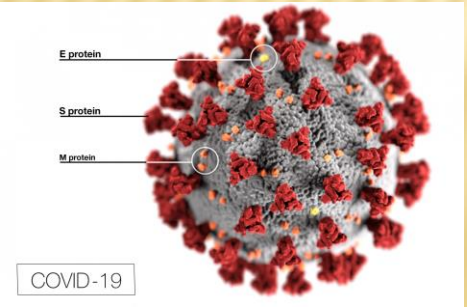
IN THE NAME OF GOD

NEUROLOGICAL COPMLICATIONS OF COVID

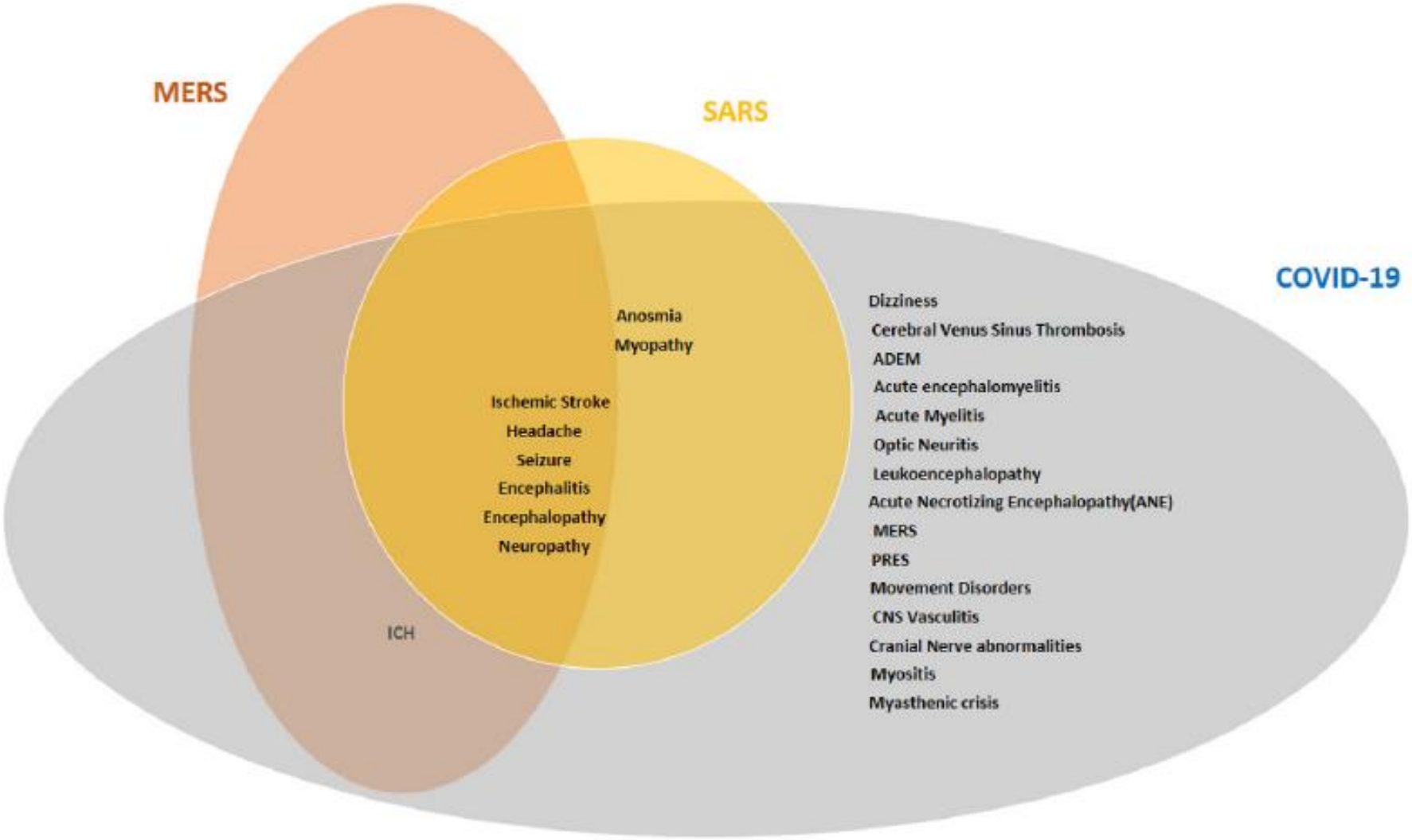
Dr.Leila Poorsaadat

Assistant Professor of Neurology,AUMS



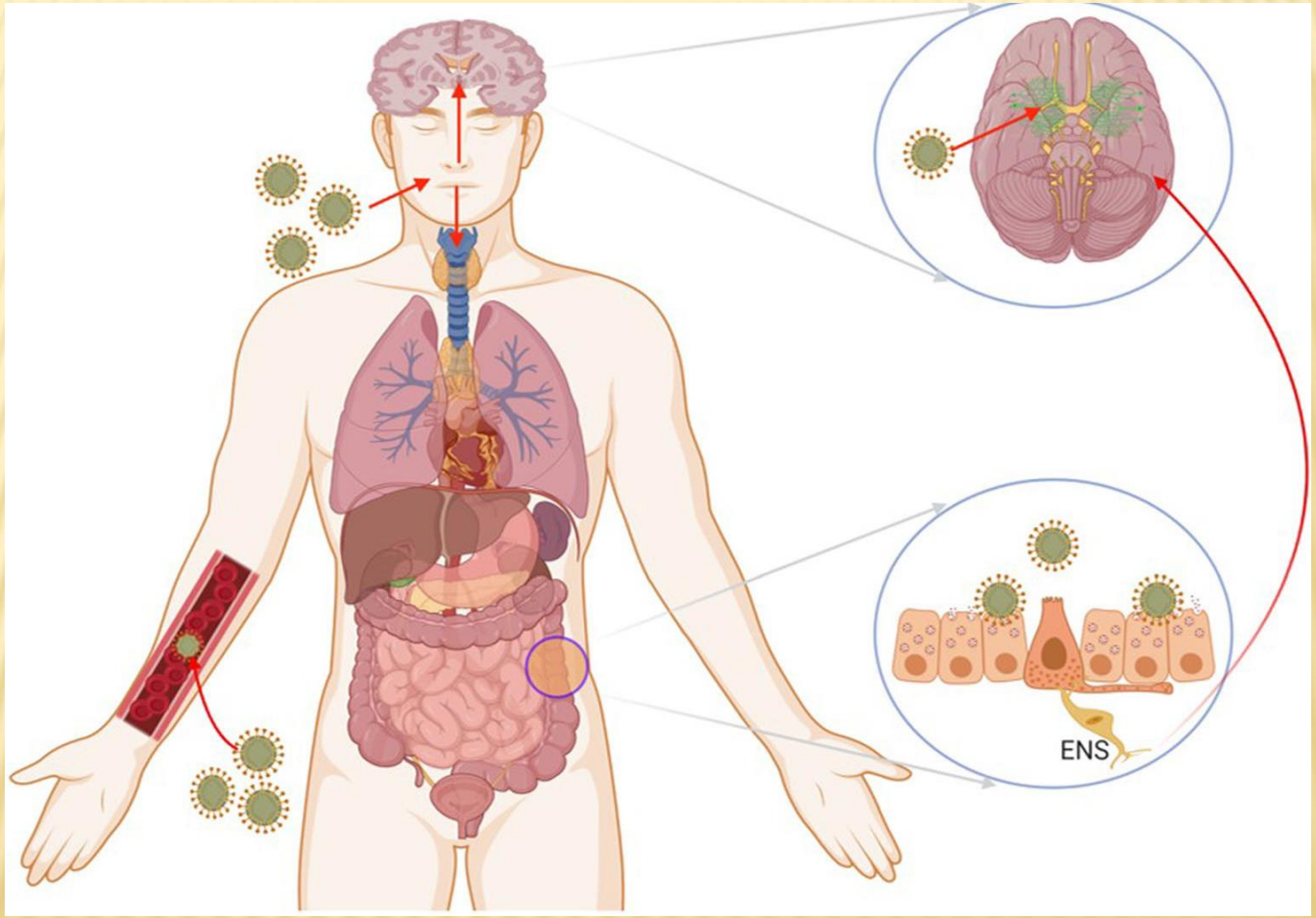
- The COVID-19 is a single-stranded positively sensed RNA virus, consisting of 26–32 kb-sized genome.
- The average diameter is 100 nm, spherical, or oval-shaped.
- The rate of recombination is up to 25% and is externally covered by a crown shaped like spike (S) proteins, which also can mutate frequently .
- These characteristics illustrate the adaptability of the virus to change its infectivity over time.
- The angiotensin-converting enzyme 2 (ACE2) receptors, which normally helps to regulate blood pressure, is abundantly expressed in the lungs. The spike proteins of the COVID-19bind to ACE2 receptors to invade the cell and develop the infection .

