ACTION OF NAPHTHALAN OIL FROM DIFFERENT WELLS ON THE STATE OF HEMOSTASIS

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UDC 615.326:553.982].015.4:612.115].07

KEY WORDS: naphthalan oil; hemostasis

The current importance of the problem of hemostasis in modern theoretical and clinical medicine is due to the high incidence of thromboembolic diseases, which has risen considerably in recent years in many countries of the world [13]. One of the most effective resources of Azerbaijan in the field of health resorts and balneology is its unique naphthalan oil (NO) [4]. An essential factor in the beneficial therapeutic action of NO is its hypocoagulative property, for naphthalan therapy is a highly effective method of treatment of many diseases accompanied by disturbances of the hemostasis system [4, 14].

Our previous investigations showed that NO from different wells, differing from one another in their physicochemical properties, act in different ways on hemostasis [5, 6].

The aim of this investigation was to elucidate the mechanism of action of NO from different wells on hemostasis.

EXPERIMENTAL METHOD

Experiments were carried out on 110 healthy noninbred albino rats weighing 150-180 g, of both sexes, of which 100 were divided into four experimental groups and the other 10 constituted the control group. Experimental group I comprised 29 rats treated with NO from well No. 39, group II of 33 rats using NO from well No. 54, group III of 30 rats using NO from well No. 88, and group IV of eight rats using NO from a general storage reservoir. NO was used at 37°C in the form of whole-body baths, the program consisting of 10 procedures with exposure of 10 min [7]. Changes in the following parameters of hemostasis were studied before and after the procedures: blood clotting time, activated recalcification time (ART) [8], antithrombin III (AT III), the protamine sulfate test, fibrinogen B and the ethanol test [1], the blood clot retraction index [15], ADP-induced platelet aggregation with calculation of the IPA index, and the velocity of platelet aggregation (VA) [9].

EXPERIMENTAL RESULTS

The results of all four groups of experiments to study the parameters of hemostasis are given in Fig. 1.

In the experiments of group I, using NO from well No. 39, the clotting time, which reflects the rate of formation of prothrombinase, was lengthened to twice the control value, and ART was increased by 36%, indicating reduced coagulability of the blood, for activity of factors XII, XI, X, and VIII was reduced [10, 11]. Antithrombin III was activated, as shown by lengthening of its time by 62%.

Naphthalan Therapy Research Center, Azerbaijan Research Institute of Medical Rehabilitation and Remedial Physiotherapy, Baku. (Presented by Academician of the Russian Academy of Medical Sciences G. N. Kryzhanovskii.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 114, No. 9, pp. 294-296, September, 1992. Original article submitted January 9, 1992.

0007-4888/92/0009-1325$12.50

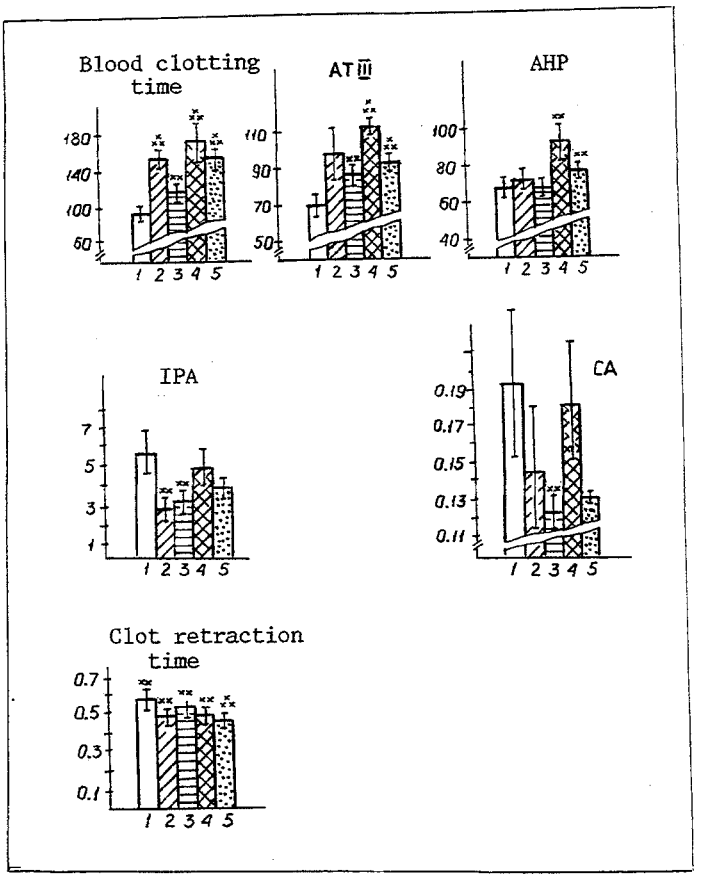

Fig. 1. Changes in some parameters of hemostasis under the influence of NO from different wells. 1) Control, 2) group III, e) group II, 4) group I, 5) group IV.

