrase strand transfer inhibitor raltegravir or dolutegravir, and protease inhibitors atazanavir/ritonavir (once daily) or darunavir/ritonavir (twice daily), are recommended. Elvitegravir or cobicistat is not recommended [21].

Dual nucleoside reverse transcriptase inhibitor (NRTI) regimens can sustain viral suppression, and reduce side effects and costs [22]. So far, no short-term neurodevelopmental toxicity has been found in fetuses exposed to dual-NRI *in utero* [23]. The dual-NRTI regimens abacavir/lamivudine, TDF/lamivudine, and TDF/emtricitabine are preferred during pregnancy. It should be noted that the use of abacavir requires detection of *HLA-B*5701*. Patients who are positive for the *HLA-B*5701* gene have a higher risk of hypersensitivity reactions caused by abacavir [24].

3.6 Herpes simplex virus

Herpes simplex virus (HSV) types 1 and 2 (HSV-1 and HSV-2) are common infections with serious sequelae, whereas infection of developing fetuses and newborns is rare (1/10000 to 1/3200) [25] but likely severe [26]. The mortality of untreated neonatal disseminated HSV is about 80% [27]. Pregnancy is a risk factor for HSV hepatitis and can result in significant mortality [28]. HSV infection can lead to genital infection, especially during pregnancy, as well as lifelong disease with unpredictable recurrences [29].

The main routes of HSV vertical transmission include intrauterine infection (about 5%) and infection through the birth canal (85% to 90%). The main risk factors for vertical transmission include high HSV load in the maternal birth canal, insufficient antibodies in newborns, delivery through the birth canal, and damaged skin barrier. Infection types and virus types also affect the risk of MTCT, as primary infection may result in higher risk of recurrent infection. In addition, HSV-1 infection may result in higher risk than HSV-2 infection [30].

To prevent severe neonatal HSV infection, antiviral treatment should be given to mothers from 36 weeks of pregnancy, together with monitoring of genital HSV lesions. Cesarean delivery is recommended for pregnant women with genital herpetic lesions [29]. There is no evidence that antiviral therapy can reduce the risk of HSV infection in pregnant women, and antiviral prevention is not recommended when there is no herpes zoster. If the potential benefits to the mother outweigh the potential risks to the fetus, it is recommended to start antiviral treatment with acyclovir in the presence of complex disease progression [31].

3.7 Cytomegalovirus

Congenital cytomegalovirus (CMV) infection is common, with infection rates of live births from 0.5% to 1.0% in the United States and Europe, and 0.6% to 6.1% in developing countries [25]. The risk of cervix shedding during pregnancy may increase as the pregnancy progresses: 5% in the first trimester, 6% to 10% in the second trimester, and 11% to 28% in the third trimester.

Both primary CMV infection and non-primary infection can lead to intrauterine transmission with probabilities of 50% and 2%, respectively [32]. CMV can transmit to infants through breast milk and horizontal transmission [33]. Congenital CMV infection can lead to permanent loss of hearing and vision, as well as severe neurological disability. In addition, CMV infection is considered a risk factor for miscarriage, and in very severe cases can lead to stillbirth. Antenatal antiviral treatment such as ganciclovir or valacyclovir is not recommended in pregnancy [34].

3.8 Varicella-zoster virus

The incidence of chickenpox may range from 0.12% to 0.60% in pregnant women [35]. Developing chickenpox during pregnancy has adverse effects on pregnant women, their fetuses, and newborns. About 10% to 20% of pregnant women with varicella zoster virus (VZV) infection will develop pneumonia, which is a significant risk factor of maternal death, as high as 40% [36].

VZV can spread through the placenta, causing congenital or neonatal chickenpox. Reactivating VZV during pregnancy does not usually result in increased fetal mortality or malformations [37]. Symptoms of newborn VZV infections can vary from infections of specific areas of the mucous membranes, skin, eyes, and central nervous system, to disseminated systemic infections [38]. Once the infection is diagnosed, it is vital to start anti-viral treatment soon. It is recommended to use antiviral therapy alone or in combination with hyperimmune globulins to VZV for the management of VZV infection during pregnancy. Acyclovir, valacyclovir, and famciclovir can be used in antiviral treatment against VZV during pregnancy [35].

3.9 Ebola virus

Ebola virus (EBOV) disease has significantly high mortality rates for all ages, and is highest in fetuses and newborns. Almost all pregnancies in women infected with EBOV end in abortion or stillbirth. MTCT of EBOV appears likely, since samples of amniotic fluid, placenta, and fetus have proved EBOV-positive, but it may also occur during childbirth and breastfeeding. Possible causes of high fetal and neonatal mortality include a weakened uterine cavity, higher intrauterine and fetal viral loads, and immature immune systems in the fetus and newborn [39].

