*Original article*

# Normovolumetric Haemodilution and Auto Transfusion in Major Operations Prevents Transfusion-Related Complications

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## Abstract

***Objective:*** To assess the efficacy and safety normovolumetric haemodilution and auto transfusion in patients undergoing major surgical operations. To compare the outcome differences between normovolumetric haemodilution and auto transfusion with allogenic transfusion group. ***Methods:*** The number and intensity of transfusion related complications in 36 patients, who received normovolumetric haemodilution and auto transfusion were compared with 36 patients who received similar amount of allogenic blood in the similar clinical environment and situation. The number and intensity of the complications encountered in study and control groups were compared and evaluated. ***Results:*** The study revealed statistically significant reduction in number and frequency of transfusion related complications in the study group comparing with the control group. The study also demonstrated reduction in number and intensity of surgery and anesthesia related complications compared with the control group without detection of harmful effect of haemodilution and auto transfusion. The study group also had statistically insignificant shorter hospital stay comparing with control group. ***Conclusion*:** Autologous transfusion with normovolemic haemodilution appears to be a safe and feasible method of reducing the need for homologous transfusion. Transfusion-related complications were significantly fewer in the auto-transfusion group in comparison with allotransfusion, in patients undergoing major operations.

**Keywords:** normovololumic; haemodilution, auto-transfusion; complications; allogenic blood and hospital stay.

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## Advances in Knowledge.

- This study significantly supplements the safety and efficacy of auto transfusion as underpinned in transfusion medicine, particularly in a situation where paucity of blood is an issue.
- Despite meticulous safety measures in transfusion process, there are reported complications related to allogenic blood transfusion. Afterall allogenic blood contain several foreign proteins, where the deleterious effect and enduring disquieting outcomes yet to be determined.
- The study conclude confidence among clinicians about this procedure, fewer complications are reported in auto transfusion group, compared to allo transfusion, thus feasibility and expediency of the procedure mandates multicentric studies.

## Application to Patient Care:

- Normovolumetric Haemodilution and Auto Transfusion study provides insight in

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"alternative to allo-transfusion". The results of this study provide clinical guidelines to clinicians: In major surgical undertaking where blood transfusion become necessary, how a safe, effective and clinically tested haemodilution and auto transfusion can be carried out.

- Clinical protocols are tested in real situation and advantages of this procedure with respect to patient safety and benefits to the health care management system are concluded.
- Safe haemodilutioncontributes in prevention of deep venous thrombosis and other complications related to haemoconcentration during prolonged surgery.

## Introduction

In major operations that inevitably require transfusion because of blood loss several kinds of transfusion-related complications may occur. Acute normovolemichaemodilution and auto transfusion is a technique that reduces the need for transfusion and the related complications.[1]After induction of anesthesia, blood is removed from the patient, and circulatory volume is maintained with infusion of crystalloid or colloid solutions. Ordinarily, up to three units of blood (1500 ml) is withdrawn and infused into the patient during or after the operation in the operating area. Patients who have normal initial haemoglobin values are expected to lose two or more units of blood may undergo isovolumetrichaemodilution and donation of 1500 ml of blood to maintain homeostasis. Adult patients who lose 20% or more of circulatory volume require replacement, but transfusion is indicated in pediatric patients with the loss of even 15% of circulatory volume. Normovolemichaemodilution and auto transfusion may be especially important when donated blood is in limited supply because of the need for specific blood type, thorough screening causes delays, or other barriers.

In contrast to auto-transfusion, allo-transfusion is associated with numerous complications: febrile reactions, circulatory overload, acute lung injury, haemolytic reactions due to ABO incompatibility, coagulopathies, biochemical disturbances (hypocalcaemia, hyperkaliemia, acid–base abnormalities), hypothermia, allergic reactions to foreign proteins, and others.[2] Numerous viral, bacterial and other infections are dangers, especially in immunocompromised patients. Delayed reactions such as antigen-antibody reactions and graft-versus-host reactions are well-known complications of allo-transfusion.[3] The actual risk of infection transmission might be higher than is described in the literature.[4]

In the current study, we compared the incidence of transfusion-related complications in surgical patients who received allo transfusions with those who received normovolumetrichaemodilution and auto transfusion.

