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Cardiopulmonary bypass. The effect on blood elements in dogs

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SUMMARY

Extracorporeal circulation (ECC) causes damage to the blood. All systems employed, such as chronic dialysis with an artificial kidney, cardiopulmonary bypass (CPB) with the heart-lung machine or long term respiratory support with the membrane oxygenator, show, apart from their life supporting functions, side effects like hemorrhages, anemia, increased susceptibility to infection, or denaturation of blood proteins. Especially in open heart surgery hematological problems have frequently been reported. The major problem is damage to the thrombocytes which can provoke hemorrhages, even more so since heparin is required to prevent clotting in the extracorporeal circuit. Destruction of erythrocytes, resulting in anemia and elevated plasma hemoglobin levels, is also regularly observed. Recently the attention is also focussed on impairment of the leukocytes and plasma proteins, which may result in an increased incidence of infection. Activation of complement factor C5a induces leukocyte aggregation, which, in turn, plugs the capillairies in the lung to cause organ dysfunction.

In this thesis the components of the heart-lung machine for CPB operations have been tested for their effects on blood elements. The purpose of the experimental investigation in dogs is:

1. To determine the hematological alterations induced by the various components from which an extracorporeal circuit for CPB is composed (circuit materials, blood pumps, oxygenators and cardiotomy suction devices) in concentrations and functions of blood cells and in fibrin formation.
2. To compose an optimal extracorporeal circuit for cardiac surgery by putting together the least traumatic components and to prove its hematological superiority.

The outline of this thesis is as follows:
Chapter 1 gives the introduction to the subject.
Chapter 2 provides an extensive description of the materials and methods used in this investigation.
Chapter 3 describes the hematological alterations caused by a simple extracorporeal circuit consisting of only tubing and pumps to demonstrate the general behaviour of blood components when exposed to an ECC. In this chapter three different tubing materials will also be compared.
Chapter 4 describes the hematological alterations caused by three different blood pumps. The results of

chapters 3 and 4 together indicate an optimal circuit.

Chapter 5 describes the hematological alterations caused by different oxygenators (one bubble oxygenator and two membrane oxygenators) in standard circuits and in the optimal circuit. The results of chapters 3, 4 and 5 together indicate a hematologically optimal heart-lung machine.

Chapter 6 describes the hematological alterations caused by two different methods of cardiotomy suction: suction of blood with and without air from the thoracic cavity. The results of chapters 3, 4, 5 and 6 together indicate the optimal equipment for cardiac surgical procedures.

Chapter 2:

Experimental setup: mongrel dogs of about 30 kgs were cannulated and connected to a standardized extracorporeal circuit consisting of tubing, blood-pump and heat exchanger. The blood flow rate was maintained at 3 l/min for an ECC period of 2 hours and total heparinization was employed. The circuit was primed with equivalent quantities of heparinized donor blood and gelatin solution. Blood samples were taken from a catheter in the femoral artery to assess to following parameters: numbers of thrombocytes, leukocytes and erythrocytes; ADP induced aggregation of the thrombocytes; bleeding time; hematocrit and plasma hemoglobin. During the experiments with a relatively simple circuit (chapter 3) also hemoglobin, SRE, rectal body temperature, and fibrin formation (APTT, PT, RT, TT) were measured. Blood samples were taken at frequent intervals during the day of the experiment and daily in the recovery period during the first week, on day 14, and on day 21. The series consisted of six experiments. In order to minimize the thrombocyte manipulation, necessary to express platelet function in relation to its number, a nomogram was created. This thrombocyte number versus function nomogram made it possible to compare aggregation curves from samples with different thrombocyte concentrations.

Chapters 3 and 4:

To demonstrate the general behaviour of the blood elements when exposed to an ECC a description is given of the changes caused by a relatively simple extracorporeal circuit consisting of PVC tubing and a roller pump. Thrombocyte numbers show an immediate and sharp drop after starting ECC, probably due to acute intravascular aggregation induced by released bioamines. This reversible process instituted stable levels after 30 minutes for the remaining period of ECC. After disconnection and consequent interruption

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of the equilibrium between aggregation and disaggregation, elimination of affected thrombocytes occurs and a secondary dip in numbers can be noticed, usually on day one after the experiment. Then a normal pattern of recovery is observed, which takes place in about one week.

Thrombocyte function, as expressed by the maximal optical density loss (ODmax) and corrected according to the nomogram, shows patterns of impairment comparable to those of the number of thrombocytes.