3.10 Zika virus

The incidence of Zika virus infection is slightly higher in women than in men. Serious manifestations in infants born to infected mothers vary across time and regions, including adult Guillain-Barre syndrome and microcephaly [40]. Zika virus infection has been linked to congenital abnormalities of the central nervous system. It can be transmitted through sexual contact, and can cause teratogenic consequences via MTCT during all trimesters, even when maternal infection is asymptomatic [41]. In cases of maternal Zika virus infections, about 26% of fetuses will be infected during the pregnancy, and 21% and 14%, respectively, will suffer serious complications at birth or abortion [42]. There are differences in fetal risks depending on the trimester of infection. Neurological and ocular defects are more common when Zika virus infection occurs early in pregnancy [43].

4. Antivirus drugs used during pregnancy

4.1 Integrase inhibitors

4.1.1 Dolutegravir

Compared with efavirenz, dolutegravir showed a stronger virologic response and stronger inhibition of HIV RNA. Dolutegravir can reduce the risk of vertical transmis-

sion [44] in mothers who start treatment in late pregnancy. Dolutegravir is highly bound to plasma proteins [45], and the free blood concentration of dolutegravir in pregnant women is similar to that of postpartum women [44]. Exposure of the fetus to dolutegravir is lower in the second trimester, and transfer through the placenta and through breastfeeding has been observed. Due to slower metabolic clearance in infants, dolutegravir may persist in infants [44]. No evidence of teratogenic or developmental toxicity has been found in pregnant animals, or in early clinical trials in pregnant women receiving dolutegravir [46]. Dolutegravir is recommended in all fertile women, including those in planned pregnancies and during pregnancies [47].

Dolutegravir-based antiretroviral therapy has similar adverse birth outcomes to efavirenz-based therapy [48]. However, studies showed that exposure to dolutegravir during pregnancy was associated with a slightly higher rate of neonatal neural tube defects compared to non-dolutegravir antiretroviral therapy [49]. In addition, compared with newborns whose mothers are HIV-negative, the prevalence of neural tube defects is slightly higher in newborns whose mothers are HIV-positive and have been taking dolutegravir during pregnancy [50]. The role of dolutegravir in terms of neural tube defects has been controversial [51], but it remains a preferred drug after consideration of risks [52].

4.1.2 Raltegravir

Tolerance of raltegravir is good during pregnancy [53]. The variation of pharmacokinetics of raltegravir is extensive [54]. Reduction of raltegravir exposure is observed in late pregnancy compared with postpartum, but it is not considered of clinical importance [55]. Raltegravir can be used in standard doses for pregnant women with HIV and is beneficial in the prevention of MTCT of HIV [21]. Raltegravir can be used in all stages of pregnancy as the preferred integrase inhibitor [56]. Raltegravir is not recommended to start during pregnancy if the patient is acutely infected, because of concerns about reduced potency with high viral loads [57].

Raltegravir can cross the placenta very easily. The ratio of raltegravir concentration in cord blood to maternal plasma is 1.48 (range, 0.32–4.33). The elimination of raltegravir varies greatly in some infants and the exposure is prolonged for a very long time [58]. At present, there is no evidence that the use of raltegravir in pregnancy will lead to fetal congenital abnormality [59].

4.2 Nucleoside analogue

4.2.1 Abacavir

Abacavir is the first-line antiretroviral drug for prevention of HIV MTCT [60]. The pharmacokinetics of abacavir and expected antiviral activity during pregnancy are comparable to that at postpartum, and no adjustment of the dosage regimen is needed during pregnancy [61]. Abacavir-containing antiretroviral therapy during pregnancy is not significantly different from anti-retroviral therapy without abacavir in a setting of adverse pregnancy events [62]. Equilibrative nucleoside transporter 1 (ENT1) is helpful for the transplacental transfer of abacavir [60]. Therefore, more attention should be paid to the drug interactions and individual differences in ENT1 in the placenta and disposition of abacavir into the fetal circulation. It has been demonstrated that a triple therapy of abacavir, dolutegravir, and lamivudine is effective and generally tolerated in the treatment of HIV infection. This triple therapy appears to have better tolerance characteristics than combined efavirenz, TDF, and emtricitabine [63].