VENN DIAGRAM OF NEUROLOGICAL PRESENTATIONS IN DIFFERENT COV INFECTIONS



THE MECHANISM OF CORONAVIRUS INFECTIONS AND NEUROLOGICAL DAMAGE

- The coronavirus can enter the nervous system directly through the olfactory nerve
- blood circulation, ACE2 in brainstem, immune injury, and neuronal pathways, resulting in neurological disorders.
- The COVID-19 infection in the gastrointestinal tract could use the enteric nervous system (ENS) and its sympathetic afferent neurons to reach the CNS


ENS

Box 1 | **Neurological disorders and COVID-19**

Neurological symptoms reported in COVID-19 patients

- Dizziness
- Headache
- Obtundation
- Hypogeusia
- Ageusia
- Hyposmia
- Anosmia
- Myalgia

Neurological disorders reported to occur with COVID-19

- Stroke (ischaemic, haemorrhagic, secondary to coagulopathy)
- Sinus venous thrombosis
- Cerebral haemorrhage
- Encephalopathy
- Altered mental status
- Meningitis
- Encephalitis
- Febrile seizures
- Acute haemorrhagic necrotizing encephalopathy
- Acute disseminated encephalomyelitis
- Myelitis
- Myasthenia gravis
- Miller–Fisher syndrome
- Guillain–Barré syndrome
- Polyneuritis cranialis

Neurological patients at risk in the context of COVID-19

- Alzheimer disease
- Parkinson disease
- Motor neuron disease
- CNS disorders with reduced mobility or immobility
- Neuromuscular disorders with reduced mobility and compromised respiratory function
- Autoimmune conditions
  - Multiple sclerosis
  - Neuromyelitis optica spectrum disorders
  - Myasthenia gravis
  - Guillain–Barré syndrome
  - Chronic dysimmune neuropathies

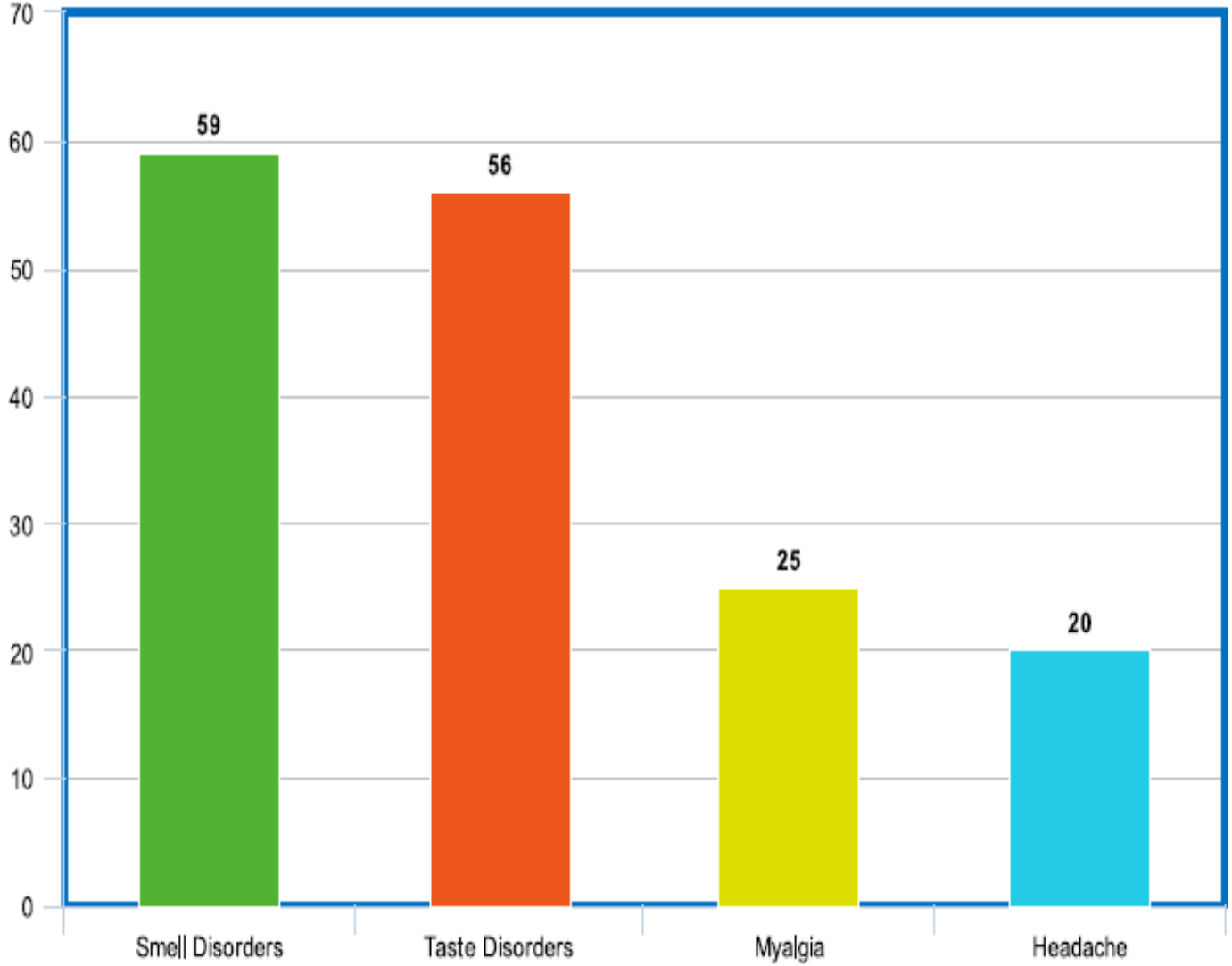


Fig. 2 Common neurological manifestations of COVID-19 expressed as percentage

NEUROLOGICAL MANIFESTATIONS

CNS manifestations

- The central nervous system manifestations include epilepsy, ataxia, encephalitis, impaired conscious, Acute Hemorrhagic Necrotizing Encephalopathy (ANE), and headache.

