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CASE REPORT

Thrombelastography during an acute normovolemic hemodilution in patient undergoing radical retropubic prostatectomy

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Abstract: The aim of our study was to monitor a patient undergoing radical prostatectomy (RP) with an extraordinary large blood loss of 3600 ml. The perioperative bleeding was minimalized through an acute normovolemic hemodilution (ANH). During the procedure we monitored the patient's hemocoagulation profile. ANH is one of the possibilities for practical and pragmatic hemotherapy. It is a safe and effective method when facing massive blood loss or when it is necessary to temporarily replace or substitute the blood with a fluid during the operation (through a transfusion of allogeneic blood); and the patient benefits from the procedure. We argue that during ANH, the hypercoagulatory state appears in the patient – and even during the introduction of a combined solution of both crystalloids and colloids. In fact, during ANH it should not be recommended to provide a substitute for the patient's blood using only a single crystalloid solution alone *(Tab. 2, Ref. 16)*. Full Text in free PDF *www.bmj.sk.*
Key words: radical prostatectomy, acute normovolaemic hemodilution, hypercoagulatory state and thrombelastography.

ANH includes a controlled transfer and storage of full-featured blood from the body of the patient immediately before surgery. The patient's intravascular volume is maintained in normovolemia through substituting solutions of crystalloids and colloids. The autologous blood thus gained is then returned to the patient either during the surgical operation, when there is a significant blood loss, or towards the end of the operation to get the bleeding under control (1).

1) We differentiate three levels of ANH according to the quantity of blood taken for achieving a defined hemocrite (Hct) goal (moderate, middle, or deep). In our case, we applied a moderate ANH with the Hct goal of 0.32. In our clinic, the ANH method has become a standard process for minimalizing blood loss and significantly limiting the application of allogeneic blood in patients undergoing RP (2).

2) When compared to ANH, other methods of pragmatic hemotherapy (such as the application of erythropoietin) are far too expensive, the perioperative recuperation of blood through the aid of cell saver is even contraindicative in RP, and the time delays demanded in a preoperational blood donation is not suitable. Another advantage of the ANH method is its outstanding economic aspect (3).

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3) The effects of ANH on blood coagulation and the processes in the human organism remains an unclear question. We would expect that during ANH a hypocoagulation state would dominate, yet certain studies have shown the opposite - a predisposition to hypercoagulation, especially during the supplement of crystalloid solution (4, 5, 6).

Our case report not only points out the unique benefits of this method for patients when eliminating the administration of allogeneic, but it also attempts to describe the changes in the coagulatory parameters and characteristics during ANH.

Case Report

We describe the case of a 50-year-old patient with prostate cancer, who underwent RP at the Urological Dept., University Hospital, Masaryk University School of Medicine, Brno, Czech Republic. Before surgery, we gave him an oral midazolam, and 12 hours before the start of the surgical procedure we gave the patient fragmin 5000, generic, subcutaneously for the prevention of thromboembolism. We launched the anesthesia with propofol at the dose of 2 mg/kg, sufentanil 2 μg, midazolam 3 mg, cisatracurium 0.15 mg/kg. After intubation, we continued with the general anesthesia and applied sufentanil, midazolam, cisatracurium, and a supplemental inhalation component: sevofluran and a stifling oxide. The entire period of the surgical operation amounted to 4 hours and 30 minutes. During the operation, blood loss reached 3600 ml.

After the introduction of the general anesthesia, we secured the monitoring of the invasive blood pressure (IBP), measuring kinaemia through the minimally invasive method (Vigileo, Edwards Lifesciences) and a 3-way central catheter for the quick

Tab. 1. Measurements of blood values and hemocoagulation.

	Htc	Hb	Ery	Leu	Tr	INR/s	aPTT R/s tests	Tromb	Fibrinogen	ATIII	DD
before ANH	0.4	143	5.06	3.83	285	1.08/14.3	1.11/36.5	17.5	2.9	87	0.21
after ANH	0.32	111	3.61	6.78	355	1.23/15.8	1.11/36.5	16.1	2.2	63	0.14
End of operation	0.26	95.7	3.27	12.8	214	1.38/17.3	1.02/33.3	17.4	1.02	55	0.37

ANH – acute normovolaemic haemodilution, Htc – haematocrit, Hb – haemoglobin, Ery – erythrocytes, Leu – leucocytes, Tr – thrombocytes, INR – international normalization ratio, aPTT – activated parcial thromboplastine time

Tab. 2. Measurements of the values of the thrombelastography.

