

An Evidence Based Case Study to Identify the Role of Bothrops Lanceolatus as a Homeopathic Anticoagulant

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ABSTRACT

In these tough times of COVID – 19 Homoeopathy has been proven as an adjuvant intervention with standard treatment prescribed according to the clinical presentation of the patient of mild to moderate categories and also as independent mode of treatment in mild cases. Here an evidence based case study is being presented of a post-covid patient which is clinically stable but haemodynamically, alterations are marked, which were brought back to normal conditions with the help of Holistic Homoeopathy.

KEYWORDS: Anticoagulant, Haemodynamics, Covid-19, D-Dimer, Homoeopathy, Ophidia Group

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INTRODUCTION

The second wave of the COVID-19 pandemic has major devastating effect with increasing number of cases, and hospitalizations.^[1,2] Effective management to address this infection is still evolving and attempts are being made to integrate complementary and alternative interventions along with standard care.^[3]

The COVID-19 infected cases are asymptomatic or symptomatic. The symptomatic cases are classified Mild, Moderate, Severe or critical according to the presentation.^[3] The common clinical features observed in mild COVID-19 cases include sore throat, fever, body-ache, nasal congestion, and dry cough without any shortness of breath. Some patients are also reporting diarrhea, loss of taste/smell etc.^[4]

WHAT IS D-DIMER?

D-dimer is a fibrin degradation product that is often used to measure and assess clot formation. Amid the COVID-19 pandemic, elevated D-dimer levels have

been associated with disease severity and mortality trends.^[5]

HOW D-DIMER IS SYNTHESIZED IN BODY?:-

- The liver produces several important proteins involved in the coagulation process, one of which includes fibrinogen. A single fibrinogen molecule is a symmetrical dimer that is made up of three pairs of three different polypeptide chains, which include a, b and g.^[5]
- Each of the intertwined polypeptide chains that comprise a single fibrinogen molecule is held together by disulfide bonds. The formation of fibrin begins with the cleaving of the a and b polypeptide chains of the fibrinogen molecule, which is achieved by thrombin. This cleaving event causes the fibrin monomers to spontaneously polymerize, which results in the formation of double-stranded fibrin protofibrils.^[6]

- To strengthen a normally weak network that exists between the fibrin monomers and the protofibrils, a transglutaminase enzyme known as factor XIIIa is activated.
- If an injury occurs, the fibrinolytic system will activate to limit the size of the clot. This system begins with the release of the plasminogen activator from the vascular endothelial cells to allow this molecule to bind to the fibrin surface of plasmin. Fibrin-bound plasmin will then degrade the fibrin network into several soluble fragments, of which will include the D-dimer of the (DD)E complex. [6]

INDICATIONS OF D-DIMER:-

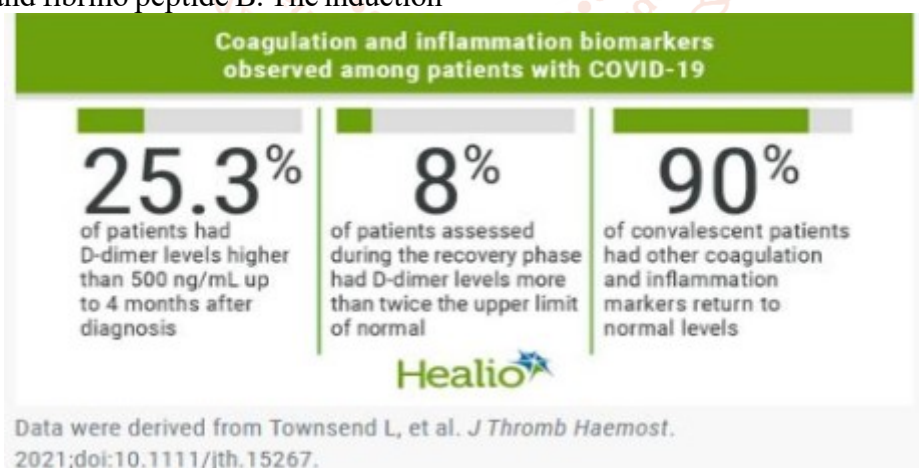
- The presence of D-dimer in the blood plasma, which has a half-life of roughly 8 hours until kidney clearance occurs, is often used as a clinical biomarker to identify thrombotic activity and therefore diagnose conditions like pulmonary embolism (PE), deep vein thrombosis (DVT), venous thromboembolism (VTE) and disseminated intravascular coagulation (DIC). [7]