4.2.2 Lamivudine

Lamivudine can be used as part of a 3-drug regimen for HIV, but should probably not be used as a first line single drug for HBV [63]. Although lamivudine is concentrated in breast milk, lamivudine cannot be effectively absorbed by infants via this pathway compared with the transplacental pathway, which suggests that breastfeeding is not a contraindication to use of lamivudine for HIV [64]. Lamivudine therapy of mothers who carry HBV from 28 weeks of gestation, may effectively interrupt the MTCT of HBV, and is safer and more effective than hepatitis B immunoglobulin [65]. If the viral load of the pregnant woman is reduced to $<10^6$ copies/mL by the use of lamivudine, HBV MTCT may be effectively interrupted [65]. In the early stage of pregnancy, the use of lamivudine in the treatment of active chronic hepatitis B also seems safe and effective for the control of the disease and interruption of MTCT [15].

4.2.3 Remdesivir

Remdesivir has become a recommended standard care for COVID-19, including during pregnancy. Note that remdesivir should only be used in pregnant women if the potential benefits justify the potential risks to the mother and fetus [66]. In a randomized clinical controlled trial, remdesivir was associated with significant shortening of recovery time of adults hospitalized with COVID-19, and relief of symptoms of lower respiratory tract infection [67]. Remdesivir has shown good efficacy and clinical safety in the treatment of coronavirus infection [68,69]. A case report shows that remdesivir was effective in treating severe COVID-19 during pregnancy [70]. Based on the early evidence, various national guidelines recommend the use of remdesivir in different patient subgroups [71].

4.2.4 Acyclovir

The use of acyclovir in the first trimester of pregnancy was not associated with any increased risk of major birth defects [72]. The pharmacokinetics of maternal acyclovir are comparable to that in non-pregnant women [35]. Yet, acyclovir can pass through the placenta, accumulate in the amniotic fluid, and result in consistent drug levels between

mother and fetus [27]. One study shows that in surviving infants with HSV central nervous system involvement, 6 months of oral acyclovir therapy can improve their neurodevelopmental conditions [73].

4.3 Nucleotide analogue reverse transcriptase inhibitor

Tenofovir

Tenofovir is safe and tolerable for both mother and fetus. The use of TDF in HBV and HIV infection is supported during pregnancy [15] and is recommended in countries with limited resources.

The exposure of infants *in utero* may be higher than through breast milk, and there is no evidence to support the prohibition of TDF during breastfeeding [74]. In $HBeAg^+$ mothers who had HBV DNA levels >200,000 IU/mL during the third trimester, HBV DNA levels and rate of MTCT were reduced by TDF treatment [14,75]. The evidence is not sufficient to suggest that additional use of TDF at low maternal HBV load can further reduce the risk of MTCT [14]. Tenofovir has a lower area under the receiver operating characteristic curve and trough during pregnancy compared with postpartum. Placental pass rates for long-term use of TDF during pregnancy are high [76]. Standard TDF doses seem suitable for most pregnant women with HIV infection, but pregnant women with large distribution volumes (weight >90 kg) or insufficient HIV RNA response should consider therapeutic drug monitoring with dose adjustment [77].

4.4 Neuraminidase inhibitor

Oseltamivir

For any adult or pediatric patient with a chronic or serious illness requiring hospitalization, if influenza is suspected, treatment with oseltamivir should be initiated immediately, regardless of the duration of the symptoms [78]. Oseltamivir carboxylate (OC) is the active metabolite of oseltamivir [79]. During pregnancy, systemic exposure of OC was reduced ~30% (19–36%), while clearance of OC increased ~45% (23–62%) [80].

Oseltamivir and OC will pass through the placenta and will likely be detected in very low concentrations of fetal septum [80]. Oseltamivir used at the clinically recommended dose is unlikely to cause adverse effects on the growth and development of the fetus [81]. No evidence of meaningful increase in risk of birth defects, preterm delivery, or small for gestational age infants was found when oseltamivir was applied in pregnancy. Using oseltamivir in pregnant women within 48 hours (or earlier) of the onset of symptoms seems to increase benefits [11].

4.5 Protease inhibitors

4.5.1 Darunavir

Darunavir is a first-line protease inhibitor recommended in pregnancy. Darunavir has mild side effects and a low resistance rate compared with other proteases [82]. A darunavir regimen can effectively inhibit HIV replication during pregnancy and prevent HIV transmission during the perinatal period with minimal sequelae [83]. During pregnancy, the total plasma concentration of darunavir (free or bound) of pregnant women was significantly lower compared with postpartum. However, because the concentration of free darunavir was comparable, the standard dose seems able to maintain antiviral activity [84]. Darunavir has a low rate of placental transfer [85]. Darunavir and atazanavir were similar in safety and activity during pregnancy, and there is no evidence that the two drugs are different regarding main pregnancy outcome [86]. Premature birth and low birth weight may be linked to darunavir exposure, but there is currently a lack of reliable evidence.

