

## AUTOLOGOUS BLOOD DONATION IN ELECTIVE SURGERY OF COLORECTAL CANCER – IS IT POSSIBLE?

**Todorov A, B. Hadzhiev, B. Sakakushev, I. Ivanov, B. Atanasov**

*Medical University Plovdiv, University Hospital St. George, Clinic of General Surgery with Coloproctology*

### ABSTRACT

Reports from recent studies indicate a causal relationship between allotransfusion, infectious complications and recurrent disease in surgical patients. The aim of the presented study is to elucidate the possibilities and indications for autologous haemotransfusion in the elective surgery of the colorectal cancer. Retrospective analysis was performed over 724 electively operated patients with colorectal cancer. The prospective part includes observation of 20 radically operated patients. In these patients autologous haemotransfusion was performed. As indications for autologous haemotransfusion we consider age up to 80 years, hemoglobin levels at least 130 g/l, plasma protein > 65 g/l, body weight > 50 kg, good general condition and absence of decompensated cardiovascular or endocrine diseases. In two patients with hemoglobin level between 90 – 110 g/l we performed stimulation by means of Erythropoetin  $\alpha$ . According to retrospective data admission hemoglobin levels varies from 54 g/l to 175 g/l (mean 119 g/l  $\pm$  22, 6). From all electively operated patients 33, 9% had hemoglobin values over 130 g/l. The frequency of postoperative infectious complications increases from 9,1% in nontransfused patients to 38,7% in patients with more than 4 units of allogenic blood transfused. The prospective part of the study is designed to establish feasibility of the autologous haemotransfusion in clinical practice. The fall of hemoglobin values on the next day after donation varies from 11g/l to 19g/l (mean 15.5 g/l  $\pm$  2,19). Erythropoetin stimulation was not found to increase hemoglobin values significantly. There were no complications in the postoperative period in autologous haemotransfusion group with exception of one superficial wound infection. Autologous haemotransfusion is feasible in approximately 1/3 of electively operated patients with colorectal cancer with no adverse effects or postoperative complications. It decreases the necessity of allogenic bioproducts and hence the risks related. Autologous haemotransfusion is easy to perform and propose benefits both from medical and logistic nature. Concerning to stimulation with Erythropoetin in our opinion it is without proven short term efficacy in general surgery so far.

**Key words:** colorectal cancer, autologous haemotransfusion, Erythropoetin

### INTRODUCTION

The development of abdominal oncosurgery and especially the elective operative treatment of colorectal cancer are impossible without use of blood and blood products today. Unfortunately in recent years of clinical practice some evidence emerged for adverse effects of allogenic blood transfusions (1). Blood transfusion-induced impairment of the immune response may reduce resistance to bacterial infection and tumor growth. Reports from clinical studies indicate a causal relationship between allotransfusion, infectious complications and recurrent disease (2,3). On the other side the possibility of HIV infection, hepatitis and graft-versus-host reactions cannot be avoided completely although allogenic transfusion has become a safer procedure as a result of better screening. Considerable problem in our country had become insufficient number of healthy, willing donors and supply with adequate amount of blood respectively.

One of the possible solutions of this problem is the use of autologous haemotransfusion in elective colorectal surgery (4,5). In the United States the method has been developed actively in the middle 1980s as a result of AIDS panic and today nearly 5% of blood transfused is autologous. In Western Europe and Japan autologous haemotransfusion became popular recently in the field of abdominal surgery because of the short period from the diagnosis of cancer to the operation and frequent presence of anemic syndrome (6).

Our intention is to answer whether autologous haemotransfusion is a method appropriate for our clinical practice with patients allocated for elective surgery due to colorectal cancer. Are there some difficulties or complications related to this method and is it possible to avoid allogenic transfusion and when?

Nowadays there are three main techniques for autologous haemotransfusion – predeposit transfusion, acute normovolemic haemodilution and intra- and postoperative blood salvage (7).

In acute normovolemic haemodilution approximately 1 liter whole blood is removed before the operation is started and simultaneously intravascular volume is replaced with colloid, crystalloid or both. The blood is then reinfused during the operation. The method is hardly to perform in real circumstances because of additional experience of the anesthetic team needed, expenses and poor studied risks for the patient so far.

Intra- and postoperative blood salvage is the oldest method used. Its disadvantages are need for elaborate instruments and risk for coagulation and electrolyte disturbances. The most important of them is that colorectal surgery is clean-contaminated procedure and the risk for bacterial contamination of operative field and collected blood is always presented.

Because of disadvantages described above we decided to use the first method - predeposit transfusion (8) as we think it is safer and easy to perform.

## AIM

The aim of the presented study is to elucidate the possibilities and indications for autologous haemotransfusion in the elective surgery of the colorectal cancer. The main question to be answered is whether the method can be used routinely in our clinical practice and what is the benefit for the patients.

## MATERIALS AND METHODS:

In order to accomplish the aim of the study retrospective analysis of the admission hemoglobin levels before surgery, the need for haemotransfusion and its correlation with postoperative infectious complications rate was done. Retrospective analysis was performed over 724 patients operated in our Clinic electively due to colorectal cancer for the last 10 years.