## Patients and Methods

This is a prospective study of patients undergoing elective major surgery between 2014 and 2019. Thirty-six patients received normovolemichaemodilution and auto-transfusion (study group), and 36 received homologous blood transfusion of the same number of blood units (control group). The patients with a preoperative hematocrit greater than 36%, American Society of Anesthesiologists were class I or II, and were without known cardiovascular or pulmonary disease[5]. Preoperatively, all patients underwent routine investigations like: liver and renal functions, and coagulation profile, while where appropriate special radiological, biochemical and haematological and other investigations were carried out. All patients received standardized general anaesthesia.

For patients undergoing normovolemichaemodilution and auto transfusion, the haemodilution process was initiated just after the induction. Blood was taken from an arm vein, and the same volume of colloid solution was infused via a high-flow (8.5 French) central venous catheter to a target hematocrit of 24%. Three units of blood were removed into standard citrate–phosphate–dextrose blood storage bags. The circulatory volume was replaced by colloid solutions (3% hydroxyethyl starch) in quantities approximately 1.1 times the volume of blood removed.[6]Other blood-conserving measures, such aspre-deposit of autologous blood and intraoperative cell salvage techniques were not used. In the intraoperative period, patients in both groups received continuous crystalloid (Ringer's lactate solution) infusion. To maintain adequate urine output and systolic blood pressure greater than 100 mm Hg, additional volume of 500 ml was administered intermittently in bolus forms. Subsequent volumes of blood were replaced with Ringer's lactate solution in a 3:1 volume. Succeeding blood loss was estimated by assessment of the volume in suction bottles, sponges, surgical drapes, and anesthetists' gowns.

The transfusion threshold for either autologous or allogeneic erythrocytes was hematocrit less than

20%. Autologous blood was labeled andstored in the operating area and was reinfused at the conclusion of surgery or when a minimum hematocrit value was reached.

All patients were kept under surveillance in the post-operativeperiod. Blood haemotology, coagulation, liver and renal profiles were determined. Adverse outcomes and complications were recorded by the examining physician and where required validated by the relevant investigations. On a predesigned proforma, we compared the expected number and level of complications in both the groups. Patients who required allogeneic transfusion during the intraoperative and perioperative period of the first 72 h after operation were excluded entirely. Safety profile and complications were assessed by comparing mortality, morbidity, clinical and laboratory values reported in the study group with those variables in the control group.

Differences between the means of the two groups and the median units transfused were compared by use of Student *t* test and Mann-Whitney test, respectively. Data within study and control group were analyzed using analysis of variance for repeated measurements.

**Ethical considerations:** Theprotocol of the study was reviewed and approved by the Institutional Review Board (IRB) prior to the start of study. The study was conducted in accordance with the ethical guide lines and approved for publication by the IRB. All patients provided written informed consent prior to study entry.

## Results

Clinical variables in the study and control groups shows:Male/female ratio of 20/16 and 19/17 respectively. The mean age of the study and control groups were46± 14 and 47± 16 (years) respectively. The mean height in the study and control groupswere 145± 11 and 150 ±8 (cm) and the mean weightwas 65± 11and 68± 12 (Kg) respectively.There were no statistically significant differences between the groups in sex, age, height, weight or American Society of Anesthesiologists class. The total number (n36) of operations that patients underwent were similar in both the groups. The common surgical procedures were; Head &Neck, abdominal, vascular, pancreatic, pelvic and hepatic in both the groups. Although there were differences between the groups, both groups underwent major, complicated operations. Blood transfusion requirements were similar in the two groups.

The haematologic and haemodynamic variables of the study (auto-transfusion) group are listed in Table 1.