- Encephalitis refers to the inflammatory lesions in the brain, which includes nerve tissue lesions and neuronal damage

- Headaches and dizziness are considered the non-specific minor symptom, associated with COVID-19 patients.
- The encephalopathy is reported in 40% of the patients
- The Acute Hemorrhagic Necrotizing Encephalopathy (ANE) is developed because of the cytokine storm and causes disruption in the blood-brain barrier,and neuroinflammation which leads to the dysfunction of the brain.

- During the COVID-19 infection, patients are likely to develop cerebrovascular accidents.
- the dysregulation of ACE2 receptors leads to cerebral autoregulation, sympatho-adrenal system and cerebral blood flow could have resulted in the bleed.
- patient infected with COVID-19 showed the abnormal clotting of blood. The blocking of arteries in the brain due to blood clots cancause stroke
- Cytokine storms and hyperinflammatory responses can cause acute myelitis.

COVID-19 Respiratory Illness and Subsequent Cerebrovascular Events, the Initial Iranian Experience

Behnam Sabayan, MD, PhD,* Mohsen Moghadami, MD,†
Farhad Assarzadegan, MD,‡ Sahar Hojjat-Anasri Komachali, MD,§
Leila Poorsaadat, MD,¶ Zabihollah Babaeepour, MD,‖
Seyed Amir Ebrahimzadeh, MD,# Ava Hamidi, MD,**
Zeinab Sadat Hasheminejad, MD,‡ Elahe Mohammadi-Vosough, MD,**
Hamid Reza Mirkarimi, MD,** Sepideh Paybast, MD,†† Nasrin Rahimian, MD,‡‡
Anahid Safari, MD,§§ Mersedeh Sepehrnia, MD,‡ Reza Nematollahi, MD,¶¶
Reza Bavarsad Shahripour, MD,‖‖ Ayush Batra, MD,*
Farzaneh Sorond, MD, PhD,* and Afshin Borhani-Haghighi, MD##

Results: Fifteen patients (12 men and 3 women) with an age range of 38 to 93 years old (median: 65 years old) were included. Fourteen patients had a first-ever acute ischemic stroke and one patient had a subarachnoid hemorrhage. Eleven patients (73%) had previous cardiovascular comorbidities. The median time between respiratory symptoms and neurological symptoms was seven days (range 1-16 days). Stroke severity in two patients was mild (NIHSS 6), in six patients moderate (NIHSS: 7-12), and in seven patients severe (NIHSS 13). One patient received intravenous tissue plasminogen activator (IV-tPA) with improved neurological symptoms

JAMA Neurology | Original Investigation

Risk of Ischemic Stroke in Patients With Coronavirus Disease 2019 (COVID-19) vs Patients With Influenza

Alexander E. Merkler, MD; Neal S. Parikh, MD, MS; Saad Mir, MD; Ajay Gupta, MD, MS; Hooman Kamel, MD, MS; Eaton Lin, MD; Joshua Lantos, MD; Edward J. Schenck, MD; Parag Goyal, MD; Samuel S. Bruce, MD, MA; Joshua Kahan, MBBS, PhD; Kelsey N. Lansdale, BA; Natalie M. LeMoss, BS; Santosh B. Murthy, MD, MPH; Philip E. Stieg, PhD, MD; Matthew E. Fink, MD; Costantino Iadecola, MD; Alan Z. Segal, MD; Marika Cusick, MS; Thomas R. Campion Jr, PhD, MS; Ivan Diaz, PhD; Cenai Zhang, MS; Babak B. Navi, MD, MS

The proportion of patients with ED visits and hospitalizations with COVID-19 who had an acute ischemic stroke was higher than the proportion seen in patientswhovisited theED orwere hospitalizedwith influenza.Thesefindings suggest that clinicians should be vigilant for symptoms and signs of acute ischemic stroke in patients with COVID-19 so that timesensitive interventions, such as thrombolysis and thrombectomy, can be instituted if possible to reduce the burden of longterm disability

- Another study confirmed that coagulation dysfunction is common in patients with COVID-19, especially fibrinogen and D-dimer elevation, and the degree of elevation is related to the severity of the disease. As the patient recovers, fibrinogen and activated partial thromboplastin time also return to norma

ENCEPHALOPATHY AND DELIRIUM

- Delirium has been reported to occur in COVID-19, especially among older persons.

- Encephalopathy and delirium may be due to direct invasion of the CNS by SARS-CoV-2, inflammation secondaryto a cytokine storm or as a result of septic encephalopathy