IMPORTANCE OF D-DIMER IN COVID-19:-

- More than one-quarter of patients with COVID-19 had elevated D-dimer levels up to 4 months after diagnosis, according to study results published in *Journal of Thrombosis and Haemostasis*. Platelets after getting exposed to Covid infection triggers the release of Platelet microbial proteins, peptides, Platelet factor (PF)-4, RANTES, and fibrino peptide B. The induction

of a cytokine storm, suppression of antiviral immunity and the activation of proinflammatory response is the root cause of pathogenicity both in SARS and COVID-19.

- CoV-2 differs from SARS-CoV in interferon-antagonizing and inflammasome-activating properties. “Elucidating the biological mechanisms responsible for sustained D-dimer increases may be of relevance in long COVID-19 pathogenesis and has implications for clinical management of these patients,” Claimed in In research study **Liam Townsend**, PhD candidate in the department of infectious diseases at St. James’s Hospital in Dublin, and colleagues.
- “Persistent fatigue, breathlessness and reduced exercise tolerance have been reported after acute COVID-19 infection. Although immunothrombosis has been implicated in acute COVID-19 pathogenesis, the biological mechanisms underpinning long COVID-19 remain unknown.” Nearly one-third (29%) of patients with increased convalescent D-dimer levels received care exclusively in the outpatient setting. Other coagulation and inflammation markers returned to normal levels among more than 90% of convalescent patients.
- “Despite ongoing symptoms and elevated D-dimers, CT pulmonary angiogram screening in eight patients failed to demonstrate pulmonary embolism,” the researchers wrote. [8]



HOMOEOPATHIC MANAGEMENT OF D-DIMER IN COVID-19:-

- As the Important cause of Covid-19 deaths is Coagulopathies, focus is to be viewed on reducing complementary cascade activation & Proinflammatory markers in the body preventing multi organ damage. Homoeopathy the alternative system of medicine acts in the best way when prescribed according to the routine case taking, analysis evaluation and systematic Repertorization technique. But in acute severe Infectious diseases the method of systematic analysis and Repertorization may be overlooked due to the emergency care for the patient as the need of the hour. [9]
- In this view some of the Homeopathic remedies which are having action on Thrombosis phenomenon were searched out. There are many Homoeopathic Remedies acting on blood vessels or plasma causing or initiating coagulation cascade. As an Alternative system of Medicine to give relief to the covid -19 sufferers,

our Homoeopathic medicines can act as adjuvants where there are many failures in conventional system and still are under trials. Though many research trials are conducted showing Homoeopathic Medicines action at Nano-particulate level, and though not fully evidenced, these medicines can be used as adjuvant to Modern system of Medicine ^[9]

➤ Following homoeopathic remedies have potential to carry out thromboembolism and coagulopathies in the organism can be used to treat high D-Dimer values in the COVID-19 patients-

- Bothrops Lanceolatus
- Arnica Montana
- Lachesis
- Vipera
- Fluoric Acid
- Cardus Mur
- Aspidosperma Quebracho
- Arsenic alb
- Ammonium Carbonicum ^[10]

CASE PRESENTATION:-

PRESENTING COMPLAIN:-

A 61-years-old Male, approached with his reports and complaints of generalized weakness, muscular cramps and twitching in calf muscles and minor coughing remaining after getting recovered from COVID-19. Clinically the patient was found very much stable but his reports showed variation in his haemodynamic state.

In his reports the value of D-DIMER was highly raised even after getting recovered from COVID-19.