The expected decline in haemoglobin and hematocrit values after donation, with return towards normal values after transfusion, are evident. Heart rate and mean arterial pressure did not change significantly with donation and haemodilution, which is evidence that haemodynamic stability was maintained with these procedures.

**Table 1.** Haemotological and Haemodynamic Variables in the Study Group

| No. | Variable | Pre-op, pre-donation | Post Donation | After Haemodilution | After Transfusion |
|---|---|---|---|---|---|
| 1 | Haemoglobin (gm/dl) | 12.8 ± 1.6 | 10.0 (±1,2) | 9,2 ± 1,01 | 10,8 ± 1, 41 |
| 2 | Hematocrit (%) | 38,6 ± 3.80 | 29.98 ± 3.10 | 26.9 ± 3.10 | 33,42 ± 2.44 |
| 3 | Heart rate (beats/ min) | 88,59 ± 10,2 | 96,41 ± 17.42 | 90,98 ± 16,41 | 85, 92 ± 11,23 |
| 4 | Mean Arterial Pressure | 91, 82 ± 6,41 | 89,49 ± 18,70 | 93,37 ± 18,24 | 89,24 ± 11, 82 |

In Table 2 we have listed the total transfusion-related complications; the total complications were significantly more in the control (homologous transfusion) group than in the study (auto-transfusion) group (p=0.020). Most notably, allergic reactions, viral infections and graft vs host disease were present in the control group but not in the study group. In Table 3 we have listed the immediate transfusion-related allergic reactions; whereas only 2 (5.6%) reactions occurred in the study group, 9 (25%) occurred in the control group (p=0.026).

We also recorded other kinds of complications that occurred in the post-operative period (Table 4). The total number was more in the control group than in the study group (p=0.009).Although it seems unlikely that these complications were related to the transfusion method used, it may be noteworthy that deep-vein thrombosis/pulmonary embolus occurred in 3 patients in the control group but in none in the study group. On the other hand, wound infections, wound dehiscence, incisional hernia respiratory complications, cardiovascular complications and renal complications occurred in both groups.

**Table 2. Transfusion-related complications in study and control group**

| No. | | Study Group (N-36) | Control Group (N-36) |
|---|---|---|---|
| 1 | Immediate haemolytic reaction | 0 | 0 |
| 2 | Delayed hemolytic reaction | 0 | 1 |
| 3 | Febrile non-haemolytic reaction | 0 | 2 |
| 4 | Chills and rigors | 0 | 2 |
| 5 | Transfusion-related circulatory overload | 0 | 0 |
| 6 | Transfusion-related acute lung injury | 0 | 0 |
| 7 | Acute haemolytic reaction due to ABO incompatibility | 0 | 0 |
| 8 | Dilutional coagulopathy | 1 | 0 |
| 9 | Hypocalcaemia | 1 | 0 |
| 10 | Hyperkaliemia | 0 | 1 |
| 11 | Acid-base abnormalities | 1 | 1 |
| 12 | Hypothermia | 0 | 0 |
| 13 | Allergic reaction | 0 | 3 |
| 14 | Transfusion-related viral /bacterial infection | 0 | 0 |
| 15 | Transfusion-related viral infection (non-HBV, HBC, HCV) | 0 | 2 |
| 16 | Transfusion-associated graft vs host disease | 0 | 1 |
| 17 | Immunomodulation | 0 | 1 |
| | Total complications n (%) | 3 (8.3%)[1] | 14 (38.9%)[1] |

[1] μ=490, p=0.020

**Table 3. Immediate Transfusion-Related Allergic Reactions in study and control group**

| No. | | Study Group (N-36) | Control Group (N-36) |
|---|---|---|---|
| 1 | Flushing | 0 | 1 |
| 2 | Chills | 0 | 1 |
| 3 | Myalgia | 1 | 1 |
| 4 | Fever | 0 | 2 |
| 5 | Haemoglobinuria | 0 | 1 |
| 6 | Transfusion-related lung injury<br>Blood-gas hypoxemia<br>Chest radiograph lung infiltrate | <br>1<br>0 | <br>1<br>1 |
| 7 | Purpura | 0 | 1 |
| | Total n (%) | 2 (5.6%)[1] | 9 (25%)[1] |

