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1. On the use of corticosteroids for 2019-nCoV pneumonia.

Authors Shang L; Zhao J; Hu Y; Du R; Cao B
Source Lancet (London, England); ; vol. 395 (no. 10225); p. 683-684
Publication Type(s) Letter; Comment
PubMedID 32122468
Database PubMed
Available at Lancet (London, England) from ClinicalKey
Available at Lancet (London, England) from Kent and Canterbury Hospital Library (lib327265) Local Print Collection Kent and Canterbury Hospital Library.
Available at Lancet (London, England) from Unpaywall

2. Clinical evidence does not support corticosteroid treatment for 2019-nCoV lung injury.

Authors Russell CD; Millar JE; Baillie JK
Source Lancet (London, England); ; vol. 395 (no. 10223); p. 473-475
Publication Type(s) Journal Article
PubMedID 32043983
Database PubMed
Available at Lancet (London, England) from ClinicalKey
Available at Lancet (London, England) from Kent and Canterbury Hospital Library (lib327265) Local Print Collection Kent and Canterbury Hospital Library.
Available at Lancet (London, England) from Unpaywall

3. Erratum: Department of Error (The Lancet (2020) 395(10229) (1054-1062), (S0140673620305663), (10.1016/S0140-6736(20)30566-3))

Authors anonymous
Source The Lancet; 2020; vol. 395 (no. 10229); p. 1038
Publication Date 2020
Publication Type(s) Erratum
PubMedID 32192581
Database EMBASE
Available at Lancet (London, England) from ClinicalKey
Available at Lancet (London, England) from Kent and Canterbury Hospital Library (lib327265) Local Print Collection Kent and Canterbury Hospital Library.
Available at Lancet (London, England) from Unpaywall
Abstract Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020; published online March 9. https://doi.org/10.1016/S0140-6736(20)30566-3-In this Article, the units for d-dimer, haemoglobin, and high-sensitivity cardiac troponin I have been corrected to mug/mL (d-dimer), g/L (haemoglobin), and pg/mL (high-sensitivity cardiac troponin I). In figure 1, the start of systematic corticosteroid for non-survivors has been changed to day 13 after illness onset. The appendix has also been corrected. These corrections have been made to the online version as of March 12, 2020, and will be made to the printed version.

4. Potential benefits of precise corticosteroids therapy for severe 2019-nCoV pneumonia.

Authors Zhou W; Liu Y; Tian D; Wang C; Wang S; Cheng J; Hu M; Fang M; Gao Y
Source Signal transduction and targeted therapy; 2020; vol. 5 ; p. 18
Publication Date 2020
Publication Type(s) Journal Article
PubMedID 32133159
Database PubMed
Available at Signal Transduction and Targeted Therapy from Unpaywall

5. Cardiac Involvement in a Patient With Coronavirus Disease 2019 (COVID-19).

Authors Inciardi, Riccardo M; Lupi, Laura; Zaccone, Gregorio; Italia, Leonardo; Raffo, Michela; Tomasoni, Daniela; Cani, Dario S; Cerini, Manuel; Farina, Davide; Gavazzi, Emanuele; Maroldi, Roberto; Adamo, Marianna; Ammirati, Enrico; Sinagra, Gianfranco; Lombardi, Carlo M; Metra, Marco
Source JAMA cardiology; Mar 2020
Publication Date Mar 2020

Publication Type(s) Journal Article
PubMedID 32219357
Database Medline
Abstract ImportanceVirus infection has been widely described as one of the most common causes of myocarditis. However, less is known about the cardiac involvement as a complication of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.ObjectiveTo describe the presentation of acute myocardial inflammation in a patient with coronavirus disease 2019 (COVID-19) who recovered from the influenzalike syndrome and developed fatigue and signs and symptoms of heart failure a week after upper respiratory tract symptoms.Design, Setting, and ParticipantThis case report describes an otherwise healthy 53-year-old woman who tested positive for COVID-19 and was admitted to the cardiac care unit in March 2020 for acute myopericarditis with systolic dysfunction, confirmed on cardiac magnetic resonance imaging, the week after onset of fever and dry cough due to COVID-19. The patient did not show any respiratory involvement during the clinical course.ExposureCardiac involvement with COVID-19.Main Outcomes and MeasuresDetection of cardiac involvement with an increase in levels of N-terminal pro-brain natriuretic peptide (NT-proBNP) and high-sensitivity troponin T, echocardiography changes, and diffuse biventricular myocardial edema and late gadolinium enhancement on cardiac magnetic resonance imaging.ResultsAn otherwise healthy 53-year-old white woman presented to the emergency department with severe fatigue. She described fever and dry cough the week before. She was afebrile but hypotensive; electrocardiography showed diffuse ST elevation, and elevated high-sensitivity troponin T and NT-proBNP levels were detected. Findings on chest radiography were normal. There was no evidence of obstructive coronary disease on coronary angiography. Based on the COVID-19 outbreak, a nasopharyngeal swab was performed, with a positive result for SARS-CoV-2 on real-time reverse transcriptase-polymerase chain reaction assay. Cardiac magnetic resonance imaging showed increased wall thickness with diffuse biventricular hypokinesis, especially in the apical segments, and severe left ventricular dysfunction (left ventricular ejection fraction of 35%). Short tau inversion recovery and T2-mapping sequences showed marked biventricular myocardial interstitial edema, and there was also diffuse late gadolinium enhancement involving the entire biventricular wall. There was a circumferential pericardial effusion that was most notable around the right cardiac chambers. These findings were all consistent with acute myopericarditis. She was treated with dobutamine, antiviral drugs (lopinavir/ritonavir), steroids, chloroquine, and medical treatment for heart failure, with progressive clinical and instrumental stabilization.Conclusions and RelevanceThis case highlights cardiac involvement as a complication associated with COVID-19, even without symptoms and signs of interstitial pneumonia.

6. COVID-19 infection and rheumatoid arthritis: Faraway, so close!

Authors Favalli, Ennio Giulio; Ingegnoli, Francesca; De Lucia, Orazio; Cincinelli, Gilberto; Cimaz, Rolando; Caporali, Roberto
Source Autoimmunity reviews; Mar 2020 ; p. 102523
Publication Date Mar 2020
Publication Type(s) Journal Article Review
PubMedID 32205186
Database Medline
Available at Autoimmunity reviews from ClinicalKey
Available at Autoimmunity reviews from Unpaywall
Abstract The outbreak of the new coronavirus infections COVID-19 in December 2019 in China has quickly become a global health emergency. Given the lack of specific anti-viral therapies, the current management of severe acute respiratory syndrome coronaviruses (SARS-CoV-2) is mainly supportive, even though several compounds are now under investigation for the treatment of this life-threatening disease. COVID-19 pandemic is certainly conditioning the treatment strategy of a complex disorder as rheumatoid arthritis (RA), whose infectious risk is increased compared to the general population because of an overall impairment of immune system typical of autoimmune diseases combined with the iatrogenic effect generated by corticosteroids and immunosuppressive drugs. However, the increasing knowledge about the pathophysiology of SARS-CoV-2 infection is leading to consider some anti-rheumatic drugs as potential treatment options for the management of COVID-19. In this review we will critically analyse the evidences on either positive or negative effect of drugs commonly used to treat RA in this particular scenario, in order to optimize the current approach to RA patients.

