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Review

The combination of hemodilution and controlled hypotension: physiology and clinical application

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Introduction

The current risks of blood transfusion can be categorized as infections, reactions, and immune suppression [1]. The incidences of viral contamination associated with human immunodeficiency virus (HIV), human T-lymphotropic virus (HTLV), hepatitis C, and hepatitis B and with fetal hemolytic reaction have been reduced [2]. However, completely eliminating these risks would be impossible.

Several methods have been used to reduce blood loss and homologous transfusion during surgery. Autologous transfusion has been widely accepted in major orthopedic surgery, such as total hip or knee arthroplasty and spinal fusion. Recently, a large-scale study of transfusion requirements associated with total joint arthroplasty was performed in the United States [3], in which a total of 9482 patients were evaluated prospectively. Of those patients, 30% had a transfusion of autologous blood and 16% had a transfusion of homologous blood. Although preoperative deposit (or preoperative donation) of autologous blood decreased the risk of transfusion of allogenic blood, inefficiences in the procedure were also identified. First, 45% of the 9920 units of the predeposited autologous blood were not used; second, of the 5741 patients who had predoposited blood, 503 (9%) needed an additional transfusion of homologous blood.

Barbier-Böhm et al. [4] in 1980 reported that either controlled hypotension or normovolemic hemodilution was effective in reducing blood loss in total hip arthroplasty, and suggested that their combination could be the best technique for avoiding homologous transfusion. This combined technique was used in children's abdominal cancer surgery [5,6]. Mandel et al. [7] in 1981 reported the use of the combined technique in spinal surgery, and Hur et al. [8] reported that acute normovolemic hemodilution combined with controlled hypotension, when combined with other methods of autologous transfusion, such as predonation or semicontinuous flour centrifugation devices (e.g., Cell Saver; Haemonetics, Braintree, MA, USA), could preclude homologous transfusion in most spinal fusion surgery.

On the other hand, the combination of acute normovolemic hemodilution and controlled hypotension may impair tissue oxygenation in the important organs due to reduction in oxygen carrying capacity and perfusion pressure. This review will evaluate the effect of the combined method of hemodilution and controlled hypotension on tissue oxygenation and descute the function in the important organs and the clinical application.

Acute normovolemic hemodilution (ANH)

Efficacy to reduce homologous transfusion

Bryson et al. [9] used a metaanalysis to evaluate whether ANH was effective in reducing perioperative allogenic transfusion and suggested that although many studies reported an impressive reduction in blood transfusion, these reductions might be due to flawed study design. However, mathematical modeling has clearly demonstrated that the success of ANH depends essentially on four factors [10–12]: the initial hematocrit and red blood cell mass of the patient, the minimal safe hematocrit at which transfusion is started, the number

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of units removed during ANH, and the anticipated surgical blood loss. Kick [10,12] has concluded that ANH is most beneficial and potentially valid as a cost-effective alternative to preoperative autologous donation for healthy adults with high initial hematocrit and the capacity to tolerate dilution-induced anemia who are undergoing procedures associated with significant hemorrhage.

Limit of hemodilution

An intentional anemia without hypovolemia would activate compensatory mechanisms, i.e., increases in tissue blood flow and oxygen extraction, based on increased cardiac output.

Wilkerson et al. [13] studied the limits of cardiac decompensation during progressive normovolemic anemia in anesthetized baboons. They found that baboons tolerated anemia with increasing cardiac output and coronary blood flow when hematocrit decreased to 10%, and that cardiac decompensation followed at a hematocrit below 10%. Levine et al. [14] evaluated the effects of withholding transfusion or lowering the transfusion trigger on long-term survival in unanesthetized baboons, and suggested that the reduction of the transfusion trigger to a hematocrit of 15% could show cardiac compensation and would be safe in a normal heart. The cardiac infarction rat model tolerated a hematocrit of 25% [15], and the myocardial depression model tolerated a hematocrit of 20% [16]. Singbartl et al. [17] continuously analyzed the ST segment of the electrocardiogram during hemodilutional anemia in ASA I–III patients undergoing orthopedic surgery. They found that ST changes appeared in 6% of ASA I or II patients and 26% of ASA III patients at a hematocrit of 24%, and in 17% of ASA I or II patients and 36% of ASA III patients at a hematocrit of 14%. Tremper [18] concluded that healthy patients with good cardiac function tolerated a hematocrit of 20% or below if they were adequately volume resuscitated, and that patients with impaired myocardial function might require a hematocrit of 30%. Oxygen transport and tissue oxygenation would be well maintained in spite of a decrease in hematocrit to about 20% as long as normovolemia and myocardial function were maintained.

