Heparin vs. DOACs in Covid-19

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Abstract

Essential Question: What are the Differences Between Heparin and Direct Oral Anticoagulants in COVID-19?

Thromboembolic developments and excessive blood clotting are prominent afflictions associated with severe cases of COVID-19. Hence, the administration of anticoagulants such as heparin and Direct Oral Anticoagulants (DOACs) aids in the recovery process of patients with COVID-19. The difference between these two agents is that heparin is given by injection and has a rapid onset of action, whereas a DOAC is given orally and has a slow onset of action.

Introduction

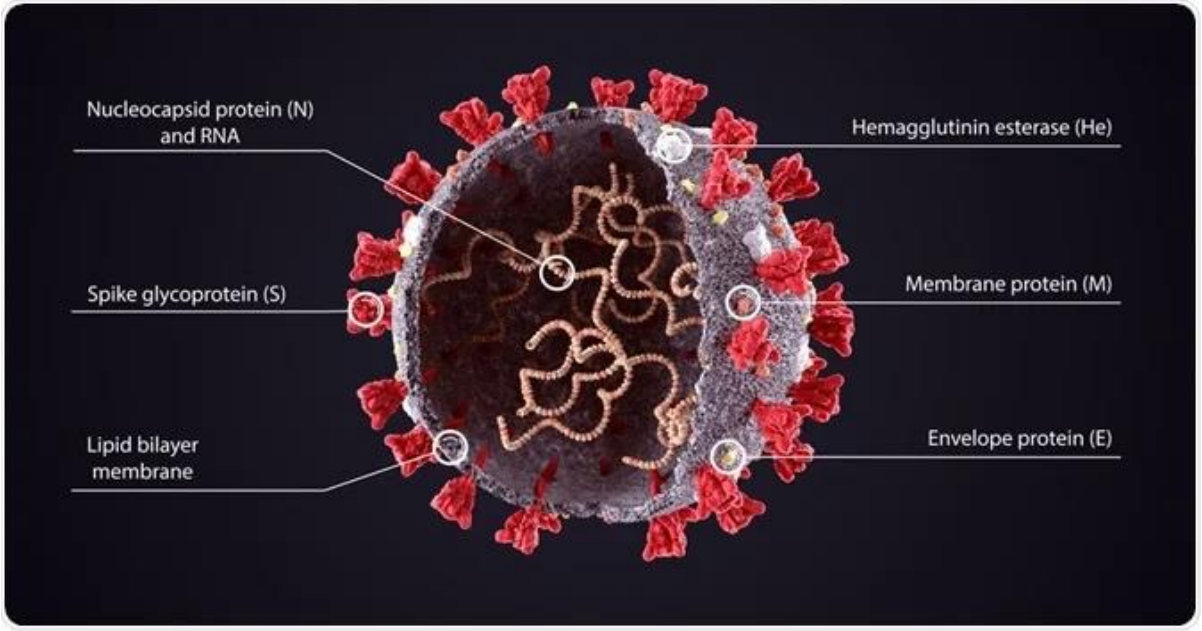
- My name is Anki Mahajan and I am a rising Junior at Johns Creek High School in Johns Creek, Georgia. I am 16 years old.
- Thromboembolic developments and excessive blood clotting are prominent afflictions associated with severe cases of COVID-19.
- The abnormal hypercoagulation in the case of coronavirus can be attributed to the interaction between the disease and the body.
- Hence, the question is raised as to the selection and administration of anticoagulants such as heparin and Direct Oral Anticoagulants (DOACs) as to which drug will best aid in the recovery process of patients with COVID-19.

Methodology

I analyzed articles and resources from PubMed.gov, the National Library of Medicine, and the US National Library of Health from the year 2019- present. I then filtered my results by selecting peer reviewed articles. Some of the key words I used were COVID-19, Thrombosis, Direct Oral Anticoagulants, Novel Oral Anticoagulants*, Heparin, Anticoagulants in Covid.

