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The Effect of Routine Maintenance Intravenous Therapy on Hemoglobin Concentration and Hematocrit during Anesthesia in Adults

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ABSTRACT

Objective: To investigate the decrease in hemoglobin concentration and hematocrit during elective surgery.
Methods: This was a prospective study being performed in Nemazee Hospital of Shiraz University of Medical Sciences. We included a total of 50 American Society of Anesthesiology (ASA) I and II patients undergoing elective minor surgeries. Perioperative fluid administration was performed for all the patients and hemoglobin and hematocrit levels were measured three times: Once before the operation, once one hour after start of operation and once in the recovery room. Values were compared using paired sample t-test.
Results: The mean age of the patients and controls was 39.66 ± 8.27 years. Hemoglobin level decreases significantly after one hour (p<0.001) and after the end of operation (p<0.001). In the same way hematocrit level was decreased significantly after one hour (p<0.001) and after the end of operation (p<0.001).
Conclusion: In this patient population undergoing elective minor operations, there was significant decrease in the hemoglobin and hematocrit levels in response to the IV fluids administration.

Keywords: Hemodilution; Hemoglobin; Hematocrit; Perioperative fluid administration**.**

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Introduction

Perioperative volume therapy primarily is based upon the use of crystalloids and colloids. When reaching a certain extent of blood loss the indication for transfusion of red blood cells (RBCs) and/or substitution of coagulation factors, primarily given as fresh frozen plasma (FFP), are considered. Compared to routine strategy some years ago, today the indication for the use of allogeneic blood transfusions is stricter due to potential adverse effects [1] costs [2], and intermittent blood shortages [3]. The obligatory consent of the patient to accept transfusion of blood and blood products exceeding a probability in case of elective surgery of 5-10% in Central Europe has increased the demand of alternatives to allogeneic blood. In this context, preoperative acute normovolemic hemodilution (ANH) is one of several procedures for conservation of autologous blood during operative procedures [4].

During operations, two concurrent events, namely blood loss and red blood cell dilution due to positive fluid balance result in precipitous hematocrit drop and need for allogeneic blood. Hemodilution has been identified as a major factor influencing the decision to transfuse. Likewise, several variables associated with total red cell mass, such as preoperative anemia, female gender and small body size, are independent predictors of transfusion in surgeries [5-7]. Existing guidelines underline the importance of limiting hemodilution, applying blood salvage techniques and using alternative therapies for transfusion and blood conservation [7].

The hemodynamic changes should be minimal during the operation in order to preserve the normal physiology of the circulation. This goal is fulfilled by intravenous (IV) fluid administration and blood transfusion if needed [4]. IV therapy is performed during operations in order to preserve oxygen delivery to target organs as well as preserving normal electrolyte concentrations and normal blood sugar. However this IV therapy during the operation will result in increase in intra-vascular volume and thus increase in plasma volume. Nevertheless, the RBC bulk doesn't change and as result a hemodilution will occur which will alleviate the patients' prognosis and outcome by disturbing oxygen delivery to target organs. The oxygen delivery acquiescence of the blood is dependent on several factors including hemoglobin concentration, oxygen pressure, organ perfusion pressure and vascular resistance [2]. Some other factors including systemic blood pressure, cardiac output and vascular tonicity have indirect influences on oxygenation. During general anesthesia vascular tonicity decreases and as a result the systemic blood pressure decreases.

Although the hemodilution during the operation is an important issue in anesthesiology, data regarding it is limited. Thus we performed this study in order to investigate the changes in hemoglobin concentration and hematocrit during elective surgery. We designed a dynamic study because the changes in the hemoglobin and hematocrit levels during the operation are important to the clinicians for deciding whether to transfuse RBCs or not.

Materials and Methods

Patients

This was a prospective study being performed in operation rooms of Nemazee Hospital, a tertiary care center affiliated with Shiraz University of Medical Sciences, during a 4 months period from October 2009 to January 2010. We included a total of 50 American Society of Anesthesiology (ASA) I and II patients undergoing elective minor surgeries including hernia repair, hydrocele correction, appendectomy, etc. in Nemazee operating room during the study period. None of these operations were accompanied by fluid shift and none needed transfusion during the operation. Patients with coronary artery disease (CAD), hypertension, those with diarrhea or vomiting in previous 48 hours, those using laxatives or diuretics in the proceeding 24 hours and those younger than 18 and older than 50 years were excluded from the study. We also excluded those with pre-existing hematologic disease or coagulation abnormality, advanced cirrhosis, renal failure and preoperative blood product transfusion.