[1] μ=508.5, p=0.026

**Table 4. Other Postoperative Complications**

| No. | | Study Group (N-36) | Control Group (N-36) |
|---|---|---|---|
| 1 | Deep-vein thrombosis/ pulmonary embolus | 0/0 | 2/1 |
| 2 | Wound infections | 2 | 5 |
| 3 | Coagulopathy | 1 | 3 |
| 4 | Wound dehiscence | 0 | 1 |
| 5 | Incisional hernia | 1 | 1 |
| 6 | Respiratory complications / ARDS | 1/0 | 2/0 |
| 7 | Post-operative cardiovascular complications<br>Myocardial infarction<br>Transient ischemic attack<br>Cerebrovascular accident | <br>1<br>0<br>0 | <br>1<br>0<br>0 |
| 8 | Median length of stay in hospital | 10 / (7-15) | 14 (8-24) |
| 9 | Renal complication | 2 | 4 |
| | Total n (%) | 8 (22.2%) | 20 (55.6%) |

[1] μ=437.5.5, p=0.009

Hospital stay was modestly shorter in patients in the study group than the control group, but this difference did not reach statistical significance. No deaths occurred in the two populations.

## Discussion

In this study, we compared the incidence of transfusion-related complications in surgical patients undergoing major operations who received allogenic transfusions with those who received normovolumetrichaemodilution and auto transfusion. The most important finding was that transfusion-related complications were significantly fewer in the auto-transfusion group than in the allo-transfusion group. Immediate transfusion-related allergic reactions, a known complication of allogenic transfusion, occurred in three cases of allogenic transfusion but in none of the patients who received auto-transfusion Moreover, other common transfusion-related complications (delayed haemolytic reaction, febrile non-haemolytic reaction, chills and rigors, viral infection, and graft vs host disease) did not occur in the autologous-transfused patients but did occur in the allogenic transfused patients. Thus,autologous transfusion with normovolemichaemodilution appears to be a safe and feasible method of reducing the need for allogenic transfusion and its related complications.

Our results are supported by the results of other studies that have reported the usefulness, safety, and cost effectiveness of auto transfusion.[7,12]This method has certain limitations, though, and cannot be applied everywhere and in all patients.

We also found that the autologous blood donation and haemodilution did not cause heamodynamic instability: no significant blood pressure falls or major changes in heart rate were recorded, others [11] have reported similar results. There are various ways to use autologous transfusion, including redeposit and cell saver techniques during the surgical procedure.[8] We used haemodilution to a target hematocrit of 27-30%, with Haemaccel 3,5% colloidal intravenous infusion solution. Others[9] also have reported that haemodilution provided good microcirculation during surgery.

Another advantage of autologous transfusion is that the blood collected on the operation table before surgery and stored has viable platelets, clotting factors and other constituents of the preserved blood. Other post-operative complications (Table4) were also significantly lower in the autologous group then in allo-transfusion group.

A limitation of this study is its small sample size, but the results are consistent with complication rates in other[19] reports on auto-transfusion in patients undergoing transfusion-requiring major operations. The small sample size does, however, prevent comparisons of complications between individual operations.

## Conclusion

In a comparison of normovolemichaemodilution and auto transfusion with allogenic transfusion in patients undergoing major operations, transfusion-related complications were significantly fewer in the auto-transfusion group. No haemodynamic instability, as determined by heart rate and mean arterial pressure, was encountered in auto-transfused patients. Thus, autologous transfusion with normovolemichaemodilution appears to be a safe and feasible method of reducing the need for allogenic

transfusion in transfusion-requiring major operations.

## Conflict of interest:

The authors have no competing interests.

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