**Although NOAC is another term for DOAC, I used both terms because some articles did not use both interchangeably and to maximize results.*

COVID-19


Nucleocapsid protein (N) and RNA
Spike glycoprotein (S)
Lipid bilayer membrane
Hemagglutinin esterase (He)
Membrane protein (M)
Envelope protein (E)

Pathophysiology

- SARS-CoV-2 is a single-stranded RNA virus that frequents mammals (including humans) and is responsible for the global scaled pandemic from 2019-2021.
- The virus is anywhere between 60-140 nanometers in diameter, and is enveloped in spikes which attach themselves to the host cell's membrane and then begin replicating themselves using the host's machinery (organelles).
- Common symptoms displayed early in infection are (in severe cases) lymphopenia, inflammation, fever, cough, chills, shortness of breath, headache, fatigue, and loss of taste and/or smell.
- COVID-19 is also responsible for the abnormal hypercoagulation leading to thrombotic risk factors heightening. The cause of death in individuals with severe cases of coronavirus was most often attributed to the thrombotic developments instead of the virus itself.

Epidemiology

- The first reported incidence of the novel coronavirus was in Wuhan, a city in the Hubei region of China.
- From there, the viral pathogen rapidly spread to other parts of China and ultimately crossed its borders and spread to the rest of the world via infected hosts (humans and select mammals).
- It is airborne and spreads through close contact between people (coughing, sneezing, touching).
- Hypercoagulation isn't a contagious symptom of the virus. The virus behaves differently in each host's body. Therefore, contracting coronavirus from someone suffering from thrombotic conditions does not necessarily mean the victim will develop thrombotic conditions themselves.

Risk Factors

- Because COVID-19 directly engages with the immune system in the body, individuals most at risk are those with immuno-deficiency disorders like HIV or AIDS, or those who are immunocompromised.
- Diabetes, cancer, chronic lung conditions,, obesity, heart conditions, and sickle cell disease are all risk factors for COVID-19. Older adults are also at a higher risk for the disease.
- The onset of thrombosis in patients hospitalized due to Covid-19 is not an uncommon incidence. Statistically, the probability of developing thrombotic conditions as a result of the virus is about 16%.
- Comparatively, the probability of developing thrombosis in relation with other respiratory diseases (e.g. pneumonia) averages at about 5%.

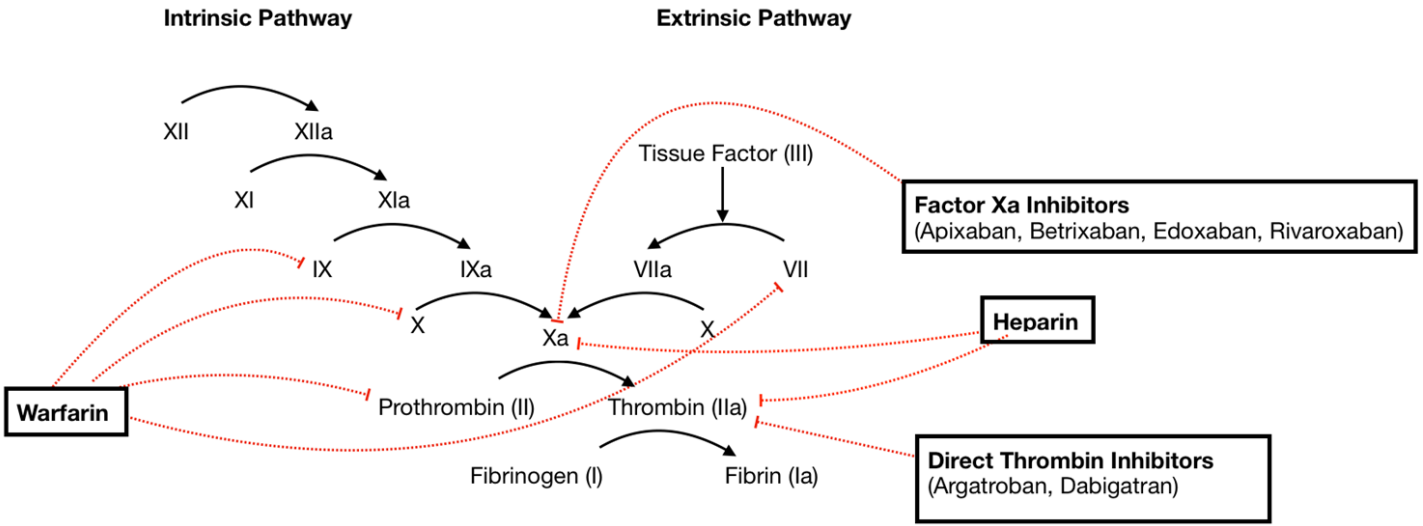
Mechanisms

- The abnormal hypercoagulation in the case of COVID-19 can be attributed to the interaction between the disease and the body.
- The angiotensin converting enzyme-2-- or ACE2 receptor-- is targeted by the virus' proteins, which bind to the receptors and degrade/damage them.
- This results in the formation of alien blood clots which then could potentially break off from the arterial wall and result in DVT, Myocardial Infarction, Pulmonary Embolism, or stroke.