Based on 95% confident intervals and an 80% power to detect a significant difference for hemoglobin level at level of 5%, 36 subjects were needed for the study. In order to compensate for non-evaluable patients, we included 50 patients undergoing elective surgeries. The study protocol was approved by the institutional review board (IRB) of Shiraz University of Medical Sciences and the approval of the Ethics Committee was achieved before beginning of the study. All the participants gave their informed consent.

Study protocol

All the patients referred to Nemazee Hospital operating rooms for undergoing surgeries. Hemoglobin and hematocrit levels were measured 3 times during the study. Before inducing general anesthesia and starting IV fluid therapy, a 2 milliliter venous blood was withdrawn to measure hemoglobin and hematocrit levels (first sample). All patients received standardized anesthesia and intraoperative care, and were operated by the same team (same surgeon, assistant and perfusionist) under standardized conditions (same operating room and setting).

All the patients received 1 gram of Ceftriaxone 30 minutes before operation as antibiotic prophylaxis. All the patients underwent the same anesthetic protocol. The patients received midazolam (0.01 mg/kg) and morphine (0.1 mg/kg) as premedication. In all patients anesthesia was induced by thiopental sodium (3-5 mg/kg) and atracurium (0.4 mg/kg). After 2-3 minutes of mask ventilation and reassurance of the muscle relaxation, the endotracheal intubation was done. During the maintenance of anesthesia patients received a (50%-50%) combination of oxygen and nitrous and also isoflurane 1.5-2.5%. After completion of the surgery, neuromuscular blockade was reversed by Neostigmine (2.5 mg) and Atropine (1.25 mg/kg). All the patients received IV fluid therapy during the operation based on sex and age. Rate of volume administration was calculated according to the previous studies (8):

Rate of fluid administration = CVE + Deficit + Maintenance + Loss + Third space

After 1 hour of the operation and receiving IV fluid therapy, another 2 milliliters of venous blood was withdrawn for measuring the hemoglobin and hematocrit levels (second sample). Patients were extubated when adequate spontaneous ventilation was established and were transferred to recovery unit. After approximately 1 hours of stay in recovery unit, patients were transferred to their respective wards. Before transferring the patients to their respective wards, another 2 milliliters of venous blood was withdrawn for measuring the hemoglobin and hematocrit levels (third sample).

Statistical analysis

The statistical package for social science, SPSS for Windows, Version 15.0 (SPSS, Chicago, IL, USA) was used for data analysis. Paired t-test was used to compare the hemoglobin and hematocrit levels before, during and after operation. Repeated measured approach MANOVA and LSD test were used to compare the differences of hemoglobin and hematocrit during the operation. Pearson's correlation coefficients were used to calculate the correlation between paired data Sets. Data are reported as the mean ± SD for 95% confidence interval with 5% degree of freedom. A two sided *p*-value less than 0.05 was considered statistically significant.

Results

We included 50 patients in this study of which 28 (56%) were men and 22 (44%) were women. Table 1 summarizes the demographic characteristics of the study population. Hemoglobin level was checked three times during the operation. Once before the operation, once one hour after start of operation and once in the recovery room. The mean hemoglobin level at these three times was found to be 13.47 ± 1.49, 12.08 ± 1.23 and 11.69 ± 1.41 mg/dL respectively. Table 2 compares the hemoglobin level during the operation. The second hemoglobin was significantly lower compared to first hemoglobin ($p<0.0001$) and was significantly higher compared to third one ($p=0.002$). In the same way, the third hemoglobin was significantly lower compared to the first one ($p<0.0001$). Figure 1 demonstrates the decrease in hemoglobin level during operation. Overall, the hemoglobin level was decreased by 13.2% in the study group. The mean IV fluid received during the operation (105.6 ± 31.2 minutes) was 2118.9 ± 343.2 milliliters. Thus it can be said that hydrating the patient with 160.4 milliliters of IV fluids during 105 minutes will results in 1% decrease in hemoglobin level. Hematocrit level was checked three times during the operation. Once before the operation, once one hour after start of operation and once in the recovery room. The mean hematocrit level at these three times was found to be 37.43 ± 5.57, 33.59 ± 3.84 and 32.39 ± 4.54% respectively. Table 3 compares the hematocrit level during the operation. The second hematocrit was significantly lower compared to first hematocrit ($p<0.0001$) and was significantly higher compared to third one ($p=0.003$). In the same way, the third hematocrit was significantly lower compared to the first one ($p<0.0001$). Figure 2 demonstrates the decrease in hematocrit level during operation. Overall, the hematocrit level was decreased by 13.4% in the study group. The mean IV fluid received during the operation (105.6 ± 31.2 minutes) was 2118.9 ± 343.2 milliliters. Thus it can be said that hydrating the patient with 158.1 milliliters of IV fluids during 105 minutes will results in 1% decrease in hematocrit level. Table 4 summarizes the main study outcomes.

