

CORRESPONDENCE

Thrombogenic Properties of Prothrombin Complex Concentrates

To the Editor:

In a recent paper White et al.¹ reported that the thrombogenic properties of prothrombin complex concentrates (PCC) are due to the presence of factors IXa and Xa. The presence of these activated factors, however, was detected indirectly by applying different inhibitors, e.g., a specific seryl reagent, phenylmethylsulfonyl fluoride (PMSF). They concluded that the effect of PMSF is due to the inactivation of factor Xa and not to that of factor IXa.

Factor IXa is a serine-protease.² It should therefore be susceptible to the seryl reagent PMSF. We have found with purified human

factor IXa³ that two seryl reagents, i.e., PMSF and diisopropyl fluorophosphate inhibit factor IXa. We may conclude, therefore that the inhibition obtained with PMSF by White et al.¹ is characteristic both for factors IXa and Xa.

The importance of factor IX activation in PCC preparations should be emphasized, since according to our experience it prevails when PCC is incubated at room temperature. We have investigated different batches of PCC, prepared in our institute, containing 10 U/ml of heparin. In spite of the presence of heparin, a significant activation of factor IX occurred in these preparations during 20-40 min of incubation at room temperature (Table 1).

The extent of factor IX activation depended on the initial factor IXa content of the preparation. Considerable activation was not detected when the initial factor IXa activity of PCC was 0.5 U/ml or less. It is interesting to note that the activation of factor X did not correlate with that of factor IX. The appearance of 5-10 U/ml of factor IXa activity during a 20-min incubation period, however, may bring about thrombogenic hazards. This risk should be considered if PCC is transfused with some delay after dissolution, even if it is a heparin-containing preparation.

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Table 1. Activation of Clotting Factors (U/ml) in PCC at Room Temperature

PCC No.	Factor Assay*	Incubation Time (min)			
		0	20	40	60
7711	IXa	1.9	6.0	10.0	10.0
	Xa	0.5	0.6	1.1	1.0
7712	IXa	5.4	10.0	13.2	13.2
	Xa	0.8	0.9	1.0	1.0
7724	IXa	2.2	4.8	4.8	5.4
	Xa	0.7	1.0	1.0	1.0

*Specific one-stage assay in a nonactivated system. One unit of activated clotting factor was arbitrarily defined as the amount of clotting factor which can be activated in 1 ml pooled normal plasma.

REFERENCES

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