7. Clinical characteristics of refractory COVID-19 pneumonia in Wuhan, China.

Authors Mo, Pingzheng; Xing, Yuanyuan; Xiao, Yu; Deng, Liping; Zhao, Qiu; Wang, Hongling; Xiong, Yong; Cheng, Zhenshun; Gao, Shicheng; Liang, Ke; Luo, Mingqi; Chen, Tielong; Song, Shihui; Ma, Zhiyong; Chen, Xiaoping; Zheng, Ruiying; Cao, Qian; Wang, Fan; Zhang, Yongxi
Source Clinical infectious diseases : an official publication of the Infectious Diseases Society of America; Mar 2020
Publication Date Mar 2020
Publication Type(s) Journal Article
PubMedID 32173725
Database Medline

Available at Clinical infectious diseases : an official publication of the Infectious Diseases Society of America from Unpaywall

Abstract BACKGROUNDSince December 2019, novel coronavirus (SARS-CoV-2)-infected pneumonia (COVID-19) occurred in Wuhan, and rapidly spread throughout China. This study aimed to clarify the characteristics of patients with refractory COVID-19.METHODSIn this retrospective single-center study, we included 155 consecutive patients with confirmed COVID-19 in Zhongnan Hospital of Wuhan University from January 1st to February 5th. The cases were divided into general and refractory COVID-19 groups according to the clinical efficacy after hospitalization, and the difference between groups were compared.RESULTSCompared with general COVID-19 patients (45.2%), refractory patients had an older age, male sex, more underlying comorbidities, lower incidence of fever, higher levels of maximum temperature among fever cases, higher incidence of breath shortness and anorexia, severer disease assessment on admission, high levels of neutrophil, aspartate aminotransferase (AST), lactate dehydrogenase (LDH) and C-reactive protein, lower levels of platelets and albumin, and higher incidence of bilateral pneumonia and pleural effusion (P<0.05). Refractory COVID-19 patients were more likely to receive oxygen, mechanical ventilation, expectorant, and adjunctive treatment including corticosteroid, antiviral drugs and immune enhancer (P<0.05). After adjustment, those with refractory COVID-19 were also more likely to have a male sex and manifestations of anorexia and fever on admission, and receive oxygen, expectorant and adjunctive agents (P<0.05) when considering the factors of disease severity on admission, mechanical ventilation, and ICU transfer.CONCLUSIONNearly 50% COVID-19 patients could not reach obvious clinical and radiological remission within 10 days after hospitalization. The patients with male sex, anorexia and no fever on admission predicted poor efficacy.

8. Understanding SARS-CoV-2-Mediated Inflammatory Responses: From Mechanisms to Potential Therapeutic Tools.

Authors Fu, Yajing; Cheng, Yuanxiong; Wu, Yuntao
Source Virologica Sinica; Mar 2020
Publication Date Mar 2020
Publication Type(s) Journal Article Review
PubMedID 32125642
Database Medline
Available at Virologica Sinica from Unpaywall

Abstract Currently there is no effective antiviral therapy for SARS-CoV-2 infection, which frequently leads to fatal inflammatory responses and acute lung injury. Here, we discuss the various mechanisms of SARS-CoV-mediated inflammation. We also assume that SARS-CoV-2 likely shares similar inflammatory responses. Potential therapeutic tools to reduce SARS-CoV-2-induced inflammatory responses include various methods to block FcR activation. In the absence of a proven clinical FcR blocker, the use of intravenous immunoglobulin to block FcR activation may be a viable option for the urgent treatment of pulmonary inflammation to prevent severe lung injury. Such treatment may also be combined with systemic anti-inflammatory drugs or corticosteroids. However, these strategies, as proposed here, remain to be clinically tested for effectiveness.

9. Clinical Features and Treatment of COVID-19 Patients in Northeast Chongqing.

Authors Wan, Suxin; Xiang, Yi; Fang, Wei; Zheng, Yu; Li, Boqun; Hu, Yanjun; Lang, Chunhui; Huang, Daoqiu; Sun, Qiuyan; Xiong, Yan; Huang, Xia; Lv, Jinglong; Luo, Yaling; Shen, Li; Yang, Haoran; Huang, Gu; Yang, Ruishan
Source Journal of medical virology; Mar 2020
Publication Date Mar 2020
Publication Type(s) Journal Article
PubMedID 32198776
Database Medline
Available at Journal of medical virology from Unpaywall

Abstract BACKGROUNDThe outbreak of the novel coronavirus in China (SARS CoV-2) that began in December 2019 presents a significant and urgent threat to global health. This study was conducted to provide the international community with a deeper understanding of this new infectious disease.METHODSEpidemiological, clinical features, laboratory findings, radiological characteristics, treatment, and clinical outcomes of 135 patients in northeast Chongqing were collected and analyzed in this study.RESULTSA total of 135 hospitalized patients with COVID-19 were enrolled. The median age was 47 years (IQR 36-55), and there was no significant gender difference (53.3% men). The majority of patients had contact with people from the Wuhan area. Forty-three (31.9%) patients had underlying disease, primarily hypertension (13 [9.6%]), diabetes (12 [8.9%]), cardiovascular disease (7 [5.2%]), and malignancy (4 [3.0%]). Common symptoms included fever (120 [88.9%]), cough (102 [76.5%]), and fatigue (44 [32.5%]). Chest CT scans showed bilateral patchy shadows or ground glass opacity in the lungs of all of the patients. All of the patients received antiviral therapy (135 [100%] (Kaletra and interferon were both used), antibacterial therapy (59 [43.7%]), and corticosteroids (36 [26.7%]). In addition, many patients received traditional Chinese medicine (124 [91.8%]). It is suggested that patients should receive Kaletra early and should be treated by a combination of western and Chinese medicine. Compared with the mild cases, the severe cases had lower lymphocyte counts and higher plasma levels of Pt, APTT, D-dimer, LDH, PCT, ALB, CRP, and AST.CONCLUSIONIn this study, the clinic features and therapies of 135 COVID-19 patients were demonstrated. Kaletra and traditional Chinese medicine played an important role in the treatment of the viral pneumonia. Further studies are required to explore the role of Kaletra and traditional Chinese medicine in the treatment of COVID-19.