However, anesthesia might alter the normal physiologic cardiovascular response to ANH [19,20]. In anesthetized patients during hemodilution, cardiac output may [21,22] or may not [19,20,23] increase, but oxygen extraction is increased [19,20, 23]. Spahn et al. [21] showed that in clinical studies with anesthetized elderly patients, the hemodiluted anemia was fully compensated by an increased cardiac output and an increased oxygen extraction.

It has been shown that hemodilution increases cerebral blood flow in normal humans [24,25], and that moderate hemodilution reduces the size of infarct volume after focal cerebral ischemia in experimental dogs [26]. However, marked hemodilution, such as that producing a hemoglobin value of $6\,g \cdot dl^{-1}$, exacerbated neurologic injury after focal cerebral ischemia in isoflurane-anesthetized rabbits [27].

Hemodynamic and hemostatic change

Large volumes of plasma substitutes, such as hydroxyethyl starch (HES), dextran (DXT), gelatin (GEL), and human albumin (ALB), are used for moderate ANH. These might be associated with some problems, such as preservation of intravascular volume, hemostasis, and renal function. Vogt et al. [28] reported that there was no significant difference in hemodynamics and hemostatic and renal functions between 6% HES (MW 200000) and 5% ALB for total hip arthroplasty. In a comparison between 6% HES and 3% GEL, HES produced better intravascular volume but prolonged bleeding time at a dose of 2000 ml or more [29]. Egli et al. [30] studied the effects of progressive (30% and 60%) in vitro hemodilution with 6% HES (MW 200000), 4% GEL, and 5% ALB on blood coagulation by thromboelastography, and concluded that the three substitutes compromised blood coagulation and that the maximum effect was found with HES.

Fukusaki et al. evaluated the effects of lactated Ringer's solution (LR), 6% HES (MW 70000), and 3% DXT (MW 40000) on the hemodynamics, endocrine system, hemostasis, and blood loss during moderate ANH for total hip arthroplasty [31]. The hemodynamics, urinary output, and endocrine system involving plasma renin activity and angiotensin-aldosterone and norepinephrine responses were best stabilized by HES. It seems that HES preserves intravascular volume better than LR or DXT. Colloids such as HES or DXT have the greatest intravascular volume effect. The HES used in this study was of low molecular weight and had a mild intravascular volume effect, with a maximum of 3 to 4 h. There were no significant differences in the incidence of coagulopathy and the amount of surgical blood loss among the three substitutes.

Preoperative acute hypervolemic hemodilution (HHD)

Trouwborst et al. [32] reported that HHD without removal of blood, which reduces loss of red blood cells, allowed major surgery to be completed safely without homologous transfusion. HHD seems to be a simple as

well as time- and cost-saving alternative for ANH in patients undergoing total hip replacement, with a predicted blood loss of about 1000 ml [33].

Controlled hypotension

Efficacy to reduce operative blood loss

Controlled hypotension is a technique that has been shown to reduce intraoperative blood loss and homologous transfusion requirements and to obtain a drier surgical field. For this purpose, systolic arterial blood pressure must be decreased to less than 80 mmHg and mean arterial blood pressure (MAP) needs to be maintained at 55–60 mmHg. Thompson et al. [34] and Barbier-Böhm et al. [4] evaluated the effect of controlled hypotension on blood loss in total hip arthroplasty, and reported that controlled hypotension was an effective means of reducing intraoperative blood loss and transfusion requirements. Fukusaki et al. also reported that intraoperative blood loss during total hip arthroplasty was significantly less in induced hypotension than in ANH (Fig. 1) [35].

