ORIGINAL RESEARCH PAPER

Neurosurgery

ROLE OF PROPHYLACTIC ANTI COAGULANTS AND ANTI PLATELETS TO REDUCE THE INCIDENCE OF THROMBOSIS, STROKE, MYOCARDIAL INFARCTION IN ASYMPTOMATIC PATIENTS OF COVID19

KEY WORDS: COVID19, Thrombosis, Stroke, Heart Attack, Vaccine

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ABSTRACT

BACKGROUND: As we are in the middle of the second year of the COVID19 Pandemic, we are observing an increased incidence of conditions like Cerebrovascular Accidents, Ischemic Heart Disease, Myocardial Infarction, Deep Vein Thrombosis, Pulmonary Embolism, and Thrombosis of Other Vessels.

MATERIALS AND METHODS: Literature Review and Analysis of Coagulation Profiles of Patients in the past 1 year treated by the author was done.

RESULTS AND CONCLUSIONS:

1. COVID19 is not just an infectious disease, but also an Immune Disease. The **Immune Part can also happen in Asymptomatic Patients and those who got the vaccine.**

2. Most of the disease processes in the body start after the virus has been cleared from the throat. **The vigil against complications must not stop when the Throat Swab becomes negative or even when the patient is discharged but must continue for months till all the disease processes stop.**

3. It is recommended that:

a. Initial Evaluation with PT, aPTT, INR is done for:

I. Those suffering from COVID 19 who have not undergone D Dimer evaluation

ii. Those recovering from COVID 19.

iii. Those likely to have had COVID 19 (based on the symptoms), but the infection was not documented.

iv. Those likely to have had asymptomatic COVID 19 (contacts of COVID19 infected patients)

v. Those planning to take Vaccines for COVID19.

b. An Abnormal Value in PT, aPTT, INR may be managed with appropriate Drugs like Aspirin, Clopidogrel, Dipyridamole, Ticlopidine, Rivaroxaban, Dabigatran, Apixaban, Edoxaban, Heparin, Low Molecular Weight Heparin, Warfarin, and other drugs.

c. Serial Evaluation of PT, aPTT, INR be done after 1 month, 3 months, 6 months (and even at more frequent intervals if indicated) and the drugs are added or removed, the dosage of the drugs is increased or reduced based on the results.

d. Standard Indication of IVC Filter may be followed.

4. It is the **knowledge of the pathogenesis of Thrombosis** that is crucial in the **prevention and management of Stroke, Heart Attack, Deep Vein Thrombosis, and Pulmonary Embolism** rather than **fancy gadgets, expensive tests, and exotic drugs.**

1. INTRODUCTION

Though COVID19 is caused by a virus, the manifestations of the infection are far and wide. In addition to damages in Lungs, there are lots and lots of various other maladies too. Some like Loss of Smell and Taste may be troublesome, but quite harmless. Others like Thrombosis may be deadly. As we are in the middle of the second year of the COVID19 Pandemic, we are observing an increased incidence of conditions like Cerebrovascular Accidents[1,2,3,4,5,6,7], ischemic heart disease[8,9,10,11], Myocardial Infarction [12,13,14,15,16,17], Deep Vein Thrombosis[18,19], Pulmonary Embolism[20] and Thrombosis of Other Vessels[21]. Such conditions are also seen in **an increased incidence in those patients who never exhibited symptoms and signs of COVID19** and who had even tested negative for various tests like Swab Test, Inflammatory Markers, and CT Scan Lungs. Hence, we must have a scientific and rational approach regarding the disease process causing these blood clots and minimize the damage.

2. Damages due to COVID 19

COVID19 Virus causes damage due to two broad mechanisms.

1. Damage by the Virus
2. Damage by the Immune System

The Damage by the Immune System happens in 4 ways.

1. Type I Hypersensitivity Reactions cause Sudden Death due to Anaphylaxis.
2. Type II Hypersensitivity Reactions causing Cytokine Storm and Multi-Organ Dysfunction
3. Type III Hypersensitivity Reactions causing Hyper Coagulable state and Thrombosis (and subsequently Heart Attack, Stroke, DVT, Pulmonary Embolism, etc.
4. Lung Damage due to Virus, Type III and Type IV Hypersensitivity Reactions

Of these,

1. We evaluate the Virus in Throat with Throat Swab.
2. We evaluate Cytokine Storm with Blood Investigations like IL6, LDH, Ferritin, CRP, NLR.
3. We evaluate the Coagulation Status with D Dimer and PT, aPTT, INR.
4. We evaluate the Lung Damage with Oxygen Saturation, CT Lungs.

However, we need to keep in mind a few tenets.

1. The negative Result is Throat Swab means that the virus is not in the throat. This does not mean that the disease has been totally cleared. In fact, **most of the disease processes in the body start after the virus has been cleared from the throat.** The vigil against complications must not stop when the patient is discharged. It must continue for months till all the disease processes stop.

2. Many would have got the virus infection and their immune system would have fought the virus and chased it away. They would not have experienced any issues like reduction in Oxygen Saturation Below 96, Cough, or Fever. **But the Type III Reactions would have started in his blood. Even if the throat swab RT PCR test had given a negative report and even if CT Lungs had revealed normal-looking lungs, the blood could have changed to have increased the chance for clot formation.** This is more common if the person already had some pathology causing a hypercoagulable state.