10. The 2019 Novel Coronavirus Outbreak - A Global Threat.

Authors Khot, Wasim Yunus; Nadkar, Milind Y
Source The Journal of the Association of Physicians of India; Mar 2020; vol. 68 (no. 3); p. 67-71
Publication Date Mar 2020
Publication Type(s) Journal Article
PubMedID 32138488
Database Medline
Abstract The 2019 Novel Corona virus infection (COVID 19) is an ongoing public health emergency of international significance. There are significant knowledge gaps in the epidemiology, transmission dynamics, investigation tools and management. In this article, we review the available evidence about this disease. Every decade has witnessed the evolution of a new coronavirus epidemic since the last three decades. The varying transmission patterns, namely, nosocomial transmission and spread through mildly symptomatic cases is an area of concern. There is a spectrum of clinical features from mild to severe life threatening disease with major complications like severe pneumonia, ARDS, acute cardiac injury and septic shock. Presence of bilateral ground glass opacity and consolidation on imaging in appropriate clinical background should raise a suspicion about COVID 19. Poor prognostic factors include Multilobular infiltration on chest imaging, Lymphopenia, Bacterial co-infection, Smoking history, Chronic medical conditions like Hypertension and age >60 years (MuLBSTA score). Diagnosis is confirmed with PCR based testing of appropriate respiratory samples. Management is primarily supportive, with newer antivirals (lopinavir ritonavir and Remdesivir) under investigation. Role of steroids is still inconclusive. Standard infection control and prevention techniques should be followed. Vigilant screening of suspected cases and their contacts is important. Isolation of symptomatic cases and home quarantine of asymptomatic contacts is recommended. To conclude, controlling this highly transmissible disease requires international co-ordination.

11. Clinical Characteristics of Children with Coronavirus Disease 2019 in Hubei, China.

Authors Zheng, Fang; Liao, Chun; Fan, Qi-Hong; Chen, Hong-Bo; Zhao, Xue-Gong; Xie, Zhong-Guo; Li, Xi-Lin; Chen, Chun-Xi; Lu, Xiao-Xia; Liu, Zhi-Sheng; Lu, Wei; Chen, Chun-Bao; Jiao, Rong; Zhang, Ai-Ming; Wang, Jin-Tang; Ding, Xi-Wei; Zeng, Yao-Guang; Cheng, Li-Ping; Huang, Qing-Feng; Wu, Jiang; Luo, Xi-Chang; Wang, Zhu-Jun; Zhong, Yan-Yan; Bai, Yan; Wu, Xiao-Yan; Jin, Run-Ming
Source Current medical science; Mar 2020
Publication Date Mar 2020
Publication Type(s) Journal Article
PubMedID 32207032
Database Medline
Available at Current medical science from Unpaywall

Abstract Since December 2019, COVID-19 has occurred unexpectedly and emerged as a health problem worldwide. Despite the rapidly increasing number of cases in subsequent weeks, the clinical characteristics of pediatric cases are rarely described. A cross-sectional multicenter study was carried out in 10 hospitals across Hubei province. A total of 25 confirmed pediatric cases of COVID-19 were collected. The demographic data, epidemiological history, underlying diseases, clinical manifestations, laboratory and radiological data, treatments, and outcomes were analyzed. Of 25 hospitalized patients with COVID-19, the boy to girl ratio was 1.27:1. The median age was 3 years. COVID-19 cases in children aged <3 years, 3.6 years, and ≥6-years patients were 10 (40%), 6 (24%), and 9 (36%), respectively. The most common symptoms at onset of illness were fever (13 [52%]), and dry cough (11 [44%]). Chest CT images showed essential normal in 8 cases (33.3%), unilateral involvement of lungs in 5 cases (20.8%), and bilateral involvement in 11 cases (45.8%). Clinical diagnoses included upper respiratory tract infection (n=8), mild pneumonia (n=15), and critical cases (n=2). Two critical cases (8%) were given invasive mechanical ventilation, corticosteroids, and immunoglobulin. The symptoms in 24 (96%) of 25 patients were alleviated and one patient had been discharged. It was concluded that children were susceptible to COVID-19 like adults, while the clinical presentations and outcomes were more favorable in children. However, children less than 3 years old accounted for majority cases and critical cases lied in this age group, which demanded extra attentions during home caring and hospitalization treatment.

12. Pharmacologic Treatments and Supportive Care for Middle East Respiratory Syndrome.

Authors Kain T; Lindsay PJ; Adhikari NKJ; Arabi YM; Van Kerkhove MD; Fowler RA
Source Emerging infectious diseases; Mar 2020; vol. 26 (no. 6)
Publication Date Mar 2020
Publication Type(s) Journal Article
PubMedID 32213260
Database PubMed
Available at Emerging infectious diseases from Europe PubMed Central - Open Access
Available at Emerging infectious diseases from Unpaywall

Abstract Available animal and cell line models have suggested that specific therapeutics might be effective in treating Middle East respiratory syndrome (MERS). We conducted a systematic review of evidence for treatment with pharmacologic and supportive therapies. We developed a protocol and searched 5 databases for studies describing treatment of MERS and deaths in MERS patients. Risk of bias (RoB) was assessed by using ROBINS-I tool. We retrieved 3,660 unique citations; 20 observational studies met eligibility, and we studied 13 therapies. Most studies were at serious or critical RoB; no studies were at low RoB. One study, at moderate RoB, showed reduced mortality rates in severe MERS patients with extracorporeal membrane oxygenation; no other studies showed a significant lifesaving benefit to any treatment. The existing literature on treatments for MERS is observational and at moderate to critical RoB. Clinical trials are needed to guide treatment decisions.

13. [Expert consensus on the use of corticosteroid in patients with 2019-nCoV pneumonia].