OTHER CNS MANIFESTATIONS

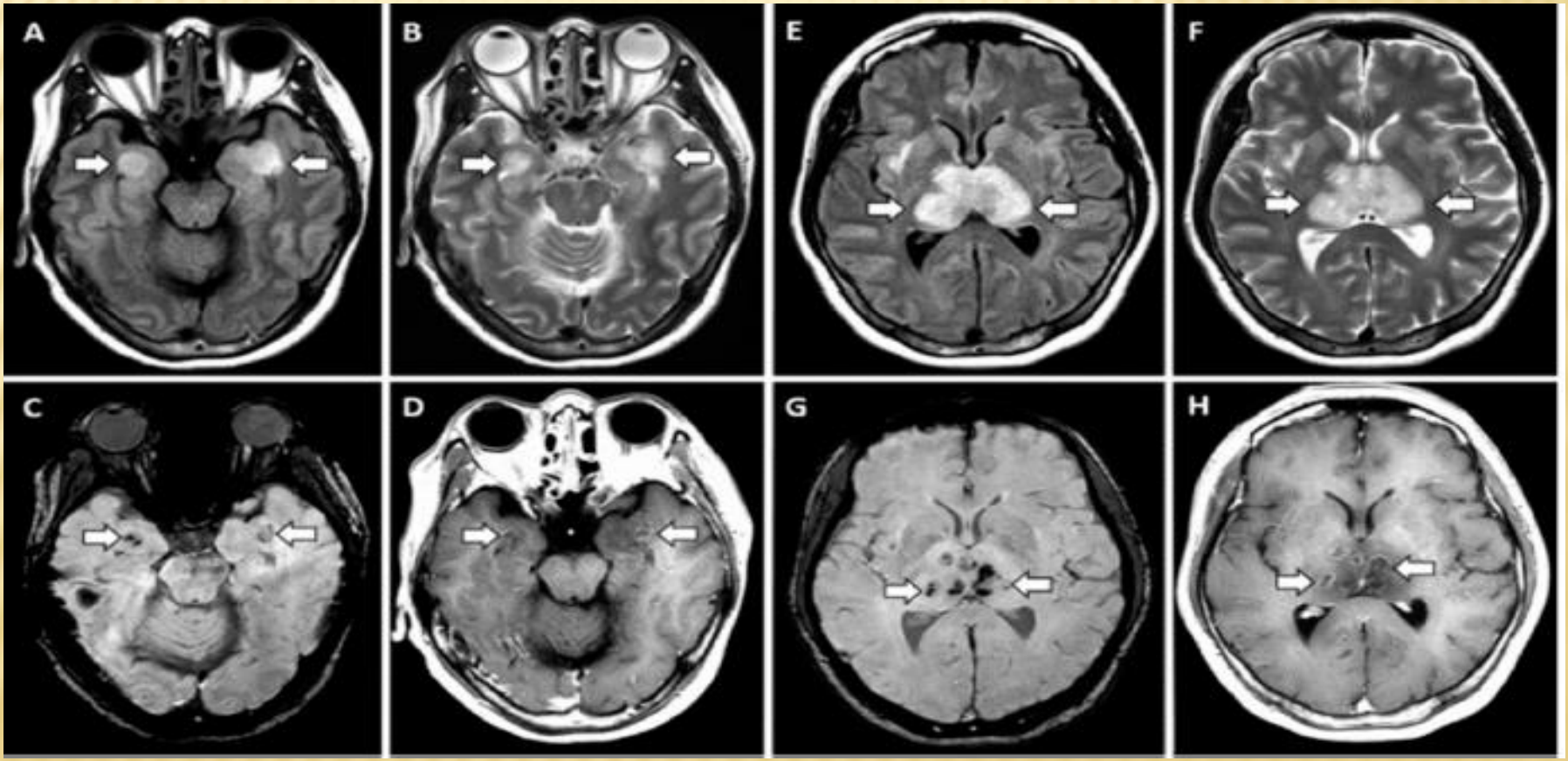
- There are reports of encephalitis and meningitis in COVID-19.

- some studies did not find an increased risk of symptomatic seizures in COVID-19 patients. At present, it isuncertain whether the seizures are coincidental or due to SARS-CoV-2 viral effects or the drugs used in treatment

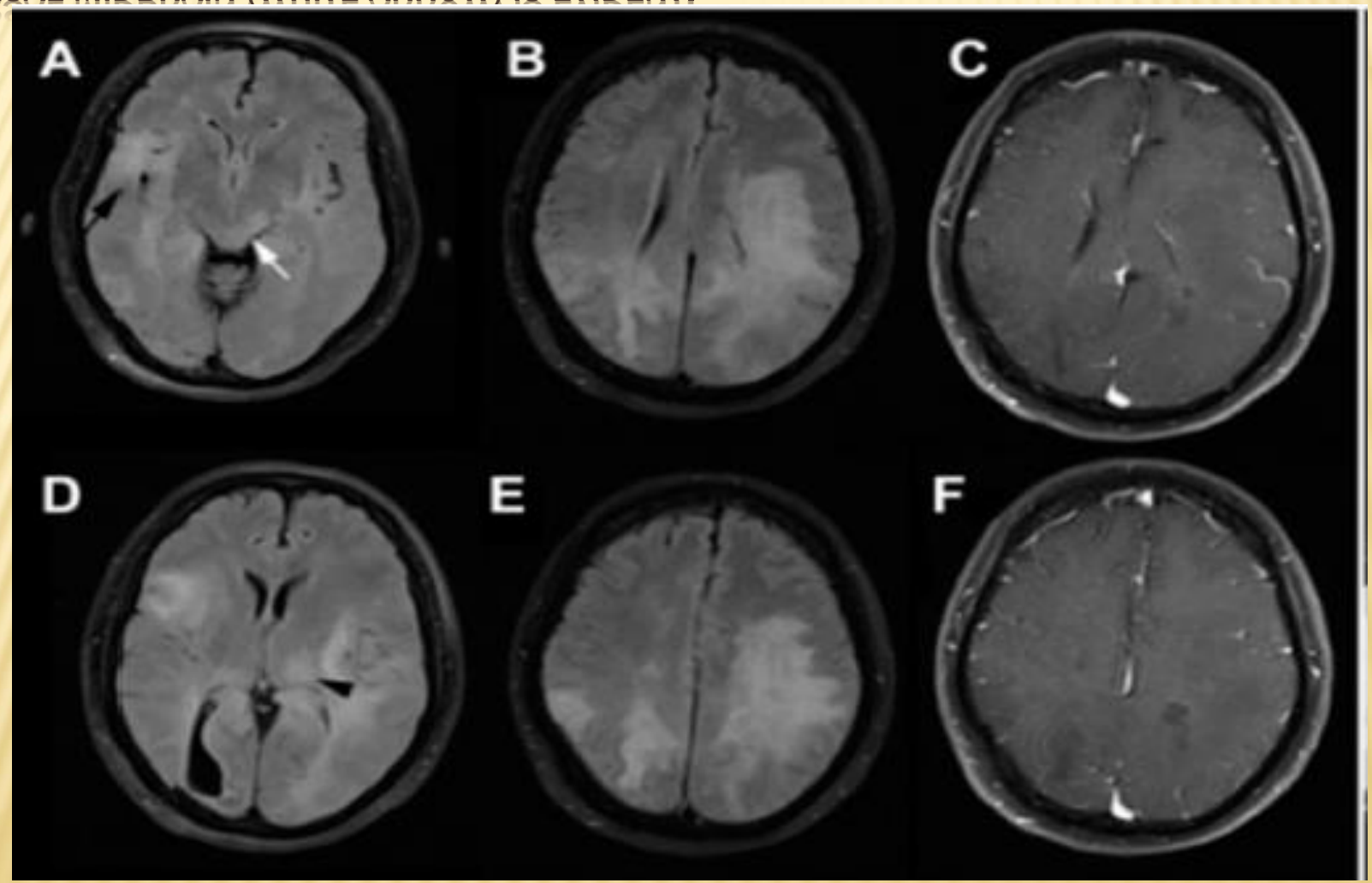
RARER CENTRAL NEUROLOGICAL FEATURES

- There are reports of rare patients with various neurological features during the course of COVID-19, including intracerebral hemorrhage, cerebral venous thrombosis, slight neck stiffness (with no SARS-Cov-2 genomes in the CSF), generalized myoclonus, seizures, acute epileptic encephalopathy, hemorrhagic posterior reversible encephalopathy syndrome, acute necrotizing encephalopathy, white matter and globus pallidum inflammatory lesions, diffuse leukoencephalopathy with microhemorrhages, neuroleptic malignant syndrome,.

