

A PRELIMINARY REPORT ON THE RELATIONSHIP BETWEEN SERUM ANTI-THROMBIN III CONCENTRATION IN PRE-AND POST-OPERATIVE PATIENTS AND IN WOMEN ON ORAL CONTRACEPTIVES

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SUMMARY

AT III values in patients undergoing surgery were found to be lower post-operatively but the fall in value was not significant while women on oral contraceptives were found to have similar AT III values as that of women not on oral contraceptives. The observed values are discussed.

INTRODUCTION

After major operations the blood is hypercoagulable in all patients irrespective of whether or not there is deep vein thrombosis. This hypercoagul-

ability is indicated by an increase in platelet number and adhesiveness, in fibrinogen concentration and a fall in fibrinolytic activity. Attention has been focused on the concentration of anti-thrombin III (AT III), the naturally occurring anticoagulant factor which neutralises thrombin and activated factor X (Abildgaard, 1969; Briggs *et al*, 1970). AT III level was reported to be lower post-operatively and that a low AT III level might play a role in post-operative venous thrombosis (Stathakis *et al*, 1973; Aberg *et al*, 1973). However, to date, no agreement has been achieved regarding the status of AT III concentration post-operatively and furthermore, there is no certainty whether alterations in these levels are related to the incidence of post-operative venous thrombosis.

Also a causal relationship between the use of oral contraceptives and thromboembolic disease, has been suspected since 1961 (Jordan, 1961). Since then, various authors have reported a positive correlation between oral contraceptives and blood clotting (Inman *et al*, 1970). Many trials published on the effect of oral contraceptives indicated some acceleration of the clotting of the procoagulants in the extrinsic and intrinsic clotting systems as well as a reduction of AT III levels. It has been found that AT III concentrations were lower in women on oral contraceptives than in control

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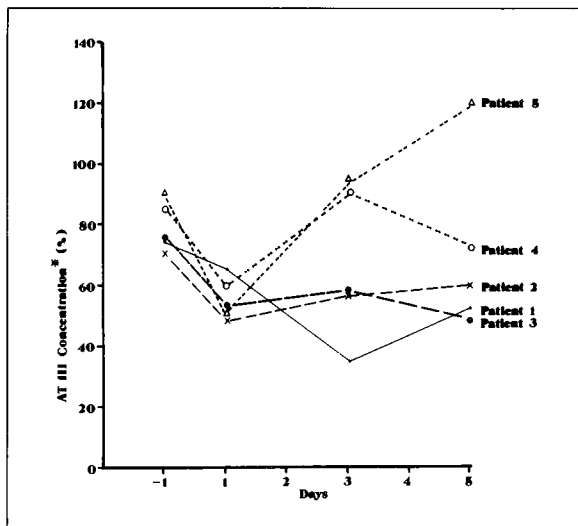


Fig. 1 Antithrombin III level before and after surgery.
* Values obtained by employing the chromogenic substrate technique.

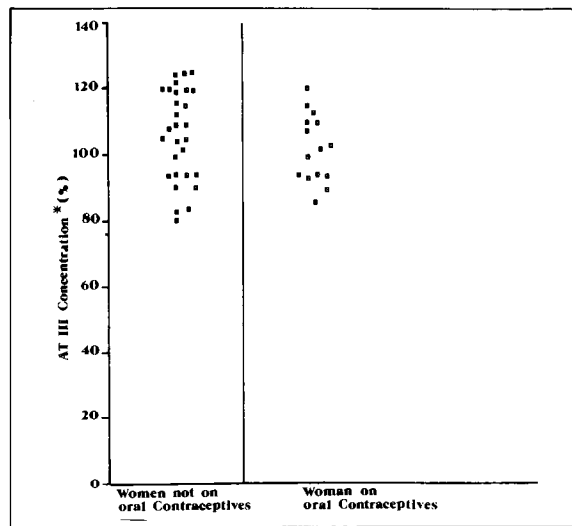


Fig. 2 Antithrombin III values of women not on oral contraceptives and women on oral contraceptives.
* AT III levels determined by the clotting method.

patients (Von Kaulla & Von Kaulla, 1970; Fagerhol & Abildgaard, 1970) and that plasma AT III activity was significantly lower pre operatively in patients on oral contraceptives (Sagar *et al*, 1976). However such studies have been done almost exclusively on Caucasian women. Thus can it be assumed that similar changes will be found in non-Caucasian women, where the thrombosis incidence is considerably lower? In an attempt to answer this question we present a preliminary report on the level of AT III in some Malaysian women who are on oral contraceptive pills and a preliminary report on AT III levels on pre-and post-operative patients.