Authors Zhao JP; Hu Y; Du RH; Chen ZS; Jin Y; Zhou M; Zhang J; Qu JM; Cao B
Source Zhonghua jie he he hu xi za zhi = Zhonghua jiehe he huxi zazhi = Chinese journal of tuberculosis and respiratory diseases; Mar 2020; vol. 43 (no. 3); p. 183-184
Publication Date Mar 2020
Publication Type(s) Journal Article
PubMedID 32164084
Database PubMed

14. Clinical characteristics of novel coronavirus cases in tertiary hospitals in Hubei Province.

Authors Liu, Kui; Fang, Yuan-Yuan; Deng, Yan; Liu, Wei; Wang, Mei-Fang; Ma, Jing-Ping; Xiao, Wei; Wang, Ying-Nan; Zhong, Min-Hua; Li, Cheng-Hong; Li, Guang-Cai; Liu, Hui-Guo
Source Chinese medical journal; Feb 2020
Publication Date Feb 2020
Publication Type(s) Journal Article
PubMedID 32044814
Database Medline
Available at Chinese medical journal from Europe PubMed Central - Open Access
Available at Chinese medical journal from Unpaywall

Abstract BACKGROUNDA novel coronavirus (2019-nCoV) causing an outbreak of pneumonia in Wuhan, Hubei province of China was isolated in January 2020. This study aims to investigate its epidemiologic history, and analyze the clinical characteristics, treatment regimens, and prognosis of patients infected with 2019-nCoV during this outbreak.METHODSClinical data from 137 2019-nCoV-infected patients admitted to the respiratory departments of the respiratory departments of nine tertiary hospitals in Hubei province from December 30, 2019 to January 24, 2020 were retrospectively collected, including general status, clinical manifestations, laboratory test results, imaging characteristics, and treatment regimens.RESULTSNone of the 137 patients (61 males, 76 females, aged 20-83 years, median age 57 years) had a definite history of exposure to Huanan Seafood Wholesale Market. Major initial symptoms included fever (112/137, 81.8%), coughing (66/137, 48.2%), and muscle pain or fatigue (44/137, 32.1%), with other, less typical initial symptoms observed at low frequency, including heart palpitations, diarrhea, and headache. Nearly 80% of the patients had normal or decreased white blood cell counts, and 72.3% (99/137) had lymphocytopenia. Lung involvement was present in all cases, with most chest computed tomography scans showing lesions in multiple lung lobes, some of which were dense; ground-glass opacity co-existed with consolidation shadows or cord-like shadows. Given the lack of effective drugs, treatment focused on symptomatic and respiratory support. Immunoglobulin G was delivered to some critically ill patients according to their conditions. Systemic corticosteroid treatment did not show significant benefits. Notably, early respiratory support facilitated disease recovery and improved prognosis. The risk of death was primarily associated with age, underlying chronic diseases, and median interval from the appearance of initial symptoms to dyspnea.CONCLUSIONSThe majority of patients with 2019-nCoV pneumonia present with fever as the first symptom, and most of them still showed typical manifestations of viral pneumonia on chest imaging. Middle-aged and elderly patients with underlying comorbidities are susceptible to respiratory failure and may have a poorer prognosis.

15. Inhibitory effects of glycopyrronium, formoterol, and budesonide on coronavirus HCoV-229E replication and cytokine production by primary cultures of human nasal and tracheal epithelial cells.

Authors Yamaya, Mutsuo; Nishimura, Hidekazu; Deng, Xue; Sugawara, Mitsuru; Watanabe, Oshi; Nomura, Kazuhiro; Shimotai, Yoshitaka; Momma, Haruki; Ichinose, Masakazu; Kawase, Tetsuaki
Source Respiratory investigation; Feb 2020
Publication Date Feb 2020
Publication Type(s) Journal Article
PubMedID 32094077
Database Medline
Available at Respiratory investigation from ClinicalKey
Available at Respiratory investigation from Unpaywall

Abstract BACKGROUNDCoronavirus 229E (HCoV-229E), one of the causes of the common cold, exacerbates chronic obstructive pulmonary disease (COPD) and bronchial asthma. Long-acting muscarinic antagonists and β2-agonists and inhaled corticosteroids inhibit the exacerbation of COPD and bronchial asthma caused by infection with viruses, including HCoV-229E. However, the effects of these drugs on HCoV-229E replication and infection-induced inflammation in the human airway are unknown.METHODSPrimary human nasal (HNE) and tracheal (HTE) epithelial cell cultures were infected with HCoV-229E.RESULTSPretreatment of HNE and HTE cells with glycopyrronium or formoterol decreased viral RNA levels and/or titers, the expression of the HCoV-229E receptor CD13, the number and fluorescence intensity of acidic endosomes where HCoV-229E RNA enters the cytoplasm, and the infection-induced production of cytokines, including IL-6, IL-8, and IFN-β. Treatment of the cells with the CD13 inhibitor 2'2'-dipyridyl decreased viral titers. Pretreatment of the cells with a combination of three drugs (glycopyrronium, formoterol, and budesonide) exerted additive inhibitory effects on viral titers and cytokine production. Pretreatment of HNE cells with glycopyrronium or formoterol reduced the susceptibility to infection, and pretreatment with the three drugs inhibited activation of nuclear factor-kappa B p50 and p65 proteins. Pretreatment with formoterol increased cAMP levels and treatment with cAMP decreased viral titers, CD13 expression, and the fluorescence intensity of acidic endosomes.CONCLUSIONSThese findings suggest that glycopyrronium, formoterol, and a combination of glycopyrronium, formoterol, and budesonide inhibit HCoV-229E replication partly by inhibiting receptor expression and/or endosomal function and that these drugs modulate infection-induced inflammation in the airway.

16. Critical care management of adults with community-acquired severe respiratory viral infection.

Authors Arabi, Yaseen M; Fowler, Robert; Hayden, Frederick G
Source Intensive care medicine; Feb 2020; vol. 46 (no. 2); p. 315-328
Publication Date Feb 2020
Publication Type(s) Journal Article Review
PubMedID 32040667
Database Medline
Available at Intensive care medicine from Unpaywall

Abstract With the expanding use of molecular assays, viral pathogens are increasingly recognized among critically ill adult patients with community-acquired severe respiratory illness; studies have detected respiratory viral infections (RVIs) in 17-53% of such patients. In addition, novel pathogens including zoonotic coronaviruses like the agents causing Severe Acute Respiratory Syndrome (SARS), Middle East Respiratory Syndrome (MERS) and the 2019 novel coronavirus (2019 nCoV) are still being identified. Patients with severe RVIs requiring ICU care present typically with hypoxemic respiratory failure. Oseltamivir is the most widely used neuraminidase inhibitor for treatment of influenza; data suggest that early use is associated with reduced mortality in critically ill patients with influenza. At present, there are no antiviral therapies of proven efficacy for other severe RVIs. Several adjunctive pharmacologic interventions have been studied for their immunomodulatory effects, including macrolides, corticosteroids, cyclooxygenase-2 inhibitors, sirolimus, statins, anti-influenza immune plasma, and vitamin C, but none is recommended at present in severe RVIs. Evidence-based supportive care is the mainstay for management of severe respiratory viral infection. Non-invasive ventilation in patients with severe RVI causing acute hypoxemic respiratory failure and pneumonia is associated with a high likelihood of transition to invasive ventilation. Limited existing knowledge highlights the need for data regarding supportive care and adjunctive pharmacologic therapy that is specific for critically ill patients with severe RVI. There is a need for more pragmatic and efficient designs to test different therapeutics both individually and in combination.