Effect on hemodynamics and organ function

Although many hypotensive drugs, i.e., inhaled anesthetics at higher inspired concentration, trimethaphan (TMP), nitroglycerin (NTG), sodium nitroprusside (SNP), adenosine triphosphate (ATP), and prostaglandin E_1 (PGE_1), have been used to achieve deliberate hypotension, all have potential side effects. Hypotension induced by the use of higher inspired concentrations of inhaled anesthetics alone may cause myocardial depression, resulting in reduced organ perfusion and possible hypoxia. The cardiovascular [36] and hepatic [37] effects of sevoflurane are similar to those of isoflurane, but hypotensive anesthesia with sevoflurane may cause transient impairment of renal function [38]. TMP-induced hypotension may impair important organ functions in animals [39,40] and humans [41]. The use of SNP did not affect the results of postoperative tests of cerebral, hepatic, or renal function and myocardial status in total hip arthroplasty [34]. SNP-induced hypotension produced increases in cardiac output, oxygen consumption, and intrapulmonary shunt during total hip arthroplasty [42]. In regard to renal function, Behnia et al. [43] reported that renal medullary tissue oxygenation might remain adequate in spite of a significant decrease in endogenous creatinine clearance during the SNP-induced hypotensive period. In regard to hepatic function, SNP does not lead to hepatic hypoxia during a decrease in systemic blood pressure by as much as 40% of the baseline in dogs [44]. Chauvin et al. [45] reported that hepatic plasma flow did not decrease, despite a decrease of 20% to 60% in blood pressure when the cardiac index was maintained during SNP hypotension in humans, and that cardiac output was the main factor controlling hepatic circulation. In terms of tissue oxygenation by microcirculatory investigation, NTG may be preferable to SNP for deliberate hypotension [46]. NTG-induced hypotension produces a decrease in cardiac output resulting from a reduction in central blood volume due to venous pooling of blood in humans [47]. ATP-induced hypotension may cause atrioventricular nodal block [48], transient renal vasoconstriction [49], and splanchnic ischemia. Crawford et al. [50] demonstrated that ATP was a potent vasodilator of portal tributary and hepatic arterial vasculature in the rat and that the splanchnic hemodynamic effects of ATP predominated over those of halothane and sevoflurane.

As a hypotensive agent, PGE_1 has several advantageous effects, e.g., positive inotropic action [39,51] and increase in renal blood flow and diuresis [52]. PGE_1 has been used safely to induce hypotension for reducing blood loss during mastectomy [52], total hip arthroplasty [53], and cerebral aneurysm surgery [54]. Fukusaki et al. reported that renal tubular function was well maintained during prolonged PGE_1-induced hypotension [55] and that hepatocellular damage did not occur during and after PGE_1-induced hypotension under sevoflurane anesthesia in the prone-position [56].

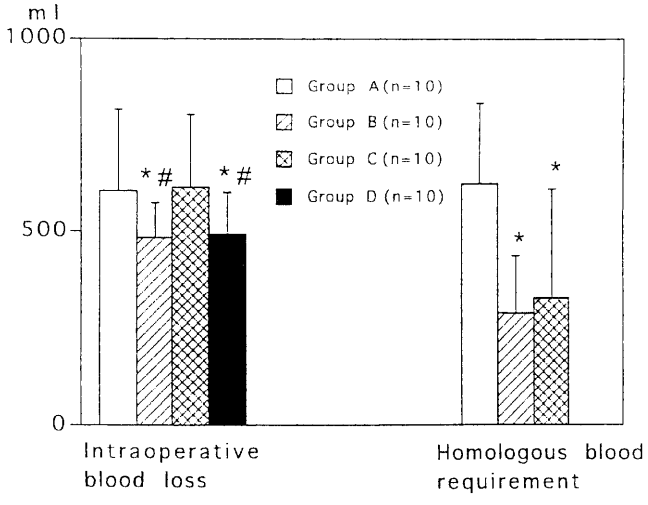

Fig. 1. Intraoperative blood loss and homologous blood requirement during total hip arthroplasty (mean ± SD) [35]. *Group A*: control. *Group B*: controlled hypotension alone. *Group C*: hemodilution alone. *Group D*: hemodilution and controlled hypotension. $^{*}P < 0.05$ *vs* group A, $^{\#}P < 0.05$ *vs* group C (from Fukusaki et al. [35])