Fluid-attenuated inversion recovery (FLAIR) image shows hyper intensities within the bilateral thalami and medial temporal lobes (arrows) and also evidence of hemorrhage on C, G, hypo intense signal (arrows) on susceptibility-weighted images(SWI) and rim enhancements in D, H.



FLUID-ATTENUATED INVERSION RECOVERY (FLAIR) MAGES SHOW DIFFUSE CONFLUENT WHITE MATTER HYPERINTENSITY
PARTICULARLY AT THE LEFT-SIDE (A-D) WITHOUT SIGNIFICANT ENHANCEMENT ON T1-WEIGHTED BRAIN MRI
(C, F). INVOLVEMENT OF (BLACK ARROW), DEEP GRAYMATTER (BLACK ARROWHEAD), AND DORSAL MIDBRAIN (WHITE ARROW) IS EVIDENT.



PNS MANIFESTATIONS

- The peripheral nervous system manifestation includes skeletal damage, anosmia, chemosensory dysfunction, and Guillain- Barre Syndrome (GBS). Anosmia and chemosensory dysfunction

- 85.6% patients had been diagnosed with olfactory dysfunction and 88.8% patients reported gustatory disorders.

- in 11.8% of patients, the olfactory dysfunction appeared before COVID-19 symptoms, 65.4% patients reported after COVID-19 symptoms, and 22.8% reported at the same time of COVID-19 general symptoms. Within the first 8 days,

- around 72.6% of patients recovered their olfactory functions

- **Skeletal muscle injury**
- Skeletal muscle injury was recorded in 10.7% of the COVID-
- . Creatine kinase (CK), D-dimer, C-reactive protein and lactate dehydrogenase levels were found to be elevated in patients with skeletal muscle injury.
- In another report, myalgia was noted in 34.8% of the studied COVID-19.
- Critical illness neuropathy and myopathy in ICU

Contents lists available at ScienceDirect

Journal of the Neurological Sciences

journal homepage: www.elsevier.com/locate/jns

Review Article

Neurological complications of coronavirus infection; a comparative review and lessons learned during the COVID-19 pandemic

Maryam Sharifian-Dorche[a,b], Philippe Huot[a], Michael Osherov[a], Dingke Wen[a,c], Alexander Saveriano[a], Paul S Giacomini[a], Jack P Antel[a], Ashkan Mowla[d,*]

[a] Department of Neurology and Neurosurgery, Montreal Neurological Institute, McGill University, Montreal, Quebec, Canada
[b] Clinical Neurology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran
[c] Department of Neurosurgery, West China Hospital, Sichuan University, Chengdu, Sichuan, China
[d] Department of Neurological Surgery, Keck School of Medicine, University of Southern California (USC), Los Angeles, CA, USA

Complications related to Skeletal Muscles and Neuromuscular Junction (NMJ) Reported During and After SARS-CoV-2 Infection.

No.	Neurological Symptom	Ref. No.	No. of patients	Mean Age of the patients (Range)	Notes
Symptoms related to Skeletal Muscles and Neuromuscular Junction (NMJ)					
1	Skeletal muscles injury and Rhabdomyolysis 3 Articles	[39], [58], [60]	38	NR in all articles.	
2	Myopathy	[60], [250], [251]	28	NR in all articles.	
3	Myositis	[252]	1	58 Y/O F	58 Y/O F with muscle biopsy suggestive of Myositis.
4	Myasthenic crisis	[253]	1	56 Y/O F	With history of myasthenia gravis
5	Neuroleptic Malignant Syndrome	[254]	1	Middle age man	In patient with past medical history of psychiatric disorders.

PNS Complications Reported During and After SARS-CoV-2 Infection.

No.	Neurological Symptom	Ref. No.	No. of patients	Mean Age of the patients(Range)	Notes
Cranial Nerve abnormalities					
1	Impaired Eye movement 4 Articles	[57], [58], [194], [215]	12	NR in all articles.	Pascual-Goñi E et al. [194], reported a 36 Y/O F and bilateral sixth nerve palsy with impression of Wernicke encephalopathy. Dinkin M et al. [215], reported a 36 Y/O M and third nerve palsy and impression of Miller-Fisher syndrome.
2	Trigeminal neuropathy 2 Articles	[57], [216]	9	NR in all articles.	
3	Facial nerve palsy 2 Articles	[58], [217]	4	NR in all articles.	
4	Auditory Impairment 2 Articles	[62] [57]	5	NR in all articles.	
5	Glossopharyngeal neuralgia 1 Article	[57]	9	NR	
GBS and other Neuropathies					
6	GBS and GBS variants 36 Articles	[60], [63], [101], [191], [215], [218], [219], [220], [221], [222], [223], [224], [225], [226], [227], [228], [229], [230] [231] [232] [233] [234] [235] [236], [237], [238], [239], [240] [241] [242], [243], [244] [245] [246], [247], [248]	52	NR in all articles.	Su XW et al [226], reoorted a patient GBS with dysautonomia. Juliao Caamaño DS et al. [230], reported a patient with Facial diplegia an Atypical Variant of GBS Pfefferkorn T, et al. [247] reported a 51 Y/O M acute polyradiculoneuritis.

Neurological Sciences (2020) 41:2005–2011
https://doi.org/10.1007/s10072-020-04549-5

COVID-19

Management of COVID-19 in people with epilepsy: drug considerations

Ali A. Asadi-Pooya[1,2] · Armin Attar[3] · Mohsen Moghadami[4] · Iman Karimzadeh[5]

Received: 8 June 2020 / Accepted: 21 June 2020 / Published online: 27 June 2020

Abstract

People with epilepsy (PWE) are neither more likely to be infected by the coronavirus nor are they more likely to have severe COVID-19 manifestations because they suffer from epilepsy. However, management of COVID-19 in PWE may be more complicated than that in other individuals. Drug-drug interactions could pose significant challenges and cardiac, hepatic, or renal problems, which may happen in patients with severe COVID-19, may require adjustment to antiepileptic drugs (AEDs). In this review, we first summarize the potential drug-drug interactions between AEDs and drugs currently used in the management of COVID-19. We then summarize other challenging issues that may happen in PWE, who have COVID-19 and are receiving treatment.