The clinically relevant parameter of the bleeding time, which is influenced by thrombocyte number and function and, to a less extent, by fibrin formation, shows slightly prolonged values at the end of the day of the experiment, but one day later normal values are found. In this regard the role of fibrin formation is only additional.

During the experiment the number of circulating erythrocytes after correction for differences in hematocrit does not change. Yet, erythrocytes are sublethally damaged by the procedure of ECC as can be concluded from the substantial elimination after ECC. This decrease in number causes anemia lasting for a period of over one week. The increased level of plasma hemoglobin shows that a few erythrocytes are already hemolyzed during the ECC period because of repetitive contact with high shear stresses. After disconnection the level of plasma hemoglobin is not reliable as a quantitative measure because of the complex elimination processes. Hematocrit and hemoglobin level provide the same information as the number of erythrocytes but are also influenced by the procedures of hemodilution (priming solutions, infusions etc.).

Leukocytes respond to the ECC with an initial dip, rapidly followed by a leukocytosis to about three times the baseline value. This increase within one day, which also compensates for leukocyte destruction during ECC, is explained by release of leukocytes from the marginated pool into the circulation. When this reservoir is depleted, a decrease in numbers occurs before a second increase is induced caused by formation of new cells in the bone marrow. Preoperative values are found after two to three weeks. Most probably neutrophilic leukocyte function tests are more indicative for the damage to the leukocytes than numbers alone.

This basic extracorporeal circuit consisting of tubing and blood pump does not provide spectacular damage. Still, the circuit does contribute to the overall damage caused by the heart-lung machine. Therefore it is of importance to incorporate the least traumatic tubing and blood pump available. Comparison of several tubing systems under standardized

conditions has revealed that silica free silicone rubber (SFSR) material is to be preferred to silica filled silicone rubber (SR) or PVC tubing. The slowly moving rotor blood pump also shows less traumatic results than the conventional roller pump or the centrifugal pump. The optimal circuit therefore consists of the rotor pump with silica free silicone rubber tubing.

Chapter 5:

The incorporation of an oxygenator yields more important differences than those measured between circuits. The use of conventional bubble oxygenators (BO) results in extensive destruction: low number of thrombocytes, disappearance of function and disturbed fibrin formation provoke a severely increased bleeding time, only normalizing after one week. A high level of plasma hemoglobin and severe anemia after the experiment show the damaging effect on the red cells. Leukocytes are also strongly affected. The anemia and the leukocyte disturbance last three weeks. The interconnection of a membrane oxygenator (MO) instead of the BO results in important improvements: the thrombocytes are significantly less injured and the resulting bleeding time is only slightly prolonged for a period of one day. The level of plasma hemoglobin is minimally increased and the anemia after the experiment is much less pronounced. Important differences are not observed between MO and BO with regard to the number of leukocytes.

As the MO is available in various materials and designs, a comparative study was performed between the microporous Teflo Modulung MO (TMO) and the silica free silicone rubber Kolobow MO. The thrombocyte number was better maintained with the TMO, but thrombocyte function, erythrocyte damage and leukocyte behaviour did not show differences. We have demonstrated that the combination of a TMO with silica free silicone rubber tubing and a rotor blood pump provides optimal hemocompatibility.

Chapter 6:

The hematologically crucial element in the circuit for CPB is the cardiotomy suction. The conventional suction system, in which blood is aspirated together with large amounts of air, act as true bubble oxygenator. This common system of blood with air suction has been evaluated as high vacuum suction (blood : air = 400:1000 ml/min). The results of these experiments are similar to those obtained in the BO experiments: all cellular elements are equally strongly affected and the bleeding time is severely prolonged for a week. To to avoid this blood to air contact a suction system was developed in which a detector

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connected to an electronic circuit regulates the pump speed and keeps the level of the blood above the tip of the sucker. Experiments with this controlled suction system have shown results in close relation to those obtained in the TMO experiments: thrombocytes, leukocytes and erythrocytes are all better preserved, while the bleeding time is only slightly prolonged. Replacement of high vacuum suction by controlled cardiotomy suction is therefore essential in open- heart surgery procedures in order to maintain the definite improvements of hemocompatibility obtained by introduction of the MO.

In conclusion:

In this systematic evaluation of the components of the ECC it was possible to assess hematological alterations caused by each single component of the extracorporeal circuit. From this evaluation the most hemocompatible extracorporeal circuit could be composed. This optimal equipment has been transferred from the animal laboratory to the clinical situations in which CPB is requested and has indeed been able to accomplish a decrease in blood damage.