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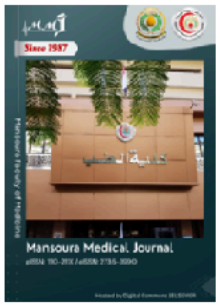

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# NAUTRAL COAGULATION INHIBITORS IN CORONARY HEART DISEASE (CHD)

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# NAUTRAL COAGULATION INHIBITORS IN CORONARY HEART DISEASE (CHD)

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## INTRODUCTION

Although it is accepted that changes in blood haemostasis can contribute to the pathogenesis of various thrombotic diseases, this concept is still a matter of controversy (Kernoff, 1989). It is thought that a hypercoagulable state may contribute to the pathogenesis of coronary artery diseases (Uno et al., 1989). Kernoff (1989), reported that test abnormalities detected in association with thrombosis may be a result rather than a causative factor. Although, coronary heart diseases (CHDs) are mostly due to atherosclerosis, they may occasionly result from one of variety of non-atherosclerotic factors leading to an occlusive insult to the coronary circulation (Harrison & Baim, 1990). Therefore, this study had been initiated to study the level of natural coagulation inhibitors (antithrombin III and protein C) which may give a clue to underline the pathogenesis and the prognosis in patients with CHDs.

## MATERIAL AND METHODS

We have screened the haemostatic system (BT, PT, PTT, TT and platelet count) and assayed AT III concentration and PC activity in 23 cases with CHD [17 males; M. age 58+10.5 years; 11 with ischemic heart disease (IHD) and 12 had acute myocardial infarction (AMI)]. Blood samples were collected prior to any therapy. Reference group consisted of 12 healthy gubjects (8 males; M. age 57.9±14.6 years).

All the necessary clinical, haematological and biochemical investigations needed for diagnosis and follow up of the cases had been carried out according to the standard methods.

AT III concentration had been assayed by single radial immunodiffusion technique; Hobb's modification of the Mancini technique (Cederholm-Williams et al., 1981). Protein-C (PC) activity had been determined by a coagulometric method modified from an assay of Kisiel (1979) and Francis & Patch (1983).

## RESULTS

The results of the studied haemostatic parameters obtained in this work has been tabulated in table (1).

## DISCUSSION

It is thought that a hypercoagulable state might contribute to the pathogenesis of coronary heart diseases (Uno et al., 1989). Therefore, a relevant understanding of the pathogeneses and prognosis of such cases may be achieved through the study of the level of the natural coagulation inhibitors particularly antithrombin III (AT III) and protein C (PC).

A highly significant reduction in AT III has been observed in IHD as well as in AMI groups compared to the control ($P<0.001$). The low AT III level in such cases might be a cause or a result. AT III deficiency has been reported to be a definite mechanism in many prethrombotic states (Kernoff, 1989). Alternatively, a thrombotic insult might induce a consumption of AT III as reported by Rao et al. ( 1984). Our data agree with those obtained by Ochler et al. (1988). On the contrary Knudsen et al. (1980) assayed AT III in patients with non complicated acute transmural myocardial infarction and they reported that AT III remained unchanged in their cases. Meade et al. (1991) concluded that both low and high levels of AT III may be associated with arterial disease particularly IHD.

On the contrary, a pronounced elevation of PC activity that was more marked in AMI patients (up to 8.6 folds of normal) than in IHD (up to 5.1

folds) as compared to the reference group. These surprising high levels of PC may be a body attempt to overcome the hypercoagulability state encountered in such cases and reported by Vigano et al. (1984). Although, PC had been described as a regulator of fibrinolysis by Zolton & Seegers (1973), these high values were insufficient to prevent the thrombotic insult (O'Connor et al., 1984). Moreover, Gensini et al. (1988) found high levels of PC and fibrinopeptide-A in patients with active as well as inactive angina. These results confirm a significant involvement of the coagulation system in IHD especially active angina. It had been shown that ischemic results induce a rapid activation of PC in the coronary microcirculation and blockage of this activation could impair recovery (Snow et al., 1991). Depending on these data, Berk (1991) suggested a potential therapeutic role that could be played by a recombinant activated PC (RAPC). Moreover, infusion of urokinase (a plasminogen activator) combined with RAPC resulted in a net additive effect of antithrombotic activities of each agent (Berk, 1991).

The haemostatic results in this study revealed a significant prolongation of PT and PTT in both IHD and AMI groups compared to the reference group ($P<0.001$). A finding that could be attributed to the marked increased activity of PC for several folds in both patient groups. This supraphysiologic level of PC is able to induce a potent inhibition of factors Va and VIIIa (Walker et al., 1979 and Ogston & Bennett, 1991). Moreover, consumption of both factors Xa and Va in the activation of PC will certainly contribute in the prolongation of CT, PT and PTT in such cases.