We performed a correlation analysis between dependent and non-dependent variables. Body weight was positively correlated to first and second hemoglobin (r=0.354, p=0.012; r=0.316, p=0.025 respectively) as well as first and second hematocrit (r=0.327, p=0.020; r=0.321, p=0.023 respectively) and negatively to hemoglobin drop during operation (r= –0.287, p=0.043). There wasn't any other significant correlation between corresponding variable.

Table 1. Demographic characteristics of the study population.

Characteristic	Value
Sex	
Male	28 (56%)
Female	22 (44%)
Age (years)	39.66 ± 8.27
Weight (kg)	65.74 ± 11.1
Operation time (minutes)	105.6 ± 31.2
Bleeding (mL)	68.7 ± 25.1
Normal Saline (cc)	1036.6 ± 348.1
Ringer (cc)	1082.3 ± 389.5

Discussion

Hemodilution during operation increases the need for RBC transfusion and thus increases the side effects of transfusion in patients undergoing minor surgeries. In the present study we tried to determine the changes in hemoglobin and hematocrit levels during elective minor surgeries with minimal bleedings in order to investigate the effect of normal fluid administration during operation on hemodilution. As hemoglobin and hematocrit are two important variables in determining acceptable blood loss (ABL) [8] and thus deciding to transfuse the patient, it is important to be aware of the impact of routine IV fluid administration

Table 2. Comparison between hemoglobin levels during the operation.

	Difference	95% Confidence Interval	*P*-value
Hb 1 – Hb 2	1.39 ± 0.81	1.15 – 1.62	<0.0001
Hb 1 – Hb 3	1.77 ± 1.01	1.48 – 2.06	<0.0001
Hb 2 – Hb 3	0.38 ± 0.84	0.14 – 0.62	0.002

Table 3. Comparison between hematocrit levels during the operation.

	Difference	95% Confidence Interval	*P*-value
Hct 1 – Hct 2	3.83 ± 4.53	2.54 – 5.12	<0.0001
Hct 1 – Hct 3	5.03 ± 5.09	3.58 – 6.48	<0.0001
Hct 2 – Hct 3	1.19 ± 2.73	0.42 – 1.97	0.003

Table 4. Main study outcomes.

Finding	Value
Hemoglobin 1 (mg/dL)	13.47 ± 1.49
Hemoglobin 2 (mg/dL)	12.08 ± 1.23
Hemoglobin 3 (mg/dL)	11.69 ± 1.41
Hb 1 – Hb 3 difference (mg/dL)	1.77 ± 1.01 (1.48 – 2.06)
Total administered IV fluid (mL)	2118.9 ± 343.2
Duration of operation	105.6 ± 31.2 minutes
IV fluid administration rate (mL/min)	20.17.3
Total hemoglobin decrease	13.2%
Total hematocrit decreases	13.4%
Amount of IV fluid for 1% decrease in Hb (mL)	160.4
Amount of IV fluid for 1% decrease in Hct (mL)	158.1

on these two variables. We found that both hemoglobin and hematocrit levels decrease significantly during an elective minor surgery with minimal bleeding after one hour of fluid administration and after the end of operation mainly because of hemodilution induced by IV fluids.

Changes in the volume of the fluid space expanded by IV infusion of Ringer's acetate solution have been analyzed recently using mathematical models [9]. Data obtained by such analyses allow simulation of the dilution of the plasma volume during infusion of the solution at different rates. Hahn and Svensén [9] obtained basic kinetic data for such simulations and measured the plasma dilution-time curves during and after IV infusion of Ringer's solution 25 ml/kg over 30 min in 15 healthy male volunteers (mean age 31 years) and over 30, 45 and 80 min in six females (mean age 32 years). Based on these experiments, nomograms were constructed from which the rate of infusion of Ringer's solution and the infusion time required to obtain a defined plasma dilution in both males and females can be estimated together with the infusion rate needed to maintain the dilution at the level reached. They showed that the infusion rate must be at least 50 ml/min in a young man to yield a plasma dilution of 20%, which corresponds to an increase in blood volume of approximately 10%. Even at this high rate, the infusion has to continue for 40 min (and requires 2000 ml of fluid) to yield the desired dilution. In contrast, an infusion rate below 40 ml/min is not capable of diluting plasma volume by 20%, regardless of how long the infusion is continued. It was also shown that a fast infusion is more effective than a slow one. Imagine we wish to increase plasma