INTERACTIONS RESULTING IN DECREASED AED PLASMA LEVELS

- Lopinavir/ritonavir decreases the plasma concentrations of lamotrigine (and possibly, phenytoin and valproate.
- A dose increment to 200% of the initial lamotrigine dose is needed to achieve concentrations similar to those with lamotrigine alone
- The therapeutic efficacy of many AEDs (e.g., carbamazepine, lacosamide, oxcarbazepine, lamotrigine, phenobarbital, phenytoin) may be decreased when used in combination with hydroxychloroquine or chloroquine

INTERACTIONS RESULTING IN INCREASED AED PLASMA LEVELS

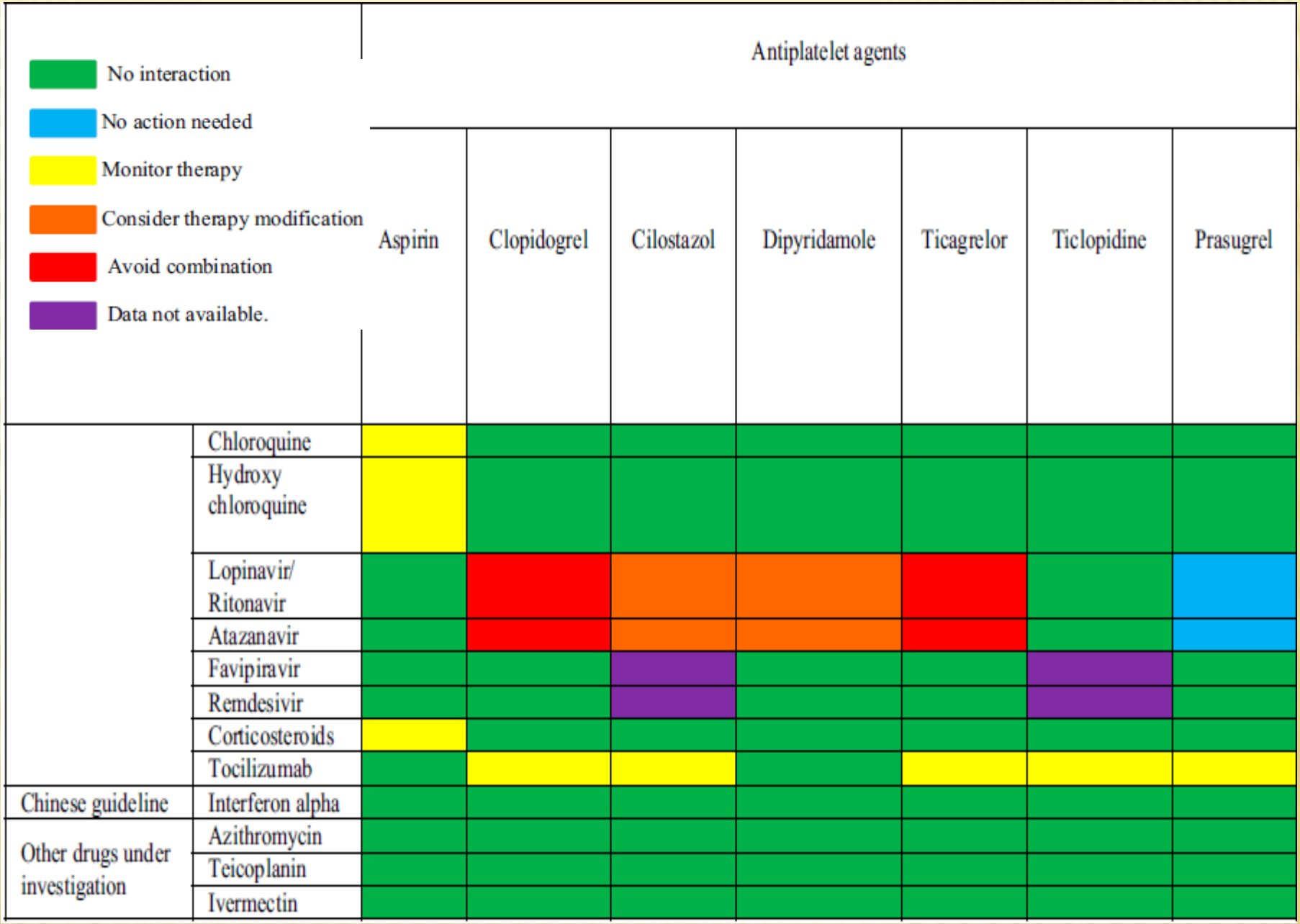
- Ritonavir is a potent inhibitor of CYP3A/ CYP2D6 and may potentially increase plasma levels of cannabidiol, carbamazepine, clonazepam, ethosuximide, lacosamide, and zonisamide

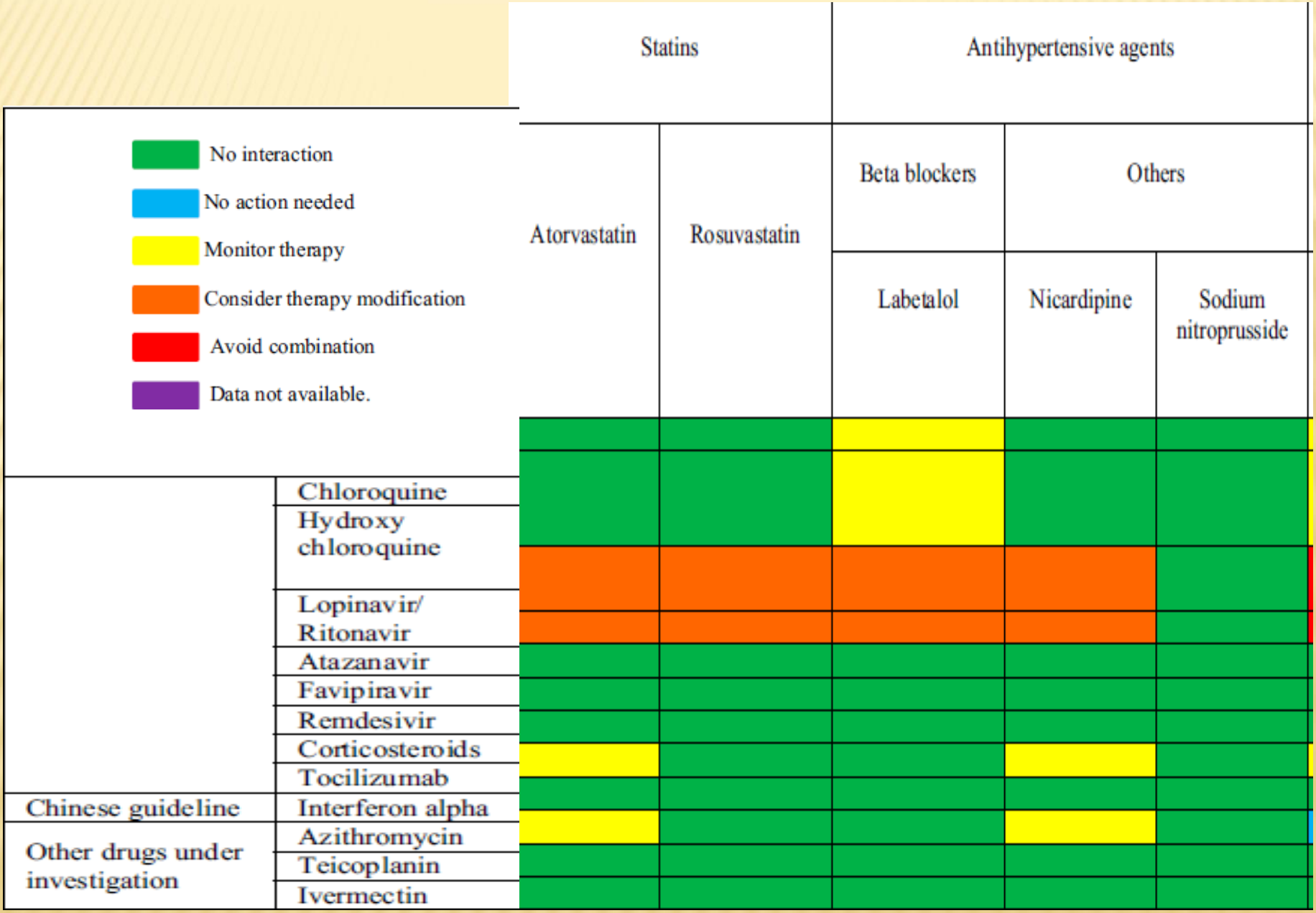
CARDIOVASCULAR ADVERSE EFFECTS OF ANTI-SEIZUREMEDICATIONS AND ANTI-COVID MEDICATIONS