4.5.2 Atazanavir

The total concentration of atazanavir is lower during pregnancy compared with postpartum and in nonpregnant populations [87]. However, the intracellular concentrations of atazanavir and unbound plasma atazanavir in HIV-infected pregnant women remain stable, which supports the use of a standard dose of atazanavir throughout pregnancy [88]. Exposure to atazanavir is associated with increased plasma bilirubin levels [86]. A study has shown that higher concentrations of atazanavir in meconium have a protective effect on developmental language delay at the age of one year, which supports the safety of atazanavir with regard to infant language development [89]. However, compared with regimens without atazanavir, intrauterine exposure to atazanavir may have a negative effect on language and socio-emotional development in the first year after birth, in uninfected infants subjected to prenatal exposure to HIV, but the absolute difference was small [90]. Atazanavir can only be used in pregnancy when combined with ritonavir, because cobicistat is contraindicated in pregnancy. Use of unboosted atazanavir is not recommended during pregnancy [91].

5. Conclusions

In recent years, EBOV, Zika virus, and 2019-nCoV have all challenged attempts at treatment. Each of these epidemics highlights how viral infections can severely and sometimes uniquely affect the health of pregnant women and their children. Pregnant women suffer much higher risk of serious illness and death when Ebola, influenza, and Lassa fever outbreaks flare, with potentially devastating consequences for the fetus.

The standard regimen may not be the best choice for pregnant women, because pharmacokinetic changes caused by pregnancy may affect drug exposure, and thus the efficacy of the drugs. Placental transport that results in fetal exposure of antiviral drugs should also be considered. The therapeutic drug and viral load should be monitored when treating pregnant women. Some placental transporters have a significant influence on placental transport of some drugs

[92]. This suggests that attention should be given to the effects of drug-drug interactions, and transporter genes that may influence fetal drug exposure.

The timing of antiviral treatment should consider the crucial windows of teratogenic effects (typically the first trimester) and vertical transmission. Since contact with perinatal blood may be an important source of vertical transmission, treatment should be completed, or viral load controlled, before delivery. In addition, when a woman continues treatment until delivery, fetal exposure should be assessed, for example by measuring cord blood concentration.

Data on the use of antiviral drugs during pregnancy are currently insufficient. Some antiviral drugs may cause adverse effects if used in pregnancy. Research is still limited regarding factors that may affect the outcome of pregnancy or cause obstetric diseases in a setting of viral infection. Such factors include the time of maternal viral exposure and viral load. Additional clinical studies are needed to understand the potential risks and benefits of antiviral therapy during pregnancy, particularly during the 2019-nCoV outbreak, and old enemies such as HIV infections. Promoting research on the ethics of drug experimentation, and pharmacokinetics, drug metabolism, and pharmacological effects of pregnancy, is essential to improve the care of pregnant women and even save lives during current and future outbreaks.

This review focused on the direct antiviral treatment during pregnancy. But we have also noticed that the development of newer pharmaceutical agents like monoclonal antibodies was raising. For example, a variety of HIV-neutralizing antibodies are also being tested, such as ub-421 [93] and PGT121 [94]. Gene therapy has also entered the clinical stage as a new HIV treatment scheme [95]. As for the emerging drugs of HBV infection, capsid assembly inhibitors and modulators are one of the main categories under development [96,97]. RNA interference is also a hot research field of the development of anti-HBV drugs in recent years, and many have entered phase II clinical trials [98]. Immunotherapy, as a type of novel antiviral therapy, has gradually attracted people's attention by preventing T cell depletion to inhibit the virus [99]. In general, in addition to traditional antiviral drugs such as polymerase and protease inhibitors, nucleic acid medicines, entry inhibitors, capsid assembly inhibitors and host targeting antiviral agents are also increasingly appearing in the R & D pipelines of major pharmaceutical enterprises. With the gradual rise of new antiviral therapy, it will be easier to achieve the ultimate goal of eliminating viral infection by jointly resisting the virus through drugs with different mechanisms.

Abbreviations

2019-nCoV, 2019 novel coronavirus; AIDS, acquired immune deficiency syndrome; CMV, cytomegalovirus; COVID-19, Coronavirus Disease 2019; EBOV, Ebola virus; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; HSV, herpes simplex virus; MERS, Middle East respiratory syndrome; MTCT, mother-to-child transmission; NRTI, nucleoside reverse transcriptase inhibitor; OC, oseltamivir carboxylate; SARS, severe acute respiratory syndrome; SARS-CoV, severe acute respiratory syndrome coronavirus; TDF, tenofovir disoproxil fumarate; VZV, varicella zoster virus.

Author contributions

XH wrote the manuscript and collected the data. JT supervised the idea and writing, revised the manuscript and directed all progress. XH and JT designed the research study. XH performed the research and wrote the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

Not applicable.

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Conflict of interest

The authors declare no conflict of interest.

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