Combination of ANH and controlled hypotension

Physiology: animal studies

Oxygen delivery to the tissues may be at risk during hemodilution combined with hypotension, in which either the oxygen-carrying capacity or the perfusion pressure is decreased. Plewes et al. [57] evaluated the cardiovascular responses to ANH and controlled hypotension induced with TMP, e.g., 23% of hematocrit and 55 mmHg of MAP, in dogs anesthetized with halothane. They found that 30 min after administration of the combination, blood flow to the heart, brain, and kidney was maintained and the calculated oxygen delivery showed minor decreases. After 90 min, blood flow and oxygen delivery showed significant decreases. They concluded that for at least 30 min the first, the effects on hemodilution and hypotension were relatively safe, but by 90 min, oxygen delivery to important tissue beds was not be preserved. Crystal et al. [58,59] studied myocardial, systemic, and regional hemodynamics during ANH and controlled hypotension in anesthetized dogs. During SNP-induced hypotension combined with hemodilution, e.g., 24% of hematocrit and 50 mmHg of MAP, for as long as 60 min, the myocardial oxygen, balance of supply and demand was well maintained under halothane anesthesia, whereas the coronary reserve and oxygen supply to the kidney were compromised [58]. A combination of ANH and ATP-induced controlled hypotension, e.g., 22% of hematocrit and 51 mmHg of MAP for 60 min, had a mixed effect on regional oxygen supply in anesthetized dogs. It increased the oxygen supply in the myocardium well above required levels, whereas it reduced the oxygen supply in most other body tissues, including the brain and kidney [59].

In a situation of hypotension with hemodilution, a protective role of anesthesia, i.e., decreased oxygen demand, also has been indicated in some tissues [60]. Oka et al. [61] investigated hemodynamics and regional blood flow under ANH and controlled hypotension in halothane-anesthetized dogs, and suggested that the combination of ANH with ATP-induced hypotension would be safer than that of ANH with TMP-induced hypotension with respect to an increase in cardiac output. However, renal cortical blood flow showed a decrease with the use of either combination.

Physiology: human studies

When controlled hypotension is combined with ANH in humans, the anesthetics and the hypotensive agent should not inhibit the normal physiologic cardiovascular response to ANH. Inhaled anesthetics depress the baroreflex-induced increase in heart rate, but isoflurane is the least depressive [62]. PGE_1 may be an appropriate hypotensive drug during hemodilution, because the compensatory mechanisms, i.e., increased flow and tissue oxygen extraction, are based on increased cardiac output. SNP is a preferred hypotensive drug with respect to cardiovascular effects, but it has potential cyanide toxicity. The combination of a hematocrit level of 22% to 25% with an MAP of 55 to 60 mmHg would be commonly used effectively to reduce surgical blood loss and homologous transfusion. We studied the effects of the combination of ANH