17. Clinical predictors of mortality of Middle East Respiratory Syndrome Coronavirus (MERS-CoV) infection: A cohort study.

Authors Alfaraj SH; Al-Tawfiq JA; Assiri AY; Alzahrani NA; Alanazi AA; Memish ZA
Source Travel medicine and infectious disease; 2019; vol. 29 ; p. 48-50
Publication Date 2019
Publication Type(s) Journal Article
PubMedID 30872071
Database PubMed
Available at Travel medicine and infectious disease from ClinicalKey
Available at Travel medicine and infectious disease from Unpaywall

Abstract BACKGROUND: Since the emergence of the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) in 2012, the virus had caused a high case fatality rate. The clinical presentation of MERS varied from asymptomatic to severe bilateral pneumonia, depending on the case definition and surveillance strategies. There are few studies examining the mortality predictors in this disease. In this study, we examined clinical predictors of mortality of Middle East Respiratory Syndrome (MERS) infection.
METHODS: This is a retrospective analysis of symptomatic admitted patients to a large tertiary MERS-CoV center in Saudi Arabia over the period from April 2014 to March 2018. Clinical and laboratory data were collected and analysis was done using a binary regression model.
RESULTS: A total of 314 symptomatic MERS-CoV patients were included in the analysis, with a mean age of 48 (±17.3) years. Of these cases, 78 (24.8%) died. The following parameters were associated with increased mortality, age, WBC, neutrophil count, serum albumin level, use of a continuous renal replacement therapy (CRRT) and corticosteroid use. The odd ratio for mortality was highest for CRRT and corticosteroid use (4.95 and 3.85, respectively). The use of interferon-ribavirin was not associated with mortality in this cohort.
CONCLUSION: Several factors contributed to increased mortality in this cohort of MERS-CoV patients. Of these factors, the use of corticosteroid and CRRT were the most significant. Further studies are needed to evaluate whether these factors were a mark of severe disease or actual contributors to higher mortality.

18. PULSED METHYLPREDNISOLONE USAGE IN ARDS DUE TO VIRAL PNEUMONIA

Authors Szeto C.H.
Source Chest; Apr 2019; vol. 155 (no. 4)
Publication Date Apr 2019
Publication Type(s) Conference Abstract
Database EMBASE

Abstract PURPOSE: Clarify the indication,timing and dosage of steroid used in ARDS due to viral pneumonia. Pulsed methylprednisolone dosage should be 0.5-1g daily.
METHOD(S): By literature review on papers on viral pneumonia, including influenza and SARS coronavirus pneumonia from 2001 to 2011,the indication and the correct steroid usage in ARDS is summarized. P<0.05 is clinically significant.Descriptive studies is included in SARS scenario.
RESULT(S): In viral pneumonia, steroid decreases the cytokines, but prolongs vthe viral replication period. Beneficial effect is shown in varicella pneumonia with decreased hospital stay,but in H1N1infected patients, a trend of increasing hospital-acquired pneumonia!, duration of mechanical ventilation, and hospital mortality,especially in patients receiving early steroid therapy.Case studies showed corticosteroid in severe flu pneumonia is beneficial in organizing pneumonia,post-viral inflammatory pneumonitis and H1N1 pneumonia in pregnant women.In SARS,nasopharyngeal aspirate reviewed viral load peaked at 10 days(early viral phase) from symptom onset.The late excessive inflammatory response started 8-14 days from onset with raised IL6,8,16,TNF alpha. Steroid usage should be given by D7 for ARDS, 1day before the late inflammatory response phase.High-dose steroid was associated with aspergillosis,avascular necrosis,myopathy and polyneuropathy.No difference in outcome was observed between patients receiving immunoglobulin/methylprednisolone versus no agents in Singapore study.Pulsed methylprednisolone dosage was 0.5-1g/d,that is compatible to the dosage used in rheumatological diseases(1g/d for 3d).
CONCLUSION(S): Pulsed methylprednisolone is given in the late immune-mediated phase as guided by the nasopharyngeal aspirate result and blood cytokine levels,in a dose of 0.5-1g/d intravenously. CLINICAL IMPLICATIONS: Methylprednisolone more than 1g/d merely clears up the lung shadows quickly,but invites avascular necrosis later without change in mortality.

19. A Rare Case of Human Coronavirus 229E Associated with Acute Respiratory Distress Syndrome in a Healthy Adult.

Authors Vassilara, Foula; Spyridaki, Aikaterini; Pothitos, George; Deliveliotou, Athanassia; Papadopoulos, Antonios
Source Case reports in infectious diseases; 2018; vol. 2018 ; p. 6796839
Publication Date 2018
Publication Type(s) Case Reports
PubMedID 29850307
Database Medline
Available at Case reports in infectious diseases from Europe PubMed Central - Open Access
Available at Case reports in infectious diseases from Hindawi Open Access Journals
Available at Case reports in infectious diseases from Unpaywall
Abstract Human coronavirus 229E (HCoV-229E) is one of the first coronavirus strains being described. It is linked to common cold symptoms in healthy adults. Younger children and the elderly are considered vulnerable to developing lower respiratory tract infections (LRTIs). In particular, immunocompromised patients have been reported with severe and life-threatening LRTIs attributed to HCoV-229E. We report for the first time a case of LRTI and acute respiratory distress syndrome developed in a healthy adult with no comorbidities and HCoV-229E strain identified as the only causative agent. A 45-year-old female with a clear medical history presented with fever, cough, and headache. Respiratory tract infection was diagnosed, and empirical antibiotics were started. Within two days, she developed bilateral pleural effusions, diffuse consolidations, and ground glass opacities involving all lung fields. She needed immediate oxygen supply, while ABGs deteriorated and chest imaging and PaO2/FiO2 indicated ARDS. Early administration of systemic corticosteroids led to gradual clinical improvement. Multiplex PCR from nasal secretions was positive only for HCoV-229E and negative for multiple other pathogens. It remains to be elucidated how an immunocompetent adult developed a life-threatening LRTI caused by a "benign considered" coronavirus strain, the HCoV-229E.

