Systematic haemostasis and intermittent pneumatic compression. Clues for the investigation of DVT prophylaxis and travellers thrombosis


Overview

This study was performed in an attempt to identify haematological markers that could be used to provide insight into the pathogenesis of travellers thrombosis.

The important outcomes were:

- Intermittent pneumatic compression (IPC) (using FLOWTRON® Excel DVT Prophylaxis System) exerted a beneficial effect, suppressing procoagulant activation whilst enhancing the fibrinolytic mechanisms.
- Measurement of specific fibrinolytic components does not reflect overall fibrinolytic activity.
- Measurement techniques can strongly influence the findings.

Design and methodology

The study population was 21 normal healthy male volunteers who were investigated during the hours of 10.30 and 14.00. Time of day tested is important, as haemostasis substances have been shown to be influenced by diurnal variation.

The FLOWTRON System was used with calf compression garments. Peripheral blood samples were obtained from the subjects before and after 60 and 120 minutes of IPC using the FLOWTRON System. Blood samples were also obtained from the same subjects when they were resting for these time periods but not using IPC; these acted as controls in order to demonstrate that the changes had not been caused by resting.

The method of taking the blood sample was carefully controlled and performed, no tourniquet was used and cannulae were not left indwelling, as these factors had previously been shown to significantly alter coagulation markers.

Measurements recorded and results

1. For the control experiments without IPC, tissue plasminogen activator (tPA) was raised after 120 minutes. Although the change is described as ‘slight’, it was sufficient to be statistically different to baseline levels.

   **Explanation:** tPA is produced by the endothelium. It initiates fibrinolysis and the breakdown of the fibrin clot. Within healthy persons at rest, the body naturally prevents development of thrombi by production of tPA.

2. Use of IPC in the same individuals led to significant falls in factor VIIa.

   **Explanation:** In the extrinsic clotting pathway, injury leads to production of tissue factor by non-vascular cells when they come into contact with blood. Tissue factor has a high affinity for factor VIIa and they link together activating factor X, prothrombin and thrombin. Application of IPC reduced the amounts of factor VIIa, which in turn would then reduce further clotting factors and make blood less likely to clot.
3. There were increased levels of tissue factor pathway inhibitor (TFPI), factor XII, urokinase plasminogen activator (uPA) and tPA after IPC.

**Explanation:** TFPI is produced by the endothelium and inhibits production of factor VIIa and factor X. Active factor XII results in the production of kinins which ultimately assist in fibrinolytic breakdown. uPA and tPA are released by the endothelium and both initiate fibrinolysis. They convert plasminogen into plasmin which then degrades fibrin.

4. uPA levels using one particular method were increased; however measurement using a different laboratory technique indicated they were not raised.

**Explanation:** This highlights how important the test itself is at detecting changes in the levels of these biological markers within the blood.

5. Although tPA levels increased and also the levels of global fibrinolytic activity increased too, these 2 measurements could not be correlated.

**Explanation:** The authors discuss how fibrinolytic activity within the body is augmented by a number of interactions and that testing for specific components in isolation may not be appropriate. This finding also illustrates how some researchers have previously found no changes in haematological markers after IPC – it really depends on what is being looked for and the method in which it is being done. These researchers have identified that it is likely that there is another mechanism by which IPC depresses factor VIIa; there is considerable current interest in the role of a substance called Thrombin Activatable fibrinolysis Inhibitor (TAFI).

### Pro-coagulant suppression mechanisms:

Reduction in factor VII

### Fibrinolysis mechanisms:

Increased production of TFPI, factor XII, uPA and tPA

### Conclusion

- ‘IPC enhances fibrinolysis and suppresses pro-coagulant activation.’
- This study demonstrated that fibrinolysis is affected by several mechanisms.

‘Measurements of specific fibrinolytic components do not reflect overall fibrinolytic activity and are highly dependent on the method of assay’ (measurement).

The full picture of how IPC works is not yet fully understood.