

Original Article

Comparison between Management and Pharmacotherapy of COVID-19 in Iran and Switzerland

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Abstract

Background: On 30 January 2020, the WHO declared the outbreak of SARS-CoV-2 as a public health emergency. In the present study, we compared the preventative and therapeutic strategies and the success rates of Iran and Switzerland during the COVID-19 outbreak.

Materials and Methods: This study was conducted using electronic databases such as PubMed, Scopus, and Web of Science. In addition, the official documents of developed countries and WHO from 1st February until 15th May 2020 were studied. Relevant documents were reviewed in detail, and vital data were extracted.

Results: Both countries have restriction policies to reduce the infection rate in the prevention setting. These policies, such as the recommendation to all citizens to stay home unless necessary, army participation, and non-face-to-face counseling, were surveyed by similar techniques in both countries. Some policies were implemented in both countries with different protocols. These policies, including social distancing practices, smart distancing methods, business activities, border closures, border controls, and restrictions, travel restrictions, testing and screening for infection and fever, and decreased working hours, were performed in both countries. In the treatment setting, the therapeutic strategy used in Iran consisted of hydroxychloroquine or chloroquine phosphate and anti-viral drugs. Switzerland followed the guidelines of the European countries. The infection rate, recovery rate, and death rate were 0.139%, 78.73%, and 5.91% in Iran, while these rates were 0.352%, 88.81%, and 6.15% in Switzerland, respectively.

Conclusion: Due to the lack of special treatment for the disease, prevention must be considered the most important factor in policymaking. Importantly, observing social distance is the most effective method among the preventative strategies. The capacity of the health care systems to provide optimal services and facilities is an important factor for patients' recovery.

Keywords: Management and Pharmacotherapy, COVID-19, Iran, Switzerland

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Introduction

A sudden dubious prevalence of respiratory disease caused by a novel virus made physicians and healthcare workers suspicious in Wuhan, China, in December 2019, followed by a quick spread throughout the country¹. The pathogen for this respiratory disease was identified and isolated later and named the 2019 Wuhan novel coronavirus (2019-nCoV)². World Health Organisation (WHO) named this pathogen severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). On January 30, 2020, the WHO declared the outbreak of SARS-CoV-2 as a public health emergency of international concern. After that, WHO used COVID-19 as an official name for the SARS-CoV-2-infection³. Compared to the SARS-CoV leading to an outbreak of SARS in 2003, this novel pathogen has a stronger transmission capacity. An increase in infected cases makes the prevention and control of COVID-19 extremely momentous⁴.

The coronavirus is a family of viruses common in animals worldwide. However, few cases have been known to affect humans. Infected cases may present various clinical manifestations, such as pneumonia, fever, and dyspnea⁵. While the symptoms of the disease are mild in most patients, the disease course could be life-threatening in old patients and patients with underlying diseases, finally leading to death⁶.

There are no cure strategies. Therefore, supportive and symptomatic treatments, prevention of disease transmission, and keeping the R0 index (primary reproduction ratio) as low as possible are the best strategies for saving human lives⁷. WHO recommended several guidelines in order to prevent COVID-19 contaminations, including washing hands frequently, especially after contact with infected people or suspicious subjects, avoiding contact with wild animals, practicing social guidelines such as social distancing, covering coughs or sneezes with disposable tissues or clothes, and avoiding to touch the face after touching subjects, especially outside

tenancy area⁸.

After the outbreak of COVID-19 in Wuhan, China, the disease rapidly spread from a single city to the entire world in just 30 days, which intensively impacted the daily life of numerous people all around the world. It quickly overwhelmed healthcare workers and public health services in China. Because there were no specific treatment and prevention options for COVID-19, China focused on traditional public health outbreak response strategies. It concluded that self-isolation, quarantine, social distancing, community containment, and activities help "them hold up the time to help scientists catch up before COVID-19 becomes a nationwide disaster"⁹.