20. Corticosteroid Therapy for Critically Ill Patients with Middle East Respiratory Syndrome.

Authors Arabi, Yaseen M; Mandourah, Yasser; Al-Hameed, Fahad; Sindi, Anees A; Almekhlafi, Ghaleb A; Hussein, Mohamed A; Jose, Jesna; Pinto, Ruxandra; Al-Omari, Awad; Kharaba, Ayman; Almotairi, Abdullah; Al Khatib, Kasim; Alraddadi, Basem; Shalhoub, Sarah; Abdulmomen, Ahmed; Qushmaq, Ismael; Mady, Ahmed; Solaiman, Othman; Al-Aithan, Abdulsalam M; Al-Raddadi, Rajaa; Ragab, Ahmed; Balkhy, Hanan H; Al Harthy, Abdulrahman; Deeb, Ahmad M; Al Mutairi, Hanan; Al-Dawood, Abdulaziz; Merson, Laura; Hayden, Frederick G; Fowler, Robert A; Saudi Critical Care Trial Group
Source American journal of respiratory and critical care medicine; Mar 2018; vol. 197 (no. 6); p. 757-767
Publication Date Mar 2018
Publication Type(s) Multicenter Study Journal Article
PubMedID 29161116
Database Medline
Available at American journal of respiratory and critical care medicine from ProQuest (Health Research Premium) - NHS Version

Abstract RATIONALECorticosteroid therapy is commonly used among critically ill patients with Middle East Respiratory Syndrome (MERS), but its impact on outcomes is uncertain. Analyses of observational studies often do not account for patients' clinical condition at the time of corticosteroid therapy initiation.OBJECTIVESTo investigate the association of corticosteroid therapy on mortality and on MERS coronavirus RNA clearance in critically ill patients with MERS.METHODSICU patients with MERs were included from 14 Saudi Arabian centers between September 2012 and October 2015. We performed marginal structural modeling to account for baseline and time-varying confounders.MEASUREMENTS AND MAIN RESULTSOf 309 patients, 151 received corticosteroids. Corticosteroids were initiated at a median of 3.0 days (quartile 1 [Q1]-Q3, 1.0-7.0) from ICU admission. Patients who received corticosteroids were more likely to receive invasive ventilation (141 of 151 [93.4%] vs. 121 of 158 [76.6%]; P < 0.0001) and had higher 90-day crude mortality (112 of 151 [74.2%] vs. 91 of 158 [57.6%]; P = 0.002). Using marginal structural modeling, corticosteroid therapy was not significantly associated with 90-day mortality (adjusted odds ratio, 0.75; 95% confidence interval, 0.52-1.07; P = 0.12) but was associated with delay in MERS coronavirus RNA clearance (adjusted hazard ratio, 0.35; 95% CI, 0.17-0.72; P = 0.005).CONCLUSIONSCorticosteroid therapy in patients with MERS was not associated with a difference in mortality after adjustment for time-varying confounders but was associated with delayed MERS coronavirus RNA clearance. These findings highlight the challenges and importance of adjusting for baseline and time-varying confounders when estimating clinical effects of treatments using observational studies.

21. Systemic Corticosteroid Therapy May Delay Viral Clearance in Patients with Middle East Respiratory Syndrome Coronavirus Infection.

Authors Hui, David S
Source American journal of respiratory and critical care medicine; Mar 2018; vol. 197 (no. 6); p. 700-701
Publication Date Mar 2018
Publication Type(s) Editorial Comment
PubMedID 29227752
Database Medline
Available at American journal of respiratory and critical care medicine from ProQuest (Health Research Premium) - NHS Version

22. Current medical treatment for middle east respiratory syndrome: A systematic review

Authors Van Le T.; Tran T.N.; Nguyen V.L.; Ghazy A.A.; Morra M.E.; Altibi A.M.; Lu D.M.; Kamel M.G.; Ahmed S.I.; Mostafa M.R.; Elabd S.S.; Farrag M.A.; Fathima S.; Tran V.L.; Memish Z.; Omrani A.S.; Hirayama K.; Nguyen H.T.
Source American Journal of Tropical Medicine and Hygiene; Nov 2017; vol. 97 (no. 5); p. 262
Publication Date Nov 2017
Publication Type(s) Conference Abstract
Database EMBASE
Abstract Middle East Respiratory Syndrome (MERS) is a novel viral respiratory disease caused by MERS-Coronavirus (MERS-CoV), and the first reported case was in Saudi Arabia in 2012. There is no specific treatment for MERS, and it ranges from supportive treatment to antiviral treatment like interferon (IFN) a 1a, IFN b 1a, and ribavirin. We conducted a systematic search on ten databases Studies published after 1/1/2012 and reporting information about treatment of MERS-CoV infection were included in our review. We used Mann-Whitney U, Chi2 and Fisher's exact tests to investigate the relation between the mortality outcome and independent variables. Classification tree model was used to find the best predictors of the mortality. We included 16 papers including ten case reports, two case series, and four observational studies. Despite receiving treatment with ribavirin plus IFN, the mortality rate was as high as 71% of 68 patients in IFN-treatment group and exactly the same (71% of 48 patients) in patients who received supportive treatment only. There was a significant difference between died and survived patients in chronic respiratory disease (CRD), diabetes mellitus (DM), hypertension, renal replacement therapy and ventilation. Indicating that having CRD, hypertension or DM and being ventilated increase the risk of mortality (for all of these factors). While there was no significant difference between died and survived patients in gender, ribavirin, corticosteroid, oseltamivir, IFN beta 1a, IFN alpha 2b, IFN alpha 2a, congestive heart failure (CHF), other comorbidities (p less than 0.05). There was a significant difference between died and survived patient in age, being older in died patients, and time from admission to antiviral treatment start being larger in died patients as well (p less than 0.05). The IFN treatment has shown no efficacy over supportive treatment only. Antiviral treatment delay, older age group, and co-morbidities preexistence (hypertension, diabetes mellitus, chronic kidney disease, dialysis dependent) were associated with worse outcome.

23. A review of candidate therapies for Middle East respiratory syndrome from a molecular perspective.

Authors Rabaan, Ali A; Alahmed, Shamsah H; Bazzi, Ali M; Alhani, Hatem M
Source Journal of medical microbiology; Sep 2017; vol. 66 (no. 9); p. 1261-1274
Publication Date Sep 2017
Publication Type(s) Journal Article Review
PubMedID 28855003

Database Medline
Available at Journal of medical microbiology from Unpaywall

Abstract There have been 2040 laboratory-confirmed cases of Middle East respiratory syndrome coronavirus (MERS-CoV) in 27 countries, with a mortality rate of 34.9%. There is no specific therapy. The current therapies have mainly been adapted from severe acute respiratory syndrome (SARS-CoV) treatments, including broad-spectrum antibiotics, corticosteroids, interferons, ribavirin, lopinavir-ritonavir or mycophenolate mofetil, and have not been subject to well-organized clinical trials. The development of specific therapies and vaccines is therefore urgently required. We examine existing and potential therapies and vaccines from a molecular perspective. These include viral S protein targeting; inhibitors of host proteases, including TMPRSS2, cathepsin L and furin protease, and of viral M(pro) and the PL(pro) proteases; convalescent plasma; and vaccine candidates. The Medline database was searched using combinations and variations of terms, including 'Middle East respiratory syndrome coronavirus', 'MERS-CoV', 'SARS', 'therapy', 'molecular', 'vaccine', 'prophylactic', 'S protein', 'DPP4', 'heptad repeat', 'protease', 'inhibitor', 'anti-viral', 'broad-spectrum', 'interferon', 'convalescent plasma', 'lopinavir ritonavir', 'antibodies', 'antiviral peptides' and 'live attenuated viruses'. There are many options for the development of MERS-CoV-specific therapies. Currently, MERS-CoV is not considered to have pandemic potential. However, the high mortality rate and potential for mutations that could increase transmissibility give urgency to the search for direct, effective therapies. Well-designed and controlled clinical trials are needed, both for existing therapies and for prospective direct therapies.