The age of the patient included in retrospective study varies from 22 to 92 years - (mean 63,  $1 \pm 10, 5$ ). Allocation by gender is: men 409 (56.5%) women 315 (43.5 %). Patients with colorectal cancer are stratified by N (9) as: Stage 0 - 0,3%, st. - 16.5%, Stage - 52.2 %, Stage 10.7%, V Stage - 19.8 % and in 0,5 % - there is not enough evidence to define the stage.

The prospective part of the study includes observation of 20 radically operated patients due to colorectal cancer in last 18 months. In these patients autologous haemotransfusion was performed. All of the patients were diagnostically evaluated before surgery by means of endoscopy or barium enema, abdominal echography and/or CT and were biopsied. The age of the patients included varies from 47 to 69 - (mean 56,  $5 \pm 8, 4$ ). Allocation by gender is: men 13 (65 %) women 7 (35 %). All of the patients included were in I or II clinical stage of the neoplastic disease.

As indications for autologous haemotransfusion we consider age under 80 years, plasma protein > 65 g/l, body

weight > 50 kg, good general condition and the absence of decompensated cardiovascular or endocrine concomitant diseases. Concerning the most important indicator - blood hemoglobin - we adopted extremely conservative approach and defined values at least 130 g/l as an inclusion factor for autologous donation.

No patient had severe complications before the operation and none of them had received preoperative chemotherapy or radiotherapy.

The autologous blood transfusion program involved one or two donations of 450 ml each according to hemoglobin levels. Interval between donations and operation should be no less than 3 days. Donated amount was stored as liquid whole blood till the moment of use.

We analyze the fall in hemoglobin values on the day after each donation of autologous blood.

In two patients with hemoglobin level between 90 - 110 g/l we performed stimulation of erythropoiesis by means of Erythropoetin, twice of 5000 IU between 5 days intravenously in combination with Venofer one vial daily.

Statistical analysis was performed with the use of SPSS software.

## RESULTS AND DISCUSSION

The absence of anemic syndrome in patients prepared for surgery is presumably of main significance for accomplishing an autologous donation. It is clear that not every patient is suitable for such a procedure. From this point of view it is important to know the admission hemoglobin levels in patients with colorectal cancer and what is the percent of them with appropriate values.

Studying retrospective data for the last 10 years we received following results: admission hemoglobin level in our patient varies between 54 g/l and 175 g/l (mean 119 g/l  $\pm 22, 6$ ). Results are shown in Diagram 1.

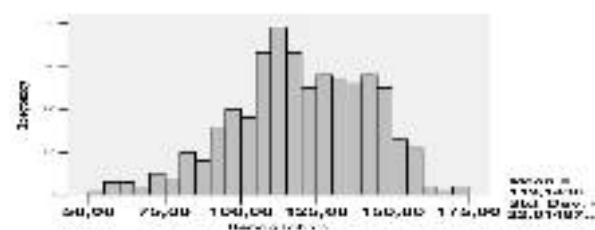


Diagram 1. Distribution of the patients according to admission hemoglobin levels

From the presented diagram it is clear that hemoglobin values of the patients with colorectal cancer before operative treatment are highly variable. It is important to point the fact that not all of patients were with profound anemic syndrome. There is a significant part of them with admission hemoglobin levels remaining in the referent values for age and gender.

Much more important is the next finding, that 33,9% from all electively operated patients due to colorectal cancer had admission hemoglobin levels over 130 g/l. Therefore autologous haemotransfusion is feasible approximately in 1/3 of the patients. Further decision to undertake or not an autologous donation should be made individually according to general condition, presence of concomitant diseases, stage of the neoplastic disease and volume of operation expected.

On the next Diagram 2 the correlation between stage of the neoplastic disease in TNM scale and percent of the patients with admission hemoglobin levels over 130 g/l is presented in details. It is obvious that patients in early stages of the disease are more suitable for the autologous haemotransfusion because of higher proportion nonanemic individuals. It could be argued that some of them do not need haemotransfusion at all. In our opinion the method is useful option in every patient even expected operation is without great blood loss. We take in consideration some reasons:

- Relative preoperative haemodilution is additive factor for prophylaxis of thromboembolism complications.
- Fresh liquid blood retains its haemostatic properties – platelets and coagulation factors.
- Completely replaces intravascular volume and thus eliminates the need for allogenic plasma transfusion or/and Humanaalbum.
- Gives a safety that bioproduct is available in cases with rare blood groups – circumstance that frequently leads to delay of the operation planned when a deficit of such blood group is present in local hemotransfusiology center.

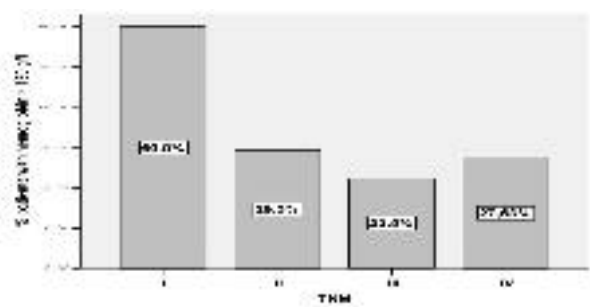


Diagram 2. Distribution of the patients with admission hemoglobin levels over 130 g/l in TNM scale.