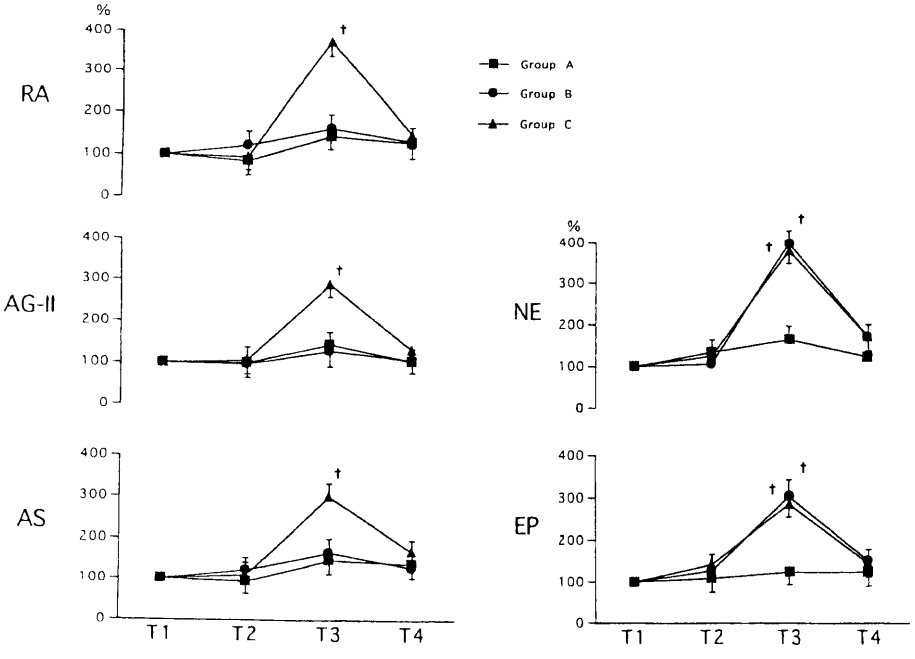

Fig. 2. Time courses of percent change in plasma renin activity (*RA*), plasma concentration of angiotensin II (*AG-II*), aldosterone (*AS*), norepinephrine (*NE*), and epinephrine (*EP*) (mean ± SEM; $n = 10$ for each value) [63]. *Group A*: hemodilution alone. *Group B*: controlled hypotension alone. *Group C*: hemodilution and controlled hypotension. *T1*, Before hemodilution in groups A and C (after induction of anesthesia in group B); *T2*, after hemodilution in groups A and C (before induction of hypotension in group B); *T3*, 80 min after start of hypotension in groups B and C (80 min after start of surgery in group A); *T4*, 60 min after recovery from hypotension in groups B and C (60 min after end of surgery in group A). $^{\dagger}P < 0.05$ *vs T1* (from Fukusaki et al. [63])

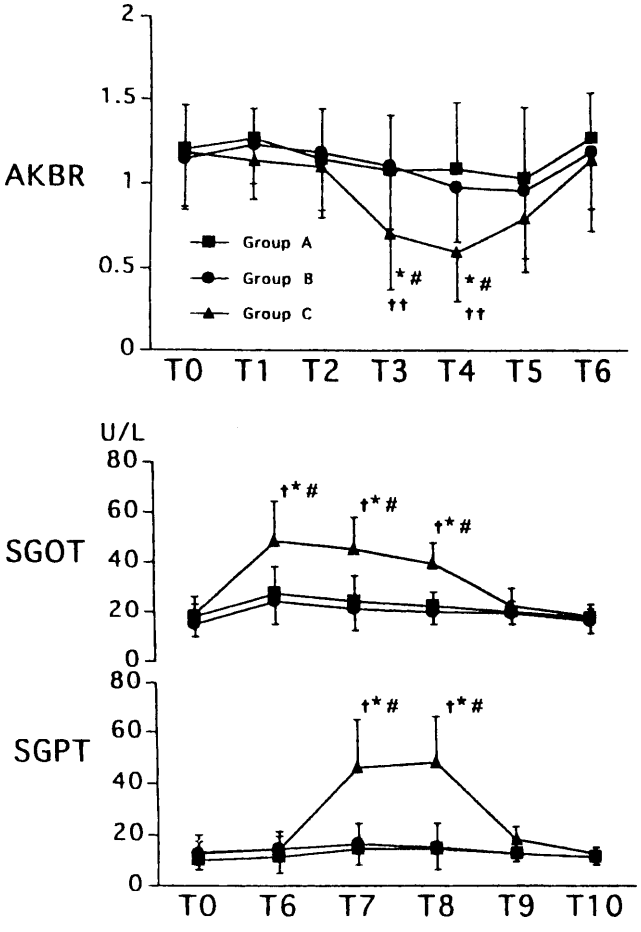

Fig. 3. Time courses of parameters for hepatic cellular function (mean ± SD; $n = 10$ for each value) [66]. *AKBR*, Aceto-acetate/3-hydroxybutyrate; *SGOT*, serum glutamic oxaloacetic transaminase; *SGPT*, serum glutamic pyruvic transaminase. *Group A*: controlled hypotension alone. *Group B*: hemodilution alone. *Group C*: hemodilution and controlled hypotension. *T0*, Before hemodilution; *T1*, after hemodilution; *T2*, 60 min after start of hypotension; *T3*, 120 min after start of hypotension; *T4*, 180 min after start of hypotension; *T5*, 60 min after recovery from hypotension; *T6*, 1st postoperative day; *T7*, 7th postoperative day; *T8*, 14th postoperative day; *T9*, 21st postoperative day; *T10*, 30th postoperative day. †$P < 0.05$ *vs* T0; ‡$P < 0.01$ *vs* T0; *$P < 0.05$ *vs* group A; #$P < 0.05$ *vs* group B [from Fukusaki et al. [66])

using DXT or HES with controlled hypotension induced by PGE_1 on endocrine responses [63], tissue oxygenation in the gastrointestinal mucosa [64], and hepatic and renal function [65] during isoflurane anesthesia for major hip surgery. Although the combined method caused an increase in catecholamine and renin-angiotensin-aldosterone activities, these responses were within physiologic range, and would play an important role in maintaining hemodynamics (Fig. 2) [63]. Hepatic function was maintained during and after use of the combination for 80 min, whereas prolonged use of the