24. A review of treatment modalities for Middle East Respiratory Syndrome.

Authors Mo, Yin; Fisher, Dale
Source The Journal of antimicrobial chemotherapy; Dec 2016; vol. 71 (no. 12); p. 3340-3350
Publication Date Dec 2016
Publication Type(s) Journal Article Review
PubMedID 27585965
Database Medline
Available at The Journal of antimicrobial chemotherapy from HighWire - Free Full Text
Available at The Journal of antimicrobial chemotherapy from Unpaywall

Abstract The Middle East Respiratory Syndrome coronavirus (MERS-CoV) has been a focus of international attention since its identification in 2012. Epidemiologically it is characterized by sporadic community cases, which are amplified by hospital-based outbreaks. Healthcare facilities in 27 countries from most continents have experienced imported cases, with the most significant outbreak involving 186 cases in Korea. The mortality internationally is 36% and guidance for clinical management has yet to be developed. Most facilities and healthcare providers outside of the Middle East receiving patients have no or little experience in the clinical management of MERS. When a case does occur there is likely little time for a critical appraisal of the literature and putative pharmacological options. We identified published literature on the management of both MERS-CoV and the Severe Acute Respiratory Syndrome coronavirus (SARS-CoV) through searches of PubMed and WHO and the US CDC websites up to 30 April 2016. A total of 101 publications were retrieved for critical appraisal. Most published literature on therapeutics for MERS are in vitro experiments, animal studies and case reports. Current treatment options for MERS can be categorized as: immunotherapy with virus-specific antibodies in convalescent plasma; polyclonal and monoclonal antibodies produced in vitro or in genetically modified animals; and antiviral agents. The use of any therapeutics in MERS-CoV remains investigational. The therapeutic agents with potential benefits and warranting further investigation include convalescent plasma, interferon-β/ribavirin combination therapy and lopinavir. Corticosteroids, ribavirin monotherapy and mycophenolic acid likely have toxicities that exceed potential benefits.

25. Coronavirus OC43-induced acute respiratory distress syndrome

Authors Pennington K.; Nolan M.; Moraes A.G.D.; Escalante P.
Source Critical Care Medicine; Dec 2016; vol. 44 (no. 12); p. 520
Publication Date Dec 2016
Publication Type(s) Conference Abstract
Database EMBASE
Available at Critical Care Medicine from Ovid (Journals @ Ovid) - Remote Access

Abstract Learning Objectives: Human Coronavirus (HCoV) 229E and OC43 most commonly cause mild, self-limiting upper respiratory infections. Newly identified HCoV species, MERS and SARS, are known to cause acute respiratory distress syndrome (ARDS); however, HCoV OC43 has never been identified as a precipitant for ARDS. HCoV 43 can cause severe lower respiratory tract infections in severely immunocompromised adults. We present a case of HCoV OC43 precipitating ARDS.
Method(s): A 39 year-old woman with poorly controlled diabetes mellitus presented with fevers, dyspnea, and cough progressing to hypoxemic respiratory failure requiring intubation and mechanical ventilation. Her PaO2 to FiO2 ratio was 93. Laboratory evaluation was notable for significantly elevated C-reactive protein and mild anemia. Chest x-ray revealed dense bilateral pulmonary infiltrates. Transthoracic echocardiogram was normal. Bronchoscopy showed scant clear secretions, no evidence of hemorrhage. Bronchial alveolar lavage bacterial and fungal cultures were sterile as were blood and urine cultures. Viral PCR studies were positive only for HCoV OC43. She was treated with lung protective ventilation for 2 days and was successfully extubated with complete functional recovery.
Result(s): Viral precipitants for ARDS are becoming increasingly recognized secondary to improved laboratory diagnostic tests. HCoV OC43 has been known to cause lower respiratory tract infections in transplant patients, HIV patients, and patients with hematologic malignancies. Poorly controlled diabetes mellitus is a known immunocompromised state traditionally believed to increase host susceptibility to bacterial infections; however, with significantly elevated glucoses, cell mediated immunity can additionally be compromised. A thorough work-up for viral etiology should be complete for patients with uncontrolled diabetes mellitus and unexplained ARDS as it may obviate the need for potentially harmful diagnostic and therapeutic interventions such as lung biopsies and corticosteroids.

26. Successful treatment of suspected organizing pneumonia in a patient with Middle East respiratory syndrome coronavirus infection: a case report.

Authors Kim, Insu; Lee, Jeong Eun; Kim, Kye-Hyung; Lee, Shinwon; Lee, Kwangha; Mok, Jeong Ha
Source Journal of thoracic disease; Oct 2016; vol. 8 (no. 10); p. E1190
Publication Date Oct 2016
Publication Type(s) Case Reports
PubMedID 27867585
Database Medline
Available at Journal of thoracic disease from Europe PubMed Central - Open Access
Available at Journal of thoracic disease from EBSCO (CINAHL Complete)
Available at Journal of thoracic disease from PubMed
Available at Journal of thoracic disease from PubMed Central
Available at Journal of thoracic disease from amegroups.com
Available at Journal of thoracic disease from doi.org
Abstract A 54-year-old man with Middle East respiratory syndrome coronavirus (MERS-CoV) infection was transferred to our hospital. We initiated anti-viral drugs and supportive care. The patient's fever and chills disappeared 3 days after admission and the results of serial follow-up reverse transcription-polymerase chain reaction testing for MERS-CoV was negative soon thereafter. He was discharged from the hospital 14 days after admission with no symptoms; however, he presented with a fever 7 days after discharge and was re-hospitalized. Chest radiographs showed newly developed consolidative opacity. His fever persisted for 3 days after commencing empirical antibiotics. Subsequent contrast-enhanced computed tomography (CT) of the chest showed focal patchy airspace consolidation and ground-glass opacities (GGOs) in a subpleural lesion of the right lower and left upper lobes, which was indicative of organizing pneumonia. We initiated empirical corticosteroid treatment for this illness, and his fever markedly subsided 1 day later. A chest radiograph showed improvement in the lung lesions, and he was discharged from the hospital 10 days after re-admission. The corticosteroid dose was gradually tapered over 2 months at the outpatient clinic, and a follow-up CT scan showed complete resolution of the consolidation and GGOs.