As WHO declared a new pandemic, each government managed the COVID-19 crisis based on its trial and error policies. In the present study, we compared Iran and Switzerland's preventative and therapeutic strategies against COVID-19. We evaluated the success rate of each country in the management and achievements in curbing the outbreak.

Methods

This study compared Iran and Switzerland's preventative and therapeutic strategies against COVID-19. For this purpose, we performed comprehensive searches of electronic databases such as PubMed and Scopus; the team reviewed all documents in different languages, such as English, Persian, and German. Moreover, we evaluated and reviewed the official documents the Iranian and Swiss governments released and the official statistics and guidelines announced by the WHO. All the literature search was conducted from 1 February 2020 until 15 May 2020.

Relevant articles were reviewed in detail, and required data were extracted and transported to prepared tables. These tables were reviewed finally, and all of the items were compared between the two countries. We utilized two independent researchers to evaluate articles and official documents. Finally, the data were analyzed by independent researchers to investigate the integrity and

validity of data to prevent any bias.

The local Ethics Committee approved the study of Shiraz University of Medical Sciences, code number EC-HP-98-01-62-21928.

Results

Prevention Strategy: This extraordinary situation, due to COVID-19, needs considering extraordinary measures to protect people, authorities, and countries. It was our goal to figure out how differences affected the results. Switzerland and Iran have issued unambiguous guidelines to prevent the spread of COVID-19^{10,11}. Table 1 presents the current policy of these two countries.

Treatment Strategy:

Iran: In Iran, physicians treating COVID-19 patients are prescribing hydroxyl chloroquine or chloroquine phosphate and anti-viral drugs such as anti-HIV-medication. Tables 2 and 3 detail these medicines' dosage and consumption guidelines.

Mentioned medicines must be adjusted and prescribed in a specific dosage in a particular population. Table 4 shows the specific dosage of each medication in special populations.

Medications used to treat COVID-19 in pregnancy:

1. Medications for high-risk cases:

This treatment could only be recommended for pregnant mothers who are at high risk (those with immune deficiency or specific health conditions)

Hydroxychloroquine sulfate 200mg OR chloroquine phosphate 250mg (equal to 150mg of drug base) q12h 2tabs / continues with q12h 1tab for at least five days

2. Pharmacologic treatment

Recommended drug regimen for in-patients:

Hydroxychloroquine/ chloroquine phosphate

Hydroxychloroquine sulfate 400mg QD or chloroquine phosphate 500mg BID QD as a single dose (Once)

First day: q12h 2tabs / continues with q12h 1tab for at least seven days and at most 14 days

One of the following drugs could be added to the therapeutic regimen under a physician's **supervision:**

Kaletra tablets (lopinavir/ ritonavir) 200/50mg; 2tabs q12h for at least 5days (atazanavir and ritonavir) tablets 300/100mg; 1tab daily with food for at least 5days

If Atazanavir / Ritonavir is started,

hydroxychloroquine 200 mg should be continued once daily until the end of the treatment period.

Switzerland: Switzerland follows the guidelines of European countries. Those advised that currently competent or licensed treatment options do not exist for Covid-19.

Randomized clinical trials, such as the WHO SOLIDARITY trial, are going on worldwide. However, there is no evidence of the effectiveness of those medicines, and unfortunately, Covid-19 medicinal managements are still experimental (Table 5).

These solidarity medicines already have a safety profile for other treatments. A combination of these medicines with other drugs may have significant side effects.

European Medicines Agency (EMA) suggested using only chloroquine and Hydroxychloroquine in clinical trials or emergency use programs. EMA has also advised that these medicines should be continued in chronic conditions and, of course, not more than the usual duration.

In order to assess the success rate of each country in the management of the COVID-19 outbreak, we extracted updated information about the number of infected cases, recovered cases, active cases, severe cases, and deaths, conducted tests from the "worldometer.info." Table 6 shows the latest information about COVID-19 in Iran and Switzerland¹² (15 May 2020).