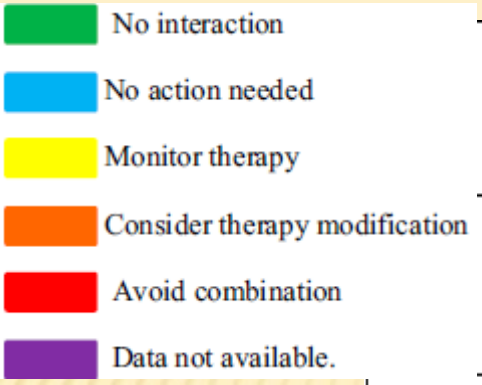
Carbamazepine	Atrioventricular block, cardiac arrhythmias or arrhythmia exacerbation, and congestive heart failure
Cenobamate	QT shortening
Clobazam	—
Clonazepam	—
Eslicarbazepine acetate	—
Ethosuximide	—
Phenobarbital/primidone	May prolong QT interval
Phenytoin	Cardiac conduction abnormalities (e.g., bundle-branch block)
Valproic acid	—
Gabapentin	—
Lacosamide	Prolongation in PR interval, first-degree atrioventricular (AV) block, second degree, and complete AV blocks
Lamotrigine	—
Levetiracetam	—
Oxcarbazepine	—
Perampanel	—
Pregabalin	Exacerbation of heart failure
Rufinamide	QT shortening
Topiramate	—
Vigabatrin	—
Zonisamide	—
Anti-COVID-19 medication	
Remdesivir	—
Lopinavir/ritonavir	Bradyarrhythmias, QTc prolongation, AV block, torsade de pointes, and prolongation of the PR interval
Chloroquine/hydroxychloroquine	Direct myocardial toxicity vs. exacerbation of underlying cardiomyopathy, altered cardiac conduction: QTc prolongation, AV block, bundle branch block, torsade de pointes, and ventricular tachycardia/fibrillation
Interferon beta	Direct myocardial toxicity vs. exacerbation of underlying cardiomyopathy, hypotension, arrhythmia, and myocardial infarction
Favipravir	—
Tocilizumab	—

THE COMMON CENTRAL NERVOUS SYSTEM (CNS) AND PERIPHERAL NERVOUS SYSTEM (PNS) ADVERSE EFFECTS OF DRUGS USED IN COVID

Drug	CNS Adverse Reactions	PNS Adverse Reactions
Chloroquine (CQ)	Acute confusional state,[28] delirium,[29] decreased deep tendon reflex, depression, extrapyramidal disorders,[30] seizure[31]	Myopathy,[32] neuromuscular disease, polyneuropathy
Hydroxychloroquine (HCQ)	Ataxia, vertigo, dizziness, sensorineural hearing loss, neurosis, psychosis, seizure	Myopathy[33]
Umifenovir	Dizziness, psychiatric symptoms (0.83%)[34]	
Lopinavir/Ritonavir	Fatigue, headache, anxiety (4%), insomnia	Weakness, myalgia
Interferon alpha	Fatigue, headache, depression, drowsiness (1 to 33%), dizziness, vertigo, malaise, paresthesia, confusion (≤12), insomnia	Myalgia, asthenia, musculoskeletal pain, arthralgia, back pain
Favipiravir	Psychiatric reactions (1.72%)[34]	
Remdesivir	Have not reported yet.	Have not reported yet.
Tocilizumab	Headache, dizziness (rare)	Chronic inflammatory demyelinating polyneuropathy (<1%)
Corticosteroids	Psychosis (14%),[35,36] mania (28%), depression (41%), delirium,[36] anxiety,[36] insomnia,[36] seizure, vertigo, paresthesia,[37] pseudotumor cerebri[38,39]	Myopathy,[40] neuropathy[41,42]


No interaction
No action needed
Monitor therapy
Consider therapy modification
Avoid combination
Data not available.
Antiplatelet agents
Aspirin
Clopidogrel
Cilostazol
Dipyridamole
Ticagrelor
Ticlopidine
Prasugrel
Chloroquine
Hydroxy chloroquine
Lopinavir/ Ritonavir
Atazanavir
Favipiravir
Remdesivir
Corticosteroids
Tocilizumab
Chinese guideline
Interferon alpha
Other drugs under investigation
Azithromycin
Teicoplanin
Ivermectin


No interaction
No action needed
Monitor therapy
Consider therapy modification
Avoid combination
Data not available.
Statins
Antihypertensive agents
Atorvastatin
Rosuvastatin
Beta blockers
Others
Labetalol
Nicardipine
Sodium nitroprusside
Chloroquine
Hydroxy chloroquine
Lopinavir/ Ritonavir
Atazanavir
Favipiravir
Remdesivir
Corticosteroids
Tocilizumab
Chinese guideline
Interferon alpha
Other drugs under investigation
Azithromycin
Teicoplanin
Ivermectin



	Oral Anticoagulants					Thrombolytic agents (tPA)	Contrast agents	
	NOACs				Warfarin	Alteplase	Iodinated contrast media (Non-ionic)	Gadolinium-containing contrast media (Ionic)
	Rivaroxaban	Apixaban	Edoxaban	Dabigatran etexilate			Iohexol, Iopamidol, Iopromid, Iodixanol	Gadoterate meglumine
Chloroquine								
Hydroxy chloroquine								
Lopinavir/ Ritonavir								
Atazanavir								
Favipiravir								
Remdesivir								
Corticosteroids								
Tocilizumab								
Interferon alpha								
Azithromycin								
Teicoplanin								
Ivermectin								

DELIRIUM IN COVID PATIENTS

- Other complications derived from long-lasting in ICU, like impaired consciousness ranging from somnolence to confusion, delirium, stupor and coma, have been reported in almost 15% of hospitalized patients with COVID-19

- In patients with COVID-19, delirium may be a manifestation of direct central nervous system (CNS) invasion, induction of CNS inflammatory mediators, a secondary effect of other organ system failure, an effect of sedative strategies, prolonged mechanical ventilation or environmental factors including social isolation.