27. Emerging respiratory tract viral infections.

Authors Hui, David S; Zumla, Alimuddin
Source Current opinion in pulmonary medicine; May 2015; vol. 21 (no. 3); p. 284-292
Publication Date May 2015
Publication Type(s) Research Support, Non-u.s. Gov't Journal Article Review
PubMedID 25764021
Database Medline

Abstract PURPOSE OF REVIEWThis article reviews the clinical and treatment aspects of avian influenza viruses and the Middle East Respiratory Syndrome coronavirus (MERS-CoV).RECENT FINDINGSAvian influenza A(H5N1) and A(H7N9) viruses have continued to circulate widely in some poultry populations and infect humans sporadically. Sporadic human cases of avian A(H5N6), A(H10N8) and A(H6N1) have also emerged. Closure of live poultry markets in China has reduced the risk of A(H7N9) infection. Observational studies have shown that oseltamivir treatment for adults hospitalized with severe influenza is associated with lower mortality and better clinical outcomes, even as late as 4-5 days after symptom onset. Whether higher than standard doses of neuraminidase inhibitor would provide greater antiviral effects in such patients requires further investigation. High-dose systemic corticosteroids were associated with worse outcomes in patients with A(H1N1)pdm09 or A(H5N1). MERS-CoV has continued to spread since its first discovery in 2012. The mortality rates are high in those with comorbid diseases. There is no specific antiviral treatment or vaccine available. The exact mode of transmission from animals to humans remains unknown.SUMMARYThere is an urgent need for developing more effective antiviral therapies to reduce morbidity and mortality of these emerging viral respiratory tract infections.

28. ATP1A1-mediated Src signaling inhibits coronavirus entry into host cells.

Authors Burkard, Christine; Verheije, Monique H; Haagmans, Bart L; van Kuppeveld, Frank J; Rottier, Peter J M; Bosch, Berend-Jan; de Haan, Cornelis A M
Source Journal of virology; Apr 2015; vol. 89 (no. 8); p. 4434-4448
Publication Date Apr 2015
Publication Type(s) Research Support, Non-u.s. Gov't Journal Article
PubMedID 25653449
Database Medline
Available at Journal of virology from Europe PubMed Central - Open Access
Available at Journal of virology from HighWire - Free Full Text
Available at Journal of virology from Unpaywall

Abstract UNLABELLEDIn addition to transporting ions, the multisubunit Na(+),K(+)-ATPase also functions by relaying cardiotonic steroid (CTS)-binding-induced signals into cells. In this study, we analyzed the role of Na(+),K(+)-ATPase and, in particular, of its ATP1A1 α subunit during coronavirus (CoV) infection. As controls, the vesicular stomatitis virus (VSV) and influenza A virus (IAV) were included. Using gene silencing, the ATP1A1 protein was shown to be critical for infection of cells with murine hepatitis virus (MHV), feline infectious peritonitis virus (FIPV), and VSV but not with IAV. Lack of ATP1A1 did not affect virus binding to host cells but resulted in inhibited entry of MHV and VSV. Consistently, nanomolar concentrations of the cardiotonic steroids ouabain and bufalin, which are known not to affect the transport function of Na(+),K(+)-ATPase, inhibited infection of cells with MHV, FIPV, Middle East respiratory syndrome (MERS)-CoV, and VSV, but not IAV, when the compounds were present during virus inoculation. Cardiotonic steroids were shown to inhibit entry of MHV at an early stage, resulting in accumulation of virions close to the cell surface and, as a consequence, in reduced fusion. In agreement with an early block in infection, the inhibition of VSV by CTSs could be bypassed by low-pH shock. Viral RNA replication was not affected when these compounds were added after virus entry. The antiviral effect of ouabain could be relieved by the addition of different Src kinase inhibitors, indicating that Src signaling mediated via ATP1A1 plays a crucial role in the inhibition of CoV and VSV infections.IMPORTANCECoronaviruses (CoVs) are important pathogens of animals and humans, as demonstrated by the recent emergence of new human CoVs of zoonotic origin. Antiviral drugs targeting CoV infections are lacking. In the present study, we show that the ATP1A1 subunit of Na(+),K(+)-ATPase, an ion transporter and signaling transducer, supports CoV infection. Targeting ATP1A1 either by gene silencing or by low concentrations of the ATP1A1-binding cardiotonic steroids ouabain and bufalin resulted in inhibition of infection with murine, feline, and MERS-CoVs at an early entry stage. Infection with the control virus VSV was also inhibited. Src signaling mediated by ATP1A1 was shown to play a crucial role in the inhibition of virus entry by ouabain and bufalin. These results suggest that targeting the Na(+),K(+)-ATPase using cardiotonic steroids, several of which are FDA-approved compounds, may be an attractive therapeutic approach against CoV and VSV infections.

Strategy 832658

#	Database	Search term	Results
1	Medline	(coronavirus OR corona-virus OR "corona virus").ti,ab	10852
2	Medline	(covid-19 OR covid19 OR "covid 19").ti,ab	1336
3	Medline	(sars-cov-2 OR sarscov2 OR "sars cov 2").ti,ab	419
4	Medline	(1 OR 2 OR 3)	11677
5	Medline	(steroid* OR corticosteroid*).ti,ab	300341
6	Medline	(4 AND 5)	99
7	Medline	6 [DT 2015-2020] [Languages English]	30
8	EMBASE	(coronavirus OR corona-virus OR "corona virus").ti,ab	11765
9	EMBASE	(covid-19 OR covid19 OR "covid 19").ti,ab	1143
10	EMBASE	(sars-cov-2 OR sarscov2 OR "sars cov 2").ti,ab	359
11	EMBASE	(8 OR 9 OR 10)	12485
12	EMBASE	(steroid* OR corticosteroid*).ti,ab	437863
13	EMBASE	(11 AND 12)	136
14	EMBASE	13 [DT 2015-2020] [Languages English]	50
15	PubMed	(coronavirus OR corona-virus OR "corona virus").ti,ab	16377
16	PubMed	(covid-19 OR covid19 OR "covid 19").ti,ab	2059
17	PubMed	(sars-cov-2 OR sarscov2 OR "sars cov 2").ti,ab	777
18	PubMed	(15 OR 16 OR 17)	17131
19	PubMed	(steroid* OR corticosteroid*).ti,ab	422159
20	PubMed	(18 AND 19)	132