Discussion

In the present study, we evaluated the health policies of Iran as a Middle Eastern country and Switzerland as a European country in preventing COVID-19, as well as therapeutic actions. Moreover, we compared the number of infected cases, recovery rate, and death rate between these two countries to evaluate each country's success rate in managing the SARS-CoV-2 outbreak.

Preventing policies: WHO and many other valid organizations provided some protocols for preventing COVID-19 infection. These protocols included strategies such as frequent washing, avoiding unprotected contact with animals, keeping distance, covering coughs or sneezes with disposable tissues or clothes, strengthening the application of strict hygiene measures for the prevention and control of infections in particular in emergency medicine departments, avoiding public gatherings of individuals that are immunocompromised⁸.

In order to compare the success rate of preventive strategies of two countries against the COVID-19 outbreak, evaluating the infection rate of each country

Table 1: Forward and Reverse Primer Sequence

Country Policy*	Iran	Switzerland
Recommend to all citizens to stay at home unless necessary	√ YES	√ Particularly those who are sick or aged 65 and older, as well as announcing a nationwide "Precautionary self-isolation of contacts "to mean "quarantine". The daily supplies of medicine and food are guaranteed.
Social distance	√ 1-2 meter	Ban on gatherings of more than five people.
Smart distance	√ Only non-risky** jobs by the obligation to comply with the health guidelines approved by the MOHME**.	Ban on all private and public events, and the closure of small businesses, restaurants, bars, cultural spaces, sporting facilities and schools. The business providing essential services – such as grocery and food stores, pharmacies, post offices and banks – remain open and serving the public.
The activity of the business	All businesses will be required to register and obtain code through the website of the Ministry of Health (based on compliance with health guidelines), then the activity license will be issued.	Social-distancing measures that adversely affect businesses, communities, and individuals. Only businesses providing essential goods – such as grocery stores, bakeries, and pharmacies – are to remain open. Banks and post offices will also be open.
The closures	Thenecessaryclosures (including the closure of schools, universities, stadiums, cultural and artistic centers, high-risk jobs, etc.)	Small businesses and restaurants have had to close their doors. Only businesses providing essential goods remain open. Schools are closed nationwide.
Travel	Ban on inter-provincial traffic will continue until further notice. Spring trips wererestricted.	IT WAS RESTRICTED (A nation of trains, it has cut service). Forbidding over-65-year-olds from leaving their homes outside of specific circumstances in Switzerland. Forinstance, from leaving their homes altogether, except for visits to the doctors, or a two-hour solo walk***.
Border controls and restrictions	By control	Border controls and restrictions on entry; the Swiss government extended entry restrictions to all Schengen and non-Schengen states. Only Swiss citizens, Swiss residents, those entering the country for professional reasons (e.g., those who work here and have a permit to prove it), and those transiting through can enter.
Working hours	The administrative centers will be activated with two-thirds of their employees on April 13, following the principles of health, and the working hours will be from 7 am to 2 pm.	-----
Militia participation	army √ The army has around 2000 additional beds.	√ The army has around 200 additional respirators [£] .
Testing [£]	It is limited to the vulnerable population or patients requiring hospitalization	√ YES people who had traveled from high-risk areas or had come into contact with an infected person, with a strong focus on high-risk groups or patients requiring hospitalization
Screening	Screening of the entire population with the support of the health network. **** The National Corona Management Task Force announced the health screening started with a team of 300,000 people across the country, especially in the provinces where the virus is most common.	For high-risk people
Non-face-to-face counseling related to Corona and related issues.	√ YES Launching the 4030 phone line with the help of 2,200 doctors and paramedics for answering 'people's questions about coronavirus.	√ YES

* In both countries this is the first time these legal provisions have been applied.

**Ministry of Health and Medical Education.

*** The Federal Justice Office said such measures violate the national regulations.

£ The armed forces command is considering reducing the number of troops called up to support hospitals and homes.