In the experiments of group II, in which NO from well No. 54 was used, the blood clotting time was lengthened compared with the control by 21%, but the increase was much less than in the experiments of group I, ART was almost unchanged compared with the control and AT III was increased by 24%. In the experiments of group III, in which NO from well No. 88 was used, the blood clotting time was lengthened by 70%, ART showed a very small increase, and activity of AT III was increased by 42%. When NO from the combined storage reservoir was used (experiments of series IV) the blood clotting time of the rats was lengthened by 69%, ART showed a small but not significant increase, and activity of AT III was increased by 33%.

In the experiments of group I a very small decrease was observed in IPA and VA, but clot retraction was reduced by 14%. In group II, IPA was reduced by 52%, VA by 36%, and clot retraction by 12%; in the experiments of group III IPA was reduced by 56%, VA by 26%, and clot retraction by 17%, whereas in the experiments of group IV, the changes were the same as in the previous groups: IPA fell by 30%, VA by 31%, and clot retraction by 25%.

A central place in the onset of thrombinemia and intravascular blood clotting is occupied by the appearance of soluble high-molecular-weight fibrin monomers or oligomers in the blood plasma and serum [2, 14]. In the presence of marked procoagulant activity, deposition of fibrin or degradation products of fibrin (fibrinogen) takes place on to the vascular endothelium [2, 10]. The level of fibrinogen degradation products is considered to be a basic characteristic of the state of the fibrinolysis system [2, 3]. The protamine sulfate test is used for semiqualitative determination of fibrinogen degradation products in the blood. Procoagulant tests such as the ethanol test and fibrinogen B, also are used to determine early products of fibrinolysis [3]. The results of procoagulant tests in our experiments were mainly negative.

High-molecular-weight heparin with low affinity for AT III inhibits platelet aggregation by a greater degree than the low-molecular-weight fractions, which have higher affinity for AT III [17]. These observations were confirmed by a study of healthy volunteers, in whom the bleeding time was lengthened under the influence of high doses

of heparin. On the other hand, low-molecular-weight fractions of heparin and "heparinoids," tested on animals with experimental thromboses, have antithrombotic activity equal to the activity of standard heparin, but they give rise to hemorrhages by a much lesser degree. It has been postulated that the higher relative antithrombotic effect and the bleeding tendency observed with low-molecular-weight heparins are connected with higher activity of antifactor XA. The study of the inhibitory effect of low-molecular-weight heparins relative to platelets has shown that these heparins inhibit collagen-induced platelet aggregation in vivo and in vitro by a lesser degree than standard heparin, from which the low-molecular-weight fractions were isolated [17]. Hence the antithrombotic effect of heparin is mainly due to its ability to increase AT III-dependent inactivation of the clotting factors, whereas its "hemorrhagic" effect is connected with two additional mechanisms, namely: 1) AT III-independent inhibition by heparin of thrombin generation on the surface of the platelets; 2) the ability of heparin to inhibit platelet aggregation. The AT III-dependent anticoagulative effect of heparin is more marked than the "hemorrhagic" effect, which is connected with a reversible functional defect of the platelets.

The results of the present investigation showed that NO from well No. 39 acts as a low-molecular-weight heparin, increasing AT III activity and inhibiting activity of the plasma blood clotting factors (factors XII, XI, X, and VIII, i.e., lengthening ART). The increase in AT III activity and lengthening of ART were more marked in the experiments of group I than in the rest, but inhibition of platelet aggregation in this case was less than in the other groups of experiments. It can be tentatively suggested that NO from wells Nos. 54 and 88 acts like a high-molecular-weight heparin, for in this case the antiaggregation effect of this balneotherapeutic agent is stronger.

In experiments on rats with intravenous injection of thrombin into animals previously receiving an injection of ^{125}I-heparin (low-molecular-weight heparin) and ^{35}I-heparin (high-molecular-weight heparin) gave results indicating changes in radioactivity of the blood in the second case only [16]. This fact indicates that high-molecular-weight heparin enters the blood stream and is stored in the mast cells, whereas low-molecular-weight heparin is not stored.

It can be postulated that NO from wells Nos. 54 and 88 stimulates the functions of mast cells, leading to release of endogenous heparin, which acts in the same way as high-molecular-weight heparin.

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