PAST HISTORY:-

Diseases suffered from	Age at	Duration	Medicines & treatment taken
Renal Stone	8 yrs ago	6-7 months	Allopathic treatment

FAMILY HISTORY:-

RELATION TO PATIENT	DISEASE SUFFERING FROM	ALIVE/ DEAD	CAUSE OF DEATH
Father	HTN	Dead	-----
Sister	Renal stone, DM	Dead	-----

PERSONAL HISTORY:-

- **ACCOMODATION:-** Good
- **ECONOMIC STATUS:-** Sound
- **DIET & FOOD HABITS:-** Addiction of alcohol
- **HOBBIES:-** Nothing Specific
- **LIFE SPACE INVESTIGATION:-**
 - **BIRTH & EARLY DEVELOPMENT:-**
All the milestones were achieved normally
 - **BEHAVIOUR DURING CHILDHOOD:-**
NAD
- **EDUCATION:-** Metric pass
- **OCCUPATIONAL HISTORY:-** Farmer
- **MARITAL HISTORY:-** Normal
- **CHILDREN:-** One (Male)

GENERAL SYMPTOMS

- **PHYSICAL GENERALS:-**
APPEARANCE:- Lean, thin person TASTE:- not specific

- THIRST:- Increased, feels unsatisfied even if drinks a large amount of water
- STOOL:- NAD
- URINE:- 3-4/0-1 : D/N
- SWEAT:- Profuse
- SLEEP:- sound
- THERMAL REACTIONS:- (HOT)
- CONSTITUTION: can't tolerate slight warmth)

- **THERAPEUTIC INTERVENTION:-**
As per the description given by patient and data obtained on questioning about his past history, family history and other examination, nothing specific was found except:-
 - Increased levels of D-DIMER
 - Generalized weakness after acute viral infection
 - Muscular cramps and twitching in calf muscles
 - HOT thermal state of patient
 - Remarkable thirst

➤ **PRESCRIPTION:-**

So, On the basis of discussion and referring to various homoeopathic material medica,

▪ **BOTHROPS LANCEOLATUS 200 SINGLE DOSE STAT ORALLY**

▪ **SAC-LAC 4X3X4 DAYS**

➤ **WHY BOTHROPS LANCEOLATUS?:-**

➤ **DR. BOERICKE SAYS:-**

• Its venom is most coagulating, (also *Lachesis*). We should expect to find under these remedies the symptomatology of thrombosis, also thrombotic phenomena, as hemiplegia, aphasia, inability to articulate (Linn J. Boyd).

- Nervous trembling.
- Pulmonary congestion.
- Broken-down, haemorrhagic constitutions; septic states.
- Great lassitude and sluggishness; Weakness [10]

➤ **DISTINGUISHING BETWEEN BOTHROPS & ARNICA:-**

• The Lance snake is of the family Crotolidae; found in the island of Martinique.

• Preparations.-The poison from this snake is triturated, and dilutions are made from the 6x trituration. Bothrops is marked under remedies for Aphasia and also stroke Rubrics. But how does it compete with arnica in coagulopathies is to be differentiated. [11]

• The differential with Arnica is an important one for several reasons, including the fact that because we know Arnica better, we give it more frequently. [11,12]

• When the etiology (Injury) is from the outside, the remedy is more likely to be Arnica. When the etiology is an internal process the remedy is more likely to be Bothrops. At times Bothrops is indicated even in injuries where thromboembolus arises after effects of injuries. [13]

• Though Bothrops is given under many repertories under bleeding conditions, but Bothrops is indicated especially in bleeding after intravascular clotting and thromboembolic phenomenon.

• According to a study conducted, Bothrops has got both coagulant (clotted human fibrinogen indicating presence of Thrombin like enzyme) and anticoagulant properties (Increase in Partial thromboplastin time).

• Clinical experience by Dr. Paul Herscu says that Bothrops initiates. Thrombi Formation leads to Fullness Restlessness, Inflammation which is followed by Bleeding, Weakness and Paralysis which brings back to the segment of thrombus Formation.