€ More than 6,000 tests are being carried out in Switzerland per day, and cantons have been ramping up their testing capacity (during the period of literature search). Switzerland has one of the highest per-capita rates of testing in the world

**** This is a more comprehensive strategy than what is being seen in Switzerland and elsewhere around the world.

Table 2: Drug regimen in specific cases, only for the high-risk population.

Pharmacologic treatment for patients, only for those at high risk

Hydroxychloroquine / chloroquine phosphate

Hydroxychloroquine sulfate 200mg or chloroquine phosphate 250mg (equal to 150mg of drug base)

First day: q12h 2tabs / continues with q12h 1tab for at least 5 days

Based on the patient’s clinical characterizations (in case of no improvement in early symptoms), chloroquine may be administered up to 10 days.

Table 3: Recommended anti-viral drug regimen for in-patients includes.

Recommended anti-viral drug regimen for in-patients

Hydroxychloroquine / chloroquine phosphate

Hydroxychloroquine sulfate tab 200mg OR -1 tablet of chloroquine phosphate 250mg (equal to 150mg of drug base)

First day: q12h 2tabs / continues with q12h 1tab for at least 7 days and at most 14 days

One of below drugs could be added to the therapeutic regimen, under 'physician's supervision:

- 1.Kaletra tablets (lopinavir/ ritonavir) 200/50mg; 2tabs q12h with food for at least 7 days and at most 14 days
- 2.(atazanavir and ritonavir) tablets 300/100mg; 1tab daily with food for at least 7 days and at most 14 days

*There is no proved evidence for the certain efficacy of mentioned regimens in COVID-19 for now.

* According to drug interactions, if Kaletra is chosen, hydroxychloroquine sulfate 400 mg QID or two chloroquine phosphate 500mg QID (equivalent to 150 mg of drug base) should be given as a single dose (once daily) on the first day. In contrast,if started (atazanavir/ritonavir), Hydroxychloroquine 200 mg twice daily (400 mg daily) can be continued until the end of the treatment period.

** In case of intolerance to gastrointestinal side effects, patients with a history of cardiac arrhythmias or high risk of drug interactions, the use of (Atazanavir / Ritonavir) over Clarettra (Lopinavir/ Ritonavir) is preferable.

*** Oseltamivir 75 mg twice daily for at least 5 days only if laboratory findings or epidemiological evidence is in favor of influenza and may only be recommended in hospitalized settings.

would be the best index. Currently, the total number of infected cases in Iran is 104,691. Considering that the population number of this country is 83,850,893, it means that 0.139% of the population is infected with COVID-19. Simultaneously, a total number of 30,207 cases suffer from COVID-19 infection in Switzerland, with a population of 8,646,448, 0.352% of the country's population. The infection rate is the best index for evaluating

preventative measures and policies. The infection rate in both countries is less than 1%, which shows that both countries’ preventative strategies were successful. However, the percentage of the infected population in Switzerland is two-fold higher than in Iran. Reviewing the preventative strategies chart seems to reduce the working hours. The employee number in the businesses that were obligated to be open during the outbreak was an efficient strategy that caused the lower infection rate

in Iran compared to Switzerland.

Differences in prevalence rate may be due to the

Table 4: Drug dosing in special populations.