MATERIALS AND METHODS

Platelet poor plasma from citrated whole blood from women taking oral contraceptive pills (age between 22 - 35 years and have been on the pills for at least a year) and from patients (age between 30 - 60 years) undergoing surgery were collected pre and post-operatively. The blood was processed and AT III determined as described (Ton & Lopez, 1981).

RESULTS

For the surgical patients the mean preoperative AT III concentration was $73.6 \pm 19\%$ and for the first post-operative day it was found to be $52 \pm 18\%$. This is not a significant difference ($p > 0.1$). AT III concentration of five of the patients was assayed the day before operation and on the first,

third and fifth post-operative days. The results are as shown in Fig. 1. As seen, AT III concentration of five patients showed a similar trend in the fall in AT III levels. A lower level was observed on the first post-operative day but the level rose after the third day for all the patients except patient 1 where the level continued to fall. It was found that the difference in the values of the AT III in the pre-and post-operative days were not significant as analysed by using Kendall coefficient of Concordance (Jedamus *et al*, 1976).

The mean of thirty females not on oral contraceptives was $106.4 \pm 13.6\%$ while that of 15 females on oral contraceptives was $102.3 \pm 10\%$ (Fig. 2). There was no significant difference between the two values ($p > 0.1$).

DISCUSSION

It has been reported that a significant decrease in AT III concentration between pre-and post-operative days was observed (Stathakis *et al*, 1973 ; Aberg *et al*, 1973). Stathakis *et al* (1973) noted that the fall was significant only on the first post-operative day while Aberg *et al* (1973) recorded that the difference was only significant from the second to the sixth post-operative day. However both groups reported that there was a progressive rise of AT III values from the third day onwards, after the initial fall in value. On the other hand, Donati *et al*, (1973) found no significant difference between the pre-operative and the first post-operative values of

AT III in 17 patients undergoing hysterectomy. Our results seem to agree with that of Donati *et al*, (1973) as we found no significant difference between the pre-and post-operative AT III values. Our results (Fig. 1) show the trend in decrease in AT III value post-operatively, as reported by Stathakis *et al* (1973) and Aberg *et al* (1973). The decrease however is not statistically significant. This post-operative fall in AT III is probably due to its increased consumption, brought about by hypercoagulability in the post-operative period.

As to the influence of oral contraceptives on thromboembolic disease, it has been reported that a positive correlation was found between the dose of oestrogen and the risk of pulmonary embolism, deep vein thrombosis, cerebral thrombosis and coronary thrombosis (Inman *et al*, 1970). Research had revealed that levels of AT III fell under oral contraceptive therapy from the tenth day soon after starting on the pill but the levels quickly returned to normal on cessation of therapy (Von Kaulla & Von Kaulla, 1970). In vitro experiments had shown that there is a direct action of oestrogenic derivatives upon AT III activity and that the decrease is directly proportional to the concentration of oestrogen (Nagasawa *et al*, 1975). As seen from our results, there was no significant difference between AT III level in women not on oral contraceptives and those on oral contraceptives. This could be attributed to the fact that the above women were on combined preparations of oestrogen and progestagen and that the oestrogen present in the preparation was either ethinyloestradiol or mestranol. These particular oestrogen derivatives have not been found to have effect on the coagulation mechanism (Inman *et al*, 1970). All of the above women except two were receiving 50 ug of oestrogen and this relatively low dosage might also contribute to the little change in AT III value observed (Conrad *et al*, 1972). Conrad *et al* (1972) had shown that women who received between 75 - 150ug of oestrogen had significantly lower AT III mean than normal ($p < 0.001$) whereas the level of AT III in women on the pill with low oestrogen content was not significantly different from that of women not on oral contraceptives.

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