	R (min)	K (min)	Angle	MA (mm)	CI	LY30 (%)	LY60 (%)
before ANH	6.7	1.5	64.9	65.3	1.8	0.9	5.6
after ANH	4.8	1.3	70.1	72.2	2.8	0.0	0.6
End of operation	4.8	1.4	69.0	68.8	0.6	1.4	5.4

R – time to initial fibrin formation, K, Angle – clot strengthening, rapidity of fibrin-buildup, MA – clot strength, represents maximum dynamics of fibrin and platelet bonding, CI – linear coagulation index using above parameters, LY30, LY60 – rate of clot breakdown

administration of solutions and measuring central venous pressure. After this, a removal of blood for ANH followed. We calculated the quantity of blood taken from the value of the Hct rate before surgery and from total body blood volume (TBBV), through the aid of a modified Bourke-Smith formula. We removed the blood for hemodilution out of the arteria radialis and put it in standard transfusion bags with a capacity of CPDA-1. The entire quantity of the blood amounted to 1900 m. The duration of this process did not extend into the beginning of the operation and the commencement of surgical blood loss. ANH was employed to attain normovolemia and half of the first 50 % of the blood removed with crystalloids in the relation of 2:1 and the second half colloids in the relation of 1:1. Other changes in the blood picture occurred as a subsequence of surgical bleeding. After reaching the transfusion trigger (Hct – 0.25), corresponding to the blood loss of another 1000 ml, we returned the blood into the patient from the ANH in the order, which was reverse to that it was collected. With a total surgical blood loss of 3600 ml during the operation, a Hct rate of 0.26 and hemoglobin of 95.7 g/l were ascertained. During the operation we did not administer any other blood derivatives. We maintained normovolemia through administering other solutions of crystalloids and colloids. We analyzed the coagulatory profile and blood picture both before and after the blood removal for ANH, as well as at the end of the operation (INR, aPTT, Thrombin timing, DD, AT III, and Fibrinogen). At the same moment, we carried out a TEG analysis of the blood samples, using a TEGŇ Coagulation Analyzer series 5000 (Haemoscope Corp., Niles, IL, USA). We activated the sample from the patient with kaolin, and with the aid of pipettes we inserted 0.36 ml of the sample into a cuvette in the TEG analyzer. So as to minimize any influence on the sample, the thrombelastograph went on directly in the urological ward with a constant timing of the extraction of 10 ml of blood and placing the sample into the analyzer. After previously removing 10 ml of blood for eliminating contamination of the sample by means of a rinse from the system of the invasive measuring of the blood pressure (IBP), we extracted the blood from the arteria radialis. We used cuvettes treated with heparin in the course of the thrombelastograph against any residual activity of Fragmin.

Towards the end of the surgery we gave the patient 1 amp of $CaC1_2$ for interrupting the effects of the CPDA-1 from the transfusion bags. As to preventing hypothermia, and with an effect on hemocoagulation, the patient laid on heated pad during the operation, and when the fluids were quickly replaced during ANH, we used a warm infusion (warm infusion of solutions HOTLINE). Even the actual low-flow anesthesia contributed towards minimalizing the loss of heat. After finishing the surgical operation, we brought the patient out of the general anesthesia. Then, being circulatory and ventilatory stable, the patient was moved for further care to the Intensive Care Unit of the Urological Department.

Discussion

Hemocoagulation in the human organism is a very complicated and complex process. Recognition and understanding of the coagulatory cascade is something, which is in constant development and change (7). Traditional laboratory investigations of coagulation have followed only defined and specific parameters of hemocoagulation, which by themselves only speak of the state of the coagulatory cascade. It describes the behavior of the coagulatory factors circulating in the plasma, but it does not address the function of thrombocytes, phospholipids, and the white blood cells found in whole blood. For instance, 50 % of factor XII is stored in blood plates and we find tissue factor in monocytes and macrophages (8). With our patient, his laboratory coagulation profile after ANH points to an extension of the rates of the thromboplastin test, while the rate of the APTT re-

mained constant (Tab. 1). The parameter INR only tells a story about the blood dilution we carried out using crystalloids and colloids. A reduction in the quantity of pro-coagulatory factors came about and, as a result, an extension of the coagulatory parameters. At the same time, we recorded a drop in anti-coagulatory factors, which had an effect in the overall assessment of the hemocoagulation. In our samples, there was a drop of AT III from 87 % to a rate of 63 %.