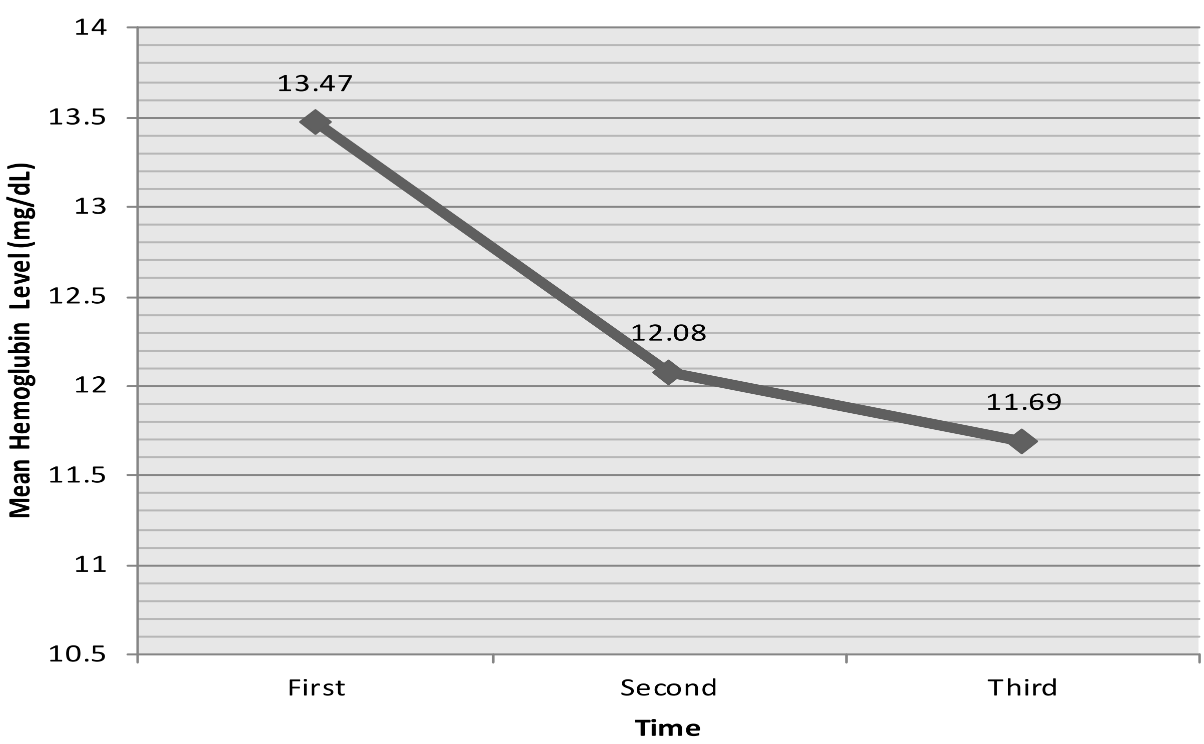

Fig. 1. Decrease in hemoglobin level during operation in 50 patients undergoing elective minor operations.