3. There is less chance for Complications like Cytokine Storm and Lung Damage after the patient is discharged from the

hospital. **But Thrombosis can happen days, weeks, or even months after discharge.**

4. Those getting Vaccines against COVID19 may not get any damages due to the Virus. **But the damages due to Hypersensitivity can occur even with the Vaccines.** Data as of date show that the incidence of Cytokine Storm, Lung Damage, etc. are almost nonexistent with vaccines, but there are cases of increased thrombosis[22]. This is more common if the person already had some pathology causing a hypercoagulable state.

3. Pathogenesis of Thrombosis

When COVID19 Virus attacks a person, his / her immune system fights back and, in that process, the virus particles are damaged. These damaged virus particles circulate in the blood. Antibodies go and attach to these particles, and they form the Ag-Ab (Antigen-Antibody) Complex. The same complex can also form after vaccination. This is the reason for the increased risk of clot formation after vaccination.

They are gradually cleared from the blood by various mechanisms. However, a few people have some genetic defects in one or many of the components involved in clearing these viral debris. So, the debris circulate for an exceptionally long time in their blood. Even if the clearing mechanism is fine, the debris can still circulate for a longer time, if the initial viral load was high or if treatment was inadequate as explained subsequently.

These Complexes circulate in the blood. However, these are "foreign particles" in the blood and the blood gets "irritated" on seeing these "dirt particles". When a dirt particle enters into an Oyster, it "irritates" the Oyster. The Oyster secretes a fluid to cover the dirt and a Pearl is formed. Our body tries to cover these "irritating factors" in a similar manner. In most persons, the covering is just enough to prevent irritation. However, some people have genetic or acquired defects where the "coverings" are made in ten, hundred, or even thousand layers, and hence fairly large-sized "balls" circulate in the blood.

These large complexes increase the viscosity of blood and interfere with blood flow, especially in smaller blood vessels. Further, they also promote clot formation. When such a clot forms in blood vessels supplying the heart, the patient gets myocardial infarction or heart attack. When such a clot forms in blood vessels supplying the brain, the patient gets a stroke and so on.

4. Factors Associated with Increased Risk of Thrombosis

As seen above the factors associated with increased risk of thrombosis are:

1. Increased Number of Viral Debris in the Blood due to
a. Increased Viral Load at Exposure.
b. Inborn Errors in Immune System Dealing with Viral Infections.
c. Delay in administration of Azithromycin, Ivermectin, Remdesivir, etc.
d. Inadequate dosage of Azithromycin, Ivermectin, Remdesivir, etc.
e. No Treatment (including Asymptomatic patients).
f. Inborn Errors in Immune System Dealing with the clearing of Viral Debris.
2. Pro Coagulable Thrombotic State in the Blood due to
a. nborn Errors in Coagulation Cascade.
b. Dehydration.
c. Delay in administration of Steroids and Anti-Inflammatory agents.
d. Inadequate dosage of Steroids and Anti-Inflammatory agents.
e. No Treatment (including Asymptomatic patients).

The list of conditions coming under each of the above categories is exhaustive. But the saving grace is that, in most cases, there is no need to go deep into these causes, but just **manage the problem keeping in mind the aim to achieve clotting-coagulation-fibrinolysis equilibrium.**

4. Tests to Detect Risk of Thrombosis

Irrespective of the above-mentioned causes, the Following Tests can be used to find out whether the patient has an elevated risk of Thrombosis.

1. Bleeding Time
2. Clotting Time
3. Prothrombin Time
4. INR
5. Activated Partial Thromboplastin Time
6. D Dimer

Of these tests, **the first two are bedside tests, and PT, INR, aPTT is available in almost all labs** and only D Dimer is expensive and available in few labs. **PT, INR, aPTT are done free of cost in Government Labs in Tamil Nadu.** Hence, the tests to detect the High Risk of Thrombosis are easily available, accessible, and affordable. It is the knowledge of the pathogenesis of Thrombosis that is crucial in the prevention and management of Stroke, Heart Attack, Deep Vein Thrombosis, and Pulmonary Embolism rather than fancy gadgets and expensive tests.

5. Treatment Options

The Hypercoagulable State can be caused due to various reasons. It is imperative that the exact mechanism is identified, and appropriate treatment is initiated with one or many of the following drugs, viz., Aspirin, Clopidogrel, Dipyridamole, Ticlopidine, Rivaroxaban, Dabigatran, Apixaban, Edoxaban, Heparin, Low Molecular Weight Heparin, Warfarin, etc. Of these Aspirin, Clopidogrel, Heparin, Low Molecular Weight Heparin, and Warfarin are available free of cost in all Government Hospitals in Tamil Nadu. They are also available in almost all medical shops and are not expensive. It is the knowledge of the pathogenesis of Thrombosis that is crucial in the prevention and management of Stroke, Heart Attack, Deep Vein Thrombosis, and Pulmonary Embolism rather than fancy gadgets and exotic drugs.

6. CONCLUSION

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