Another important finding from the retrospective analysis is that the more amount of allogenic blood units were transfused the more frequency of postoperative infectious complications were observed in the operated patients.

It is clear that the frequency of postoperative infectious complications of the operative wound increases from 9,1% in nontransfused patients to 38,7% in patients with more than 4 units of allogenic blood transfused. There is also a clear trend toward increased infectious wound complications rate with raise of the total amount of blood transfused. Hence, the allogenic blood transfusions should be con-

cerned as a risk factor for development of postoperative infectious complications in elective colorectal surgery.

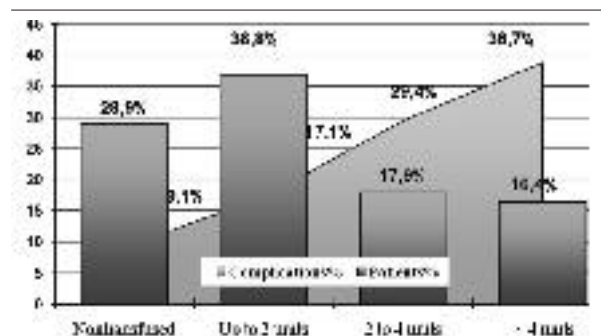


Diagram 3. Relation between amount of blood transfused and postoperative infectious complications rate.

The prospective part of the study is designed to establish feasibility of the autologous haemotransfusion in clinical practice. From this point of view is essential to evaluate the influence of 450 ml whole blood donation over the hemoglobin level of the patient several days before elective surgery planned. It is obvious that the perioperative risk should not be increased in any case after such a donation. On the following table 1 is shown how many decreases hemoglobin level in our patients measured 24 hours after auto donation.

Table 1. Changes in hemoglobin value 24 hours after auto donation.

	N	Minimum	Maximum	Mean	Std. Deviation
Hb g/l	20	11 g/l	19 g/l	15.50 g/l	2.188
Valid N	20				

It is obvious from the table that deposition of 450 ml whole blood several days before surgery do not bring additional risk for anemia for selected patients. In part of them is completely permissible donation of two portions of 450 ml between 5 – 7 days. The goal is to achieve hemoglobin levels no less than 110 – 115 g/l before the start of the operation. Results in Table 1 and also the data from the retrospective study confirm that autologous haemotransfusion is possible without risk approximately in 1/3 of the patients allocated for elective colorectal cancer surgery.

From Diagram 1 might be concluded that there is a considerable group of patients with marginal hemoglobin levels from 100 g/l to 120 g/l. In these patients is impossible to perform autologous haemotransfusion without risk from undesired additional anemia. That was the reason to explore the ways for stimulation of erythropoiesis as it was proposed from some authors in recent years (10).

Preoperative stimulation with Erythropoetin as described above was performed in two patients. On the 14 day from

the start of the stimulation unfortunately was not found significant increase in hemoglobin value of the patients. They have been excluded from autohaemotransfusion group. Similar results was reported and from other explorers. According to them clinical efficacy may to be expected only in selected patients with high iron bioavailability and for longer period of stimulation (11). It have to be taken in consideration also the high price of the medication needed and the fact that expenses for the use of Erythropoetin in general surgery is not insured by the National Health Fund so far. There were no complications in the postoperative period in autologous haemotransfusion group with exception of one superficial wound infection.

## CLINICAL CASES

. . 65 years >. Very good general condition. Dg: *Ca rectosigmoidalis*, T3, N0, M0. Histology – moderate to low differentiated adenocarcinoma. Admission hemoglobin level 166 g/l. Two donations of 450 ml whole blood each between 4 days. After the first donation Hb 155 g/l. Preoperatively 138 g/l. Operation: RRA. One unit autologous blood intraoperatively. On the third postoperative day – one more unit. Uneventful postoperative period. Without transfusion of other bioproducts. On discharge – Hb 136 g/l.

. . 62 years. +. Very good general condition. Dg: *Ca recti*. T1, N0, M0. Histology – highly differentiated adenocarcinoma. Admission hemoglobin level 133 g/l. One donation of 450 ml whole. Preoperatively 117 g/l. Operation: RRA. One unit autologous blood intraoperatively. Uneventful postoperative period with transfusion of two units fresh frozen plasma. On discharge - 84 g/l. Because the absence of complications allotransfusion was not performed. Discharged with prescribed per oral iron medication. Control examination after tree months – Hb in reference.

## CONCLUSION

The method of autologous haemotransfusion is feasible in approximately 1/3 of electively operated patients with colorectal cancer mainly in I and II clinical stage. There are no adverse effects and postoperative complications due to the method. It considerably decreases the necessity of allogenic bioproducts and hence the risks related. Autologous haemotransfusion is easy to perform in clinical

practice and propose benefits both from medical and logistic nature.

Concerning to stimulation with Erythropoetin in our opinion it is rather expensive and without proven short term efficacy in general surgery so far.

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