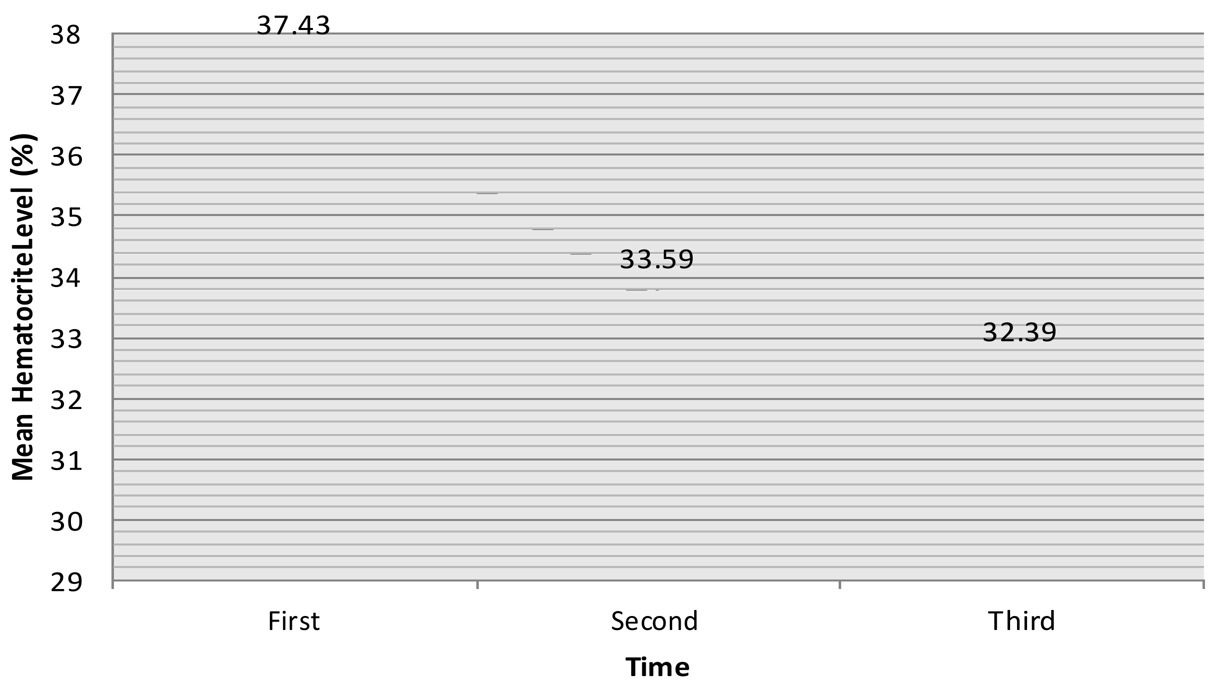

Fig. 2. Decrease in hematocrit level during operation in 50 patients undergoing elective minor operations.

volume by 10%, which corresponds to an increase in blood volume of 5%. In males, this can be achieved by infusing Ringer's solution at a rate of either 50 ml/min for 15 min (750 ml) or 25 ml/min for 45 min (1125 ml). The second infusion regimen requires 50% more fluid than the first despite the fact that the same dilution is obtained [9]. In the present study we achieved hemodilution with lower rate (26 ml/min) compared to Hahn and Svensén (50 ml/min) [9]. This can be explained due to the fact that our population underwent general anesthesia while their population were awake. General anesthesia causes a block in the sympathetic system and these results in generalized vasodilation. In the same way the cardiac output decreases secondary to decreased contractibility. All of these events result in decreased blood pressure and thus decreased glomerular filtration rate (GFR). When GFR decreases a volume overload happens which hastens the hemodilution. In addition, vasodilation causes an increase in the vascular compliance and thus decreases the extravasation of fluid towards interstitium. These two events together cause hemodilution in those undergoing general anesthesia. Hemodilution involves the infusion of a significant amount of cell-free solution. Thus not only the hematocrit is lowered, but all cellular and plasma components of the blood are diluted [10]: hence platelet counts and the concentration of coagulation factors will also be lowered, calling for attention when already preoperative parameters are found in the lower normal range. Preexisting coagulation disorders are clear exclusion criteria for preoperative hemodilution [11].

We found that hemoglobin level decreases in those adult patients undergoing general anesthesia by 1% per 160.4 milliliters of IV fluid hydration in 105 minutes. This finding was also consistent for hematocrit level (1% decrease per 158.1 milliliters of IV fluid hydration in 105 minutes). This equation can be used to estimate the amount of hemodilution in those adult patients undergoing general anesthesia.

We found a positive correlation between intraoperative bleeding and hemoglobin drop during this period. This may seems like a bias to our results. However only 12 (24%) patients had intraoperative bleeding and the maximum amount of that was 50 milliliters. Thus it can be said that the decrease in hemoglobin and hematocrit levels are associated with IV fluid administration during the operation.

As hemoglobin and hematocrit are two important variables in determining acceptable blood loss (ABL) [8] and thus deciding to transfuse the patient, it is important to be aware of the impact of routine IV fluid administration on these two variables. In this dynamic study we found that both hemoglobin and hematocrit levels decrease significantly during an elective minor surgery with minimal bleeding after one hour of fluid administration and after the end of operation mainly because of hemodilution induced by IV fluids. However this study included the patients who underwent minor surgeries with minimal bleeding during the operation. Thus its results are limited and can be interpreted only to the same population. Future studies including the patients undergoing major surgeries with significant blood losses are needed for clarifying this issue. We suggest performing prospective dynamic studies including patients undergoing major surgeries with higher amount of blood losses in order to understand the role of perioperative IV fluid administration on inducing hemodilution.

In conclusion, in this patient population undergoing elective minor operations, there was significant decrease in the hemoglobin and hematocrit levels in response to the IV fluids administration. Thus perioperative hemodilution in result of IV fluid administration should be kept in mind.

Conflict of Interest: None declared.

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