Drug	Pediatrics	Patients with renal failure	Patients with hepatic failure	pregnancy
Hydroxychloroquine	3-5 mg/Kg in 1-2 divided doses	No need to dose adjustment	No need to dose adjustment	Allowed
lopinavir/ ritonavir	230 mg/m ² body surface area 2 times a day	No need to dose adjustment	No need to dose adjustment	Allowed
Atazanavir/ ritonavir	≤15Kg: Not recommended 5 to <15 kg: 200/80 mg, if unable to tolerate this dose, 150/80 mg 15-15 to <25 Kg: 250/80 mg ≥25 Kg: same as adults	No need to dose adjustment	Not recommended in advanced hepatic failure (Child-Pugh class C)	Allowed
Osetamivir	Infants: 3mg/Kg 2 times/day Children ≤15Kg: 30mg 2 times/day Children 15-23 Kg: 40mg 2 times/day Children 23-40 Kg: 40mg 2 times/day Children ≥40 Kg: same as adults	Keratin clearance: ✓ 30-60 ml/min: 30mg/day ✓ Below 30 ml/min: 30mg/day or 75mg every other day ✓ Dialysis patients: 30mg after each dialysis session for 5 days (normal dialysis filter (Low flux)) and 75mg after each dialysis session for 5 days (High-flux filters), 3 times/week after dialysis in the 5-day period.	No need to dose adjustment	Allowed

Table 5: WHO options on potential Covid-19 treatment

Solidarity clinical trial	Non-solidarity trial
Chloroquine or Hydroxychloroquine Lopinavir and Ritonavir	IL-6 / IL-1 antagonist (tocilizumab) Favipiravir (Investigational drug)
Lopinavir / Ritonavir plus interferon Beta 1a Remdesivir (Investigational drug)	Convalescent Plasma (CP)

Table 6: The latest information COVID-19 in Iran and Switzerland

Country	Total Cases	Total Recovered	Active Cases	Serious Critical	Total Deaths	Total Tests
Iran	248,379 (~0.003 in 1million)	209,463 (~0.002 in 1million)	26,832 (~0.0003 in 1million)	3,309 (~0.000 in 1million)	12,084 (~0.0001 in 1million)	1,827,391 (~0.0217 in 1million)
Switzerland	32,498 (~0.003 in 1million)	29,400 (~0.003 in 1million)	1,132 (~0.0001 in 1million)	16 (~0.000 in 1million)	1,966 (~0.0002 in 1million)	652,413 (~0.075 in 1million)

In Switzerland, COVID-19 testing was conducted on 3.86% of the population, while in Iran just on 0.785%.

difference in the capacity of identifying the patients based on the diagnostic tests. Although in Iran a

screening program via telephone call was conducted based on patients' clinical signs and symptoms, the higher identification rate of Switzerland showed that due to probability of symptomless cases the most reliable method of identifying COVID-19 cases is conducting diagnostic laboratory test.

Treatment Policies: We evaluated two other indices in this study that would be useful for comparing therapeutic strategies between countries: recovery rate and death rate. In Iran, 5.917% of the infected cases, and in Switzerland, 6.15% have died due to the disease. However, the recovery rate was slightly different between the two countries. In Switzerland, the patients improved in 88.81% of the infected cases, while in Iran, it was 78.73% of the patients.

As mentioned previously, there is no definite treatment for SARS-CoV-2 right now. The available therapeutic regimens mostly use Hydroxychloroquine and an Anti-viral medicine since there is some evidence confirming their efficacy on viral load reduction and clinical outcome^{13,14}. During the crisis, the physicians in Switzerland and Iran also applied the mentioned regimen to treat the disease. Therefore, the therapeutic strategy does not play any role in the difference in recovery rates between Iran and Switzerland. A point not evaluated in this study but seemed to be the main reason for Switzerland's higher recovery rate is the availability of health system facilities.

In Iran, data were gathered from documented information from the ministry of health, the only authorized health organization for WHO. The total number of COVID-19 patients may be higher in Iran. However, there was no other reliable and acceptable reference to get accurate information for this country.

Conclusion

In conclusion, reducing social contact duration or number is the most crucial factor in preventing COVID-19 infection. Since there is no specific treatment for the disease, prevention can be considered the most crucial factor in policymaking. Furthermore, due to the lack of information about this novel virus and its treatment, it is still fatal in critical cases worldwide. However, the capacity of the healthcare systems to provide optimal services and facilities is most probably a crucial factor in patients'

recovery.

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