• The bleeding in Bothrops is always secondary to the coagulation, so even though there is bleeding mentioned in many locations, it rarely shows up in practice. The thrombi are much more to the point. [14]

▪ **FOLLOW UP:-**

01/05/2020 – 1st follow up:-

- Remarkable decrease in levels of D-DIMER (but still elevated)
- Improvement in weakness , ameliorated upto great extent
- Relief in muscular cramps and twitching
- Rx:- BOTHROPS LANCEOLATUS 200 SINGLE DOSE STAT ORALLY
- SAC-LAC 4 X 3 X 7 DAYS

▪ **FOLLOW UP:-**

04/05/2020 – 2nd follow up:-

- Levels of D-Dimer normalized
- Weakness absent
- Muscular cramps and twitching almost relieved
- Rx:- SAC-LAC 4 X 3 X 7 DAYS

BEFORE TREATMENT:-

TEST	RESULTS	UNIT	BIOLOGICAL REF RANGE	REMARKS
BIOCHEMICAL INVESTIGATIONS				
D-Dimer	H 452.88	ng FEU/mL	0-100	Labile parameter. Critical correlation or repeat with fresh sample

For important diseases, the following D-Dimer reference values ranges are provided:

- In the first trimester of pregnancy: 181-751 ng/mL;
- In the second trimester of pregnancy: 208-1803 ng/mL;
- In the third trimester of pregnancy: 403-2265 ng/mL;
- In those with diabetes and/or collagen: D-Dimer ranges: 181-833 ng/mL; C-reactive protein: 200-3471 ng/mL; (2nd trimester); and 484-4438 ng/mL; (3rd trimester).

Intended Use:

- It is used for quantitative immunological determination of fibrin degradation product in human plasma for exclusion of Venous Thromboembolism.
- In combination with non-high clinical probability assessment, a result value <800 ng FEU/mL indicates deep vein thrombosis (DVT) and pulmonary embolism (PE) with high sensitivity.

Clinical significance:

Thrombin converts Fibrinogen to soluble fibrin by cleaving the fibrinopeptides A and B. The fibrin monomers polymerize spontaneously. Activator (tPA) into two D-dimers and generates a soluble form (d-D) by degradation of a fibrin dimer by plasmin. Fragment containing D-Dimer are formed accordingly. D-Dimer is very sensitive marker for the activation of coagulation. When D-Dimer values below the cutoff are obtained, deep vein thrombosis and pulmonary embolism can be excluded with high sensitivity.

Note: D-Dimer values in heparin or EDTA plasma are on average 10% higher over the entire measuring range because lack of dilution effect.

----- End of Report -----

DURING TREATMENT:-

LABORATORY REPORT				
Name: [REDACTED]	Sex/Age: Male / 31 Years			
Ref. By: Dr. Self	Dis. At: [REDACTED]			
Ref. Loc: [REDACTED]	PL Loc: [REDACTED]			
Req. Date and Time: 01-May-2021 12:35	Sample Type: Plasma Citrate			
Sample Date and Time: 01-May-2021 12:45	Sample Coll. By: NBCL			
Report Date and Time: 01-May-2021 12:43	Acc. Remarks:			
TEST	RESULTS	UNIT	BIOLOGICAL REF. RANGE	REMARKS
D-Dimer (D-D)	H 542.00	ng FTV/mL	0 - 500	Labile parameter. Clinical correlation or repeat with fresh sample.

BIOCHEMICAL INVESTIGATIONS

D-Dimer (D-D)

For pregnant women, the following D-Dimer reference value ranges are proposed:
 in the first trimester of pregnancy, 0-1771 ng/mL;
 in the second trimester of pregnancy, 268-1052 ng/mL;
 and in the third trimester of pregnancy, 463-2259 ng/mL.
 In those with diabetes and/or chronic D-Dimer ranges: 151-608 ng/mL (first trimester), 202-3474 ng/mL (2nd trimester), and 434-4439 ng/mL (3rd trimester).
 [JPT - Senoo A, Kijie M, Chikazumi K, et al. Reference Values of D-Dimers and Fibrinogen in the Course of Physiological Pregnancy: The Potential Impact of Selected Risk Factors. A Pilot Study. *Diagn* 2020; 10(5):520. Published 2020 May 24; doi:10.1155/2020/5200520].