Techniques have been developed for point-of-care coagulation tests (9), among which the thrombelastography (TEG) belongs. TEG was the brainchild of the German hematologist Hartert in 1948 and, since then, it has found wide acceptance and application. This is a procedure which deals with the viscoelasticity properties of the coagulum from the origin of the first fribrinous tissue across to the acceleration of formation of the coagulum, its hardening and eventual subsequent lysis and dynamics. During measurement, whole blood is used, and so it is therefore possible to carefully monitor the hemocoagulation in vitro. As a result of the TEG measurement, there is a thrombelastographic curve. With the patient after ANH, an apparent diminishing of the values R, K and a increase of the angle a was noted, along with an extension of MA. The coagulation index shows an incline towards hypercoagulation. From the parameters LY (%), it is ensured that there is a minimal degradation of the coagulum, therefore fibrinolysis is minimal, and we can confirm the hypercoagulatory state after ANH. This is in accord with other studies, which confirm the hypercoagulation, namely when maintaining normovolemia through a solution of crystalloids (study). In our patient, we substituted the blood taken for ANH into normovolemia, using not only a solution of crystalloids but also colloids. The blood loss was substituted by crystalloids in the relation of 2:1 and colloids in the relation. Even in this case, we recorded a hypercoagulation, even when the colloids lower the adhesiveness and aggregation of the thrombocytes - coating effect (10, 11). It's likely that using a combination of colloids and crystalloids is advantageous, but the question remains, what is the most advantageous relation of crystalloids and colloids. Maintaining normovolemia only by infusion of crystalloid solutions isn't appropriate. An increase in the pool of thrombocytes after ANH can have a hand in the process of coagulation, but this, however, does not correspond exactly to the notion of the blood picture after ANH. With the measurement of SVV and CVP, we assist in excluding hypovolemia, but an increase in the quantity of thrombocytes can be caused by other factors as well (12). During the surgery, after reaching the transfusion trigger, all the blood taken from the patient in ANH was returned in the reverse order it was removed. The measurement of TEG at the end of the surgical operation showed, in comparison with the examination prior to ANH, a persistent extension of R, K, the angle a, and furthermore an augmentation of fibrinolysis with a resulting lower coagulation index CI (Tab. 2). The values correspond to the overall slight lowering of coagulatory activity following a large blood loss.

Besides substitute solutions, the patient's entire blood loss (total amount equal to 3600 ml) was replaced with only the blood gained from ANH. It wasn't necessary to administer allogeneic blood. After the surgery, we ascertained a resulting Hct value of 0.26. The effect of a lower Hct value on the circulatory system is, nevertheless, with ANH rather positive. Although the actual hemodilution leads to a reduction of the transport capacity of oxygen in the arterial blood, at same time it has an outcome of reducing the viscosity of the blood, and by that, improves the rheological attributes of the blood. As a consequence, this has an enhanced or return of venous blood towards the heart and a heightened expenditure per minute. In the tissue, it not only does an improvement in blood flow occur, but there is even a compensational heightened extraction of oxygen. This theory is supported by a study observing the effect of ANH on cardiac activity during heart surgery, where ANH leads to a cardio-protective effect (13, 14). A study dealing with complications of haemodilution shows that we can consider a value higher than 0.22 as a safety limit in patients with compromised hearts and the extracorporeal circulation (MO) threatens a rise in post-operational complications: CMP, IM, kidney failure, long-term ventilation post operation, swelling of the lungs, another operation due to bleeding, sepsis, or multi-organ failure (15). In patients with a fall in Hct under 0.20, hemodilution in the presence of MO is connected with a significant rise in post-operational mortality (16). In our case, weaning ran smoothly after the surgery, without complications in the urological ward and in the post-operational care, where neither circulatory, ventilating nor hemocoagulatory occurred.

Conclusion

ANH is a safe method, and it is one of the possibilities for efficient and practical hemotherapy, where the fundamental goal is to limit the administration of blood taken from blood donors. Using an allogeneic blood is associated with a plethora of complications and risks, jeopardizing the patient. At the same time, ANH is a technique, which is inexpensive and simple, without the need to employ time-consuming and difficult equipment. Also, it has a great potential in operations involving large blood loss. Using the TEG method in our patient, we proved the existence of hypercoagulation post ANH – and even after the substitution of normovolemia with solutions of crystalloids and colloids. However, this fact did not affect the post-operational state of the patient nor the length of hospitalization.

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