Heparin

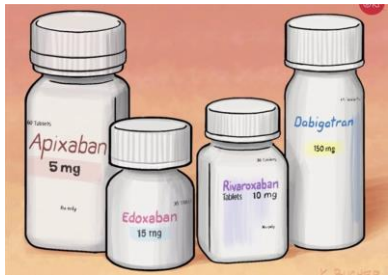
- Heparin was first discovered in 1916, and is the oldest anticoagulant used to date.
- Since its introduction into the medical field, this cost-effective drug has revolutionized the treatment of thrombosis and associated thrombotic conditions.
- Heparin effectively combats blood clots and hypercoagulation by interacting with antithrombin III, a protein in the blood that prevents the formation of abnormal clots.
- Heparin is injected directly into the bloodstream and has a rapid onset of action.
- All these factors make heparin a wise treatment option for COVID induced blood clots because it specifically interacts with antithrombin III to quickly unbind clots of an abnormal nature.

Mechanism of Action: Heparin vs. Other Anticoagulants



Direct Oral Anticoagulants (DOACs)

- Initially, DOACs were known as Novel Oral Anticoagulants (NOACs). They were first introduced in the year 2010 as Dabigatran.
- The search for a new anticoagulant was due to complications following heparin and warfarin. Heparin was short-acting and wasn't sustainable for preventing future blood clots, and warfarin needed very close INR monitoring and restricted the patient's diet because its antidote (vitamin k) frequents normal diets.
- Hence, DOACs were introduced as a long-term alternative for warfarin and heparin.
- DOACs are divided into two separate groups: direct factor Xa inhibitors (e.g. apixaban, rivaroxaban), and direct thrombin inhibitors (dabigatran).
- In recent studies, the DOAC use was proven to reduce the risk of thrombotic developments in a sample population of COVID-19 patients at risk across all age groups and gender.
- Although a great option for the long term combat or prevention of thrombosis in COVID-19, DOACs are not the best fit for immediate blood clot diffusal because of their slow onset of reaction.



Heparin vs. DOACs

	Heparin	**DOACs**
Onset of Action	Immediate action	Slow onset of action
Administration	Injection	Oral
Record	Approved in 1939 by FDA	Approved in 2010 by FDA
Antidote	Yes; Protamine Sulfate	Darucizumab
Efficacy	Works immediately, half life of ½ hour	Works in 1-3 hours, exits system in about 2-3 days
Safety	Can induce major bleeding events	Relatively safe

Conclusions

- After analyzing both Heparin and DOACs, my research concludes that both can be used for the treatment of thrombosis associated with COVID-19, but not interchangeably.
- In acute situations, Heparin should be administered to quickly remove blood clots. DOACs may be used in non-life threatening settings to decrease the risk of thrombotic developments in patients with COVID-19.
- DOACs may also be prescribed to recovering patients to prevent further thrombotic complications.

Future Directions

- The most significant challenge I encountered in the making of this presentation was with limitations on data and references.
- Because of the recency of the COVID-19 pandemic, there weren't many existing articles to choose from. My data was all recent, meaning that it has not been sufficiently followed up.
- Some data was contradicting. For example, one study claimed that the administration of DOACs procured results that were not significantly different from that of the control group, whereas other studies supported a positive correlation between DOAC usage and declining thrombotic outcomes.
- I recommend that more studies be done on the topic, especially those that contrast the effectiveness of different kinds of DOACs on patients with or at risk of thrombosis induced by Covid-19.

References

https://pubmed.ncbi.nlm.nih.gov/33181067/

https://pubmed.ncbi.nlm.nih.gov/32991251/

https://pubmed.ncbi.nlm.nih.gov/2191809/

https://pubmed.ncbi.nlm.nih.gov/29506866/

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1124446/

https://pubmed.ncbi.nlm.nih.gov/33988835/

https://pubmed.ncbi.nlm.nih.gov/33683064/