- Regarding pharmacological interventions, no drugs can be recommended for the prevention or treatment of ICU delirium other than avoidance of overuse of potent psychoactive agents like sedatives and neuromuscular blockers (NMB), unless patients require such management

DELIRIUM MANAGEMENT ADVICE FOR PATIENTS WITH CONFIRMED OR SUSPECTED

- Identify if patient is at risk – older, dementia, comorbidities.
- Identify baseline level of functioning via collateral history if needed. Drug and alcohol history is also important.
- Orientate, ensure people have their glasses and hearing aids, control pain, promote sleep hygiene, mobilise, maintain optimal hydration and nutrition, support with toileting, monitor and treat any pain or constipation, optimise oxygenation
- Optimise medication and consider anticholinergic burden
- Minimise number of changes of environment as far as possible (e.g. moves between wards)

SYMPTOMS/FEATURES OF DELIRIUM

- Disorientation Acute onset (hours/days)
- Agitation and restlessness Disturbances in attention and awareness
- Withdrawal and drowsiness Fluctuating symptoms
- Mood disturbance Disrupted sleep/wake cycle
- Delusions Perceptual disturbance including hallucinations

COMMON CAUSES OF DELIRIUM

- Pain
- Infection
- Nutrition
- Constipation
- Hydration & Hypoxia
- Medication & Metabolic
- Environment
- Central nervous sys disorders. Eg, acute stroke or non convolsive status epilepticus

MANAGEMENT

- Consider risk to self and others due to current symptoms (e.g. aggression, accident, self-neglect, physical deterioration, infection risk to others in context of COVID-19)
- Perform physical examination & investigations to identify causes
- Bloods ideally to include full confusion screen (**FBS,U+E, LFTs, TFTs, Mg, Ca .Na ,CRP, Lp as needed)**
- Consider CT if indicated (witnessed or possible fall, on anticoagulants, neuro Sx)
- Treat all underlying causes Review current medications; ensure optimal pain management (use Bolton Pain Scale if required); treat any constipation

- Address sensory impairments -make sure people have their **hearing aids and glasses**
- Ensure proper **hydration & nutrition** – make sure people have their dentures
- Optimise environment - support with sleep hygiene, use environmental cues (clock, calendar, radio etc) to aid orientation)
- Consider side room if available, **consider 1:1 nursing & aim for staff continuity, ensure adequate lighting and comfortable**
- Break down complicated tasks; **regular reorientation and explanation**; acknowledge distress and validate feelings
- EEG performing for rule out seizure
- **Inform, educate and counsel the family**; assist contact with family if possible; interact regularly as tolerated by patient

USE OF SEDATING MEDICATION FOR SEVERE AGITATION IN PATIENTS WITH DELIRIUM AND COVID-

- **Current advice is to start with low dose lorazepam or haloperidol and increase dose and frequency slowly if needed. Be aware that benzodiazepines may cause respiratory depression, and so haloperidol may be preferred in COVID delirium.**
- **Antipsychotics** should not be used for patients with Parkinson's Disease or Lewy Body Dementia
- An ECG should be obtained prior to administering antipsychotics to check QTc (upper limits 440mS in men, 470mS in women)
- If antipsychotics are contraindicated low dose lorazepam can be used, **please note lorazepam is not licensed in delirium**
- In severe cases both antipsychotics and lorazepam may be needed
- Alternative antipsychotics can be used if needed, but please note they are not licensed for delirium. **Risperidone** is licensed for use in Alzheimer's dementia for aggression, so can be considered if there is a history of this
- Avoid polypharmacy and monitor for medication side effects, after sedation vital signs must be monitored as per rapid tranquillisation policy

Medication	Route	Dose range (mg)	Daily frequency range	Recommended 24 hour max
Lorazepam	PO/IM/IV	0.5-1	OD - QDS	2mg
Haloperidol	PO/IM/SC (liquid form available)	0.5 – 2	OD - 2-4 hourly	5 mg
Risperidone	PO (liquid form available)	0.25 – 0.5	OD -BD	2 mg
Olanzapine	PO/IM (liquid form available)	2.5 - 5	OD - BD	10 mg
Quetiapine	PO (liquid form available)	12.5 - 50	OD - BD	100mg

If no improvement over 4 days, review diagnosis

Continue to treat underlying medical condition(s)

Continue to address common causes of delirium, e.g. constipation, dehydration, urinary tract infection, pain, medication side effects

DRUG INTERACTIONS BETWEEN COMMONLY USED MEDICATIONS IN DELIRIUM AND COVID- 19 DRUGS

	ATV	LPV/r	RDV	FAVI	CLQ	HCLQ	NITAZ	RBV	TCZ
Aripiprazole	↑	↑	↔	↔	↔	↔	↔	↔	↔
Haloperidol	↑♥	↑♥	↔	↔	↔♥	↔♥	↔	↔	↔
Olanzapine	↔	↓	↔	↔	↔	↔	↔	↔	↔
Quetiapine	↑♥	↑♥	↔	↔	↔♥	↔♥	↔	↔	↔
Risperidone	↑♥	↑♥	↔	↔	↑♥	↑♥	↔	↔	↔
Diazepam	↑	↑	↔	↔	↔	↔	↔	↔	↔
Lorazepam	↔	↔	↔	↔	↔	↔	↔	↔	↔
Midazolam (oral)	↑	↑	↔	↔	↔	↔	↔	↔	↔
Midazolam (parenteral)	↑	↑	↔	↔	↔	↔	↔	↔	↔
Oxazepam	↔	↔	↔	↔	↔	↔	↔	↔	↔
Zaleplon	↑	↑	↔	↔	↔	↔	↔	↔	↔
Zolpidem	↑	↑	↔	↔	↔	↔	↔	↔	↔
Zopiclone	↑	↑	↔	↔	↔	↔	↔	↔	↔

	These drugs should not be co-administered
	Potential interaction which may require a dose adjustment or close monitoring.
	Potential interaction likely to be of weak intensity. Additional action/monitoring or dosage adjustment unlikely to be required.
	No clinically significant interaction expected

Key

- ↑ Potential increased exposure of the co-medication
- ↓ Potential decreased exposure of the co-medication
- ⇑ Potential increased exposure of COVID drug
- ⇓ Potential decreased exposure of COVID drug
- ↔ No significant effect
- ♥ One or both drugs may cause QT and/or PR prolongation. ECG Monitoring is advised if co-administered

ATV	Atazanavir	CLQ	Chloroquine
LPV/r	Lopinavir/ritonavir	HCLQ	Hydroxychloroquine
RDV	Remdesivir	NITAZ	Nitazoxanide
FAVI	Favipiravir	RBV	Ribavirin
		TCZ	Tocilizumab

THANK YOU