Intended use:
 Intended for quantitative immunoassay determination of fibrin degradation product in human plasma for exclusion of Venous Thromboembolism.
 In correlation with high clinical probability assessment, a result value <500 ng FTV/mL exclusive deep vein thrombosis (DVT) and pulmonary embolism (PE) with high sensitivity.
Clinical significance:
 Thrombotic covers (fibrinogen) to soluble fibrin by cleaving the fibrinopeptide A and B. The fibrin monomers polymerize spontaneously. Active factor XIII links two D-dimers and generates a stable fibrin clot. During degradation of a fibrin clot by plasmin, fragments containing D-Dimer are formed accordingly. D-Dimer is very sensitive marker for the activation of coagulation. When D-Dimer values below the cut-off are obtained, deep vein thrombosis and pulmonary embolism can be excluded with high sensitivity.
 Note: D-Dimer values in hospital or EDTA plasma are on average 10% higher over the entire necessary range because of dilution effect.

End of Report

hospital stay by 2 days. Similarly, in Acute Encephalitis Syndrome/Japanese Encephalitis homeopathy as an adjuvant to the Institutional Management protocol could decrease death rate by 15% in comparison to those who received only Institutional Management protocol. In both the studies, adverse effect was not observed. Keeping in view the clinical success in above mentioned severe viral diseases, Homeopathy as an adjuvant to the usual care may be tried in COVID-19 patients. Thus, homeopathy can play significant therapeutic roles.

Covid-19 presenting as Acute viral pneumonia causes thrombotic complications leading to Respiratory failure and ultimately multi system dysfunction. The COVID-19- associated coagulopathy (CAC) are distinct from those seen with bacterial Sepsis-Induced Coagulopathy (SIC) and disseminated intravascular coagulation (DIC). The CAC usually shows increased D-dimer and fibrinogen levels with minimal abnormalities in Prothrombin time and platelet count.

Coagulation is the main cause to prevent complications in covid19. In pulmonary complications Hypoxia leads to thrombus and in turn Thrombosis leads to hypoxia. The complication of coagulation leads to further damage further to multi organ failure. In coagulation resulting from Covid 19, D-Dimers are of diagnostic value which predicts the severity of Coagulation and assess the prognosis of diseases. Homeopathic remedies though act well when selected on individualisation basis, in some acute emergency setups, specific remedies need to be given as the need of the hour.

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AFTER TREATMENT:-

LABORATORY REPORT				
Name: [REDACTED]	Sex/Age: Male / 31 Years			
Ref. By: Dr. Self	Dis. At: [REDACTED]			
Ref. Loc: [REDACTED]	PL Loc: [REDACTED]			
Req. Date and Time: 04-May-2021 14:20	Sample Type: Plasma Citrate			
Sample Date and Time: 04-May-2021 14:28	Sample Coll. By: NBCL			
Report Date and Time: 04-May-2021 14:10	Acc. Remarks:			
TEST	RESULTS	UNIT	BIOLOGICAL REF. RANGE	REMARKS
D-Dimer (D-D)	H 350.00	ng FTV/mL	0 - 500	Labile parameter. Clinical correlation or repeat with fresh sample.

BIOCHEMICAL INVESTIGATIONS

D-Dimer (D-D)

For pregnant women, the following D-Dimer reference value ranges are proposed:
 in the first trimester of pregnancy, 0-1771 ng/mL;
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End of Report

DISCUSSION:-

In Indian scenario, CCRH had so far undertaken clinical trials in Dengue and Acute Encephalitis syndrome/JE with Homeopathy as an add-on to usual care in tertiary care setups. In Dengue Hemorrhagic fever, add on Homeopathy could bring early improvement in platelet count and decrease in

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