Apart from a significantly elevated ESR, the other studied haematological parameters were not statistically different in both groups of IHD and AMI as well when compared to the reference group. A high ESR in CHD might be a result of tissue breakdown following cornary artery thrombosis, this finding agrees with that of Miles & Zipes (1990). In addition, Oehler et al. (1988) reported that fibrinogen, one of the acute phase reactants, is increased significantly after AMI and

also in angina pectoris resulting in elevation of ESR, (Lowe et al., 1991).

Both the haematological as well as the haemostatic parameters showed no statistical difference on comparing the group of IHD with that of AMI.

## SUMMARY AND CONCLUSION

Haemostasis may be implicated in the pathogenesis of various thrombotic dieases. Assay of natural coagulation inhibitors (AT III and PC) in coronary heart diseases may be informative in such cases.

In this work, AT III and PC were assayed for 23 patients with coronary ischaemia and infarction besides 12 controls. A highly significant reduction in AT III had been observed in patient groups which had been attributed to an activated coagulation mechanism with consequent consumption of AT III. On the other hand, a significant increase in PC activity had been observed in both studied groups. This rise may be a body attempt to overcome hypercoagulability in those patients. We recommend a trial to use AT III and recombinant APC as therapeutic lines in patients with cornary heart diseases.

**Table (1) :**

| | BT min. | CT min. | PT sec | PTT sec. | TT sec. | AT III conc g/L | PC activity % of normal |
|---|---|---|---|---|---|---|---|
| Control (n : 12) | | | | | | | |
| M | 2.125 | 6.750 | 12.752 | 26.667 | 11.167 | 0.289 | 87.333 |
| SD | 0.711 | 2.261 | 1.138 | 2.270 | 0.835 | 0.047 | 12.463 |
| IHD (n :11) | | | | | | | |
| $M_1$ | 2.136 | 7.500 | 17.182 | 57.545 | 11.273 | 0.198 | 257.727 |
| $SD_1$ | 0.778 | 2.133 | 5.706 | 23.905 | 2.328 | 0.055 | 167.143 |
| AMI (n : 12) | | | | | | | |
| $M_2$ | 2.830 | 9.670 | 17.500 | 53.670 | 12.580 | 0.195 | 411.660 |
| $SD_2$ | 1.340 | 4.260 | 5.000 | 21.660 | 2.906 | 0.070 | 244.599 |
| $t_1$ | 0.035 | 0.818 | 2.530 | 4.266 | 0.143 | 4.247 | 3.372 |
| $P_1$ | >0.05 | >0.05 | <0.05 | <0.001 | >0.05 | <0.001 | <0.01 |
| $t_2$ | 1.610 | 2.097 | 3.210 | 4.290 | 1.620 | 3.860 | 4.587 |
| $P_2$ | >0.05 | >0.05 | <0.05 | <0.001 | >0.05 | <0.001 | <0.001 |
| $t_3$ | 1.534 | 1.560 | 0.142 | 0.406 | 1.195 | 0.115 | 1.775 |
| $P_3$ | >0.05 | >0.05 | >0.05 | >0.05 | >0.05 | >0.05 | >0.05 |

* $t_1, P_1$ : IHD (Ischemic heart disease) versus control.
* $t_2, P_2$ : AMI (Acute myocardial infarction) versus control.
* $t_3, P_3$ : IHD versus AMI.
* n : number of cases.
* BT : bleeding time.
* CT : clotting time.
* PT : prothrombin time.
* PTT : partial thromboplastin time.
* TT : thrombin time.
* AT III : antithrombin III.
* PC : protein C.

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# المثبطات الطبيعية لتجلط الدم فى مرضى الشريان التاجى

**ملخص البحث :**

من المعروف أن اختلال عملية وقف النزف وتخثره تلعب دوراً فى حدوث العديد من أمراض الجلطات الدموية وتعيين مضادات التجلط الطبيعية (مضاد الثرومبين - ٣، البروتين - سى) يمكن أن تكون ذات مدلول مفيد فى مرضى الشريان التاجى. وفى هذا البحث تم تعيين هذه العوامل فى ٢٣ مريضاً بالذبحة القلبية وقصور الشريان التاجى إلى جانب ١٢ فرداً من الطبيعيين كمجموعة ضابطة. وقد لوحظ انخفاض مضاد الثرومبين - ٣ فى هؤلاء المرضى وقد عزى ذلك إلى زيادة نشاط التجلط ومايستتبع ذلك استهلاك لهذا البروتين ومن ناحية أخرى لوحظ أيضاً زيادة فى نشاط البروتين سى فى مرضى قصور الشريان التاجى وقد فسرت هذه الزيادة على أنها محاولة من الجسم للتغلب على زيادة نشاط التجلط فى هؤلاء المرضى. وبناء على هذه النتائج وكامتداد لهذا البحث فمن المقترح محاولة تقيم استعمال مضاد الثرومبين ٣ والبروتين - سى المخلق كوسائل علاجية فى مرضى جلطة الشريان التاجى.