Table 1. Blood loss and homologous blood requirement in orthopedic surgery during acute normovolemic hemodilution or controlled hypotension

Authors	Surgery	Sample size				Blood loss (ml)				Homologous blood requirement (ml)			
		Control	ANH	CH	ANH + CH	Control	ANH	CH	ANH + CH	Control	ANH	CH	ANH + CH
van der Linden et al. [19]	Hip	10	10	—	—	I: 842 P: 328	961 492	—	—	1085	165[a]	—	—
Thompson et al. [34]	Hip	9	—	21	—	I: 1200 P: 650	—	500 650	—	1330	—	250[a]	
Yukioka et al. [53]	Hip	28	—	29	—	I: 667 P: 309	—	480 320	—	468 368	—	280[a] 440	
Barbier-Böhm et al. [4]	Hip	10	9	11	—	I: 900 P: 530	1050 400	320[a] 460	—	1485	135	500	—
Fukusaki et al. [35]	Hip	10	10	10	10	I: 606 P: 568	612 506	483[a,b] 519	492[a,b] 491	622	328[a]	288[a]	0
Mielke et al. [33]	Hip	—	23	—	—	—	I: 545 P: 730	—	—	—	250	—	—
Mandel et al. [7]	Spine	—	29 (HHD)	—	119	—	1430	—	1112	—	1150	—	90[b]
Hur et al. [8]	Spine	—	68	77	—	—	1170	777[a]	—	—	975	700[b]	—

ANH, Acute normovolemic hemodilution; CH, controlled hypotension; HHD, acute hypervolemic hemodilution; I, intraoperative blood loss; P, postoperative blood loss.
[a] $P < 0.05$ *vs* control.
[b] $P < 0.05$ *vs* ANH.

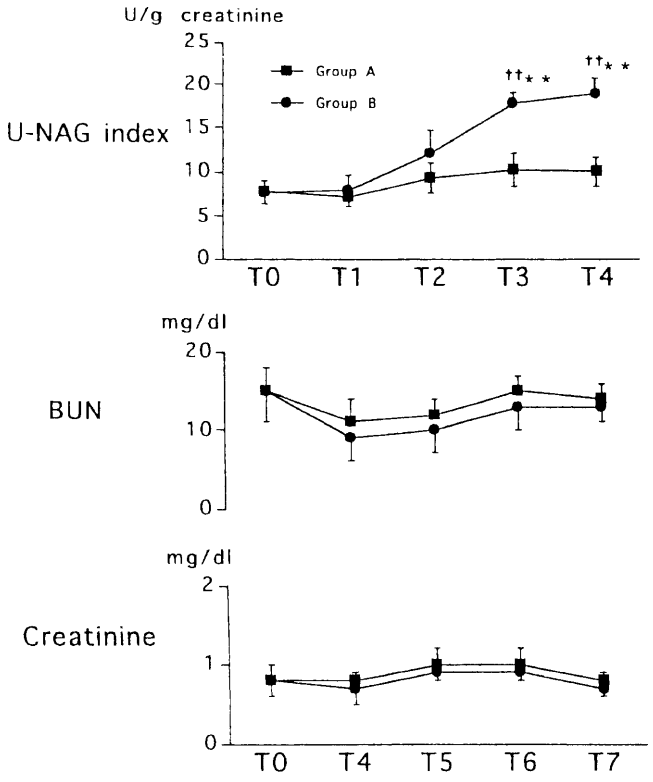

Fig. 4. Time courses of change in renal function (mean ± SEM; $n = 10$ for each value) [65]. *U-NAG index*, Urine *N*-acetyl-β-D-glucosaminidase; *BUN*, blood urea nitrogen. *Group A*: controlled hypotension with mild hemodilution. *Group B*: controlled hypotension with moderate hemodilution. *T0*, Before hemodilution; *T1*, after hemodilution; *T2*, 80 min after start of hypotension; *T3*, 60 min after recovery from hypotension; *T4*, 1st postoperative day; *T5*, 3rd postoperative day; *T6*, 7th postoperative day; *T7*, 14th postoperative day. $^{\dagger\dagger}P < 0.01$ *vs* T0; and $^{**}P < 0.01$ *vs* group A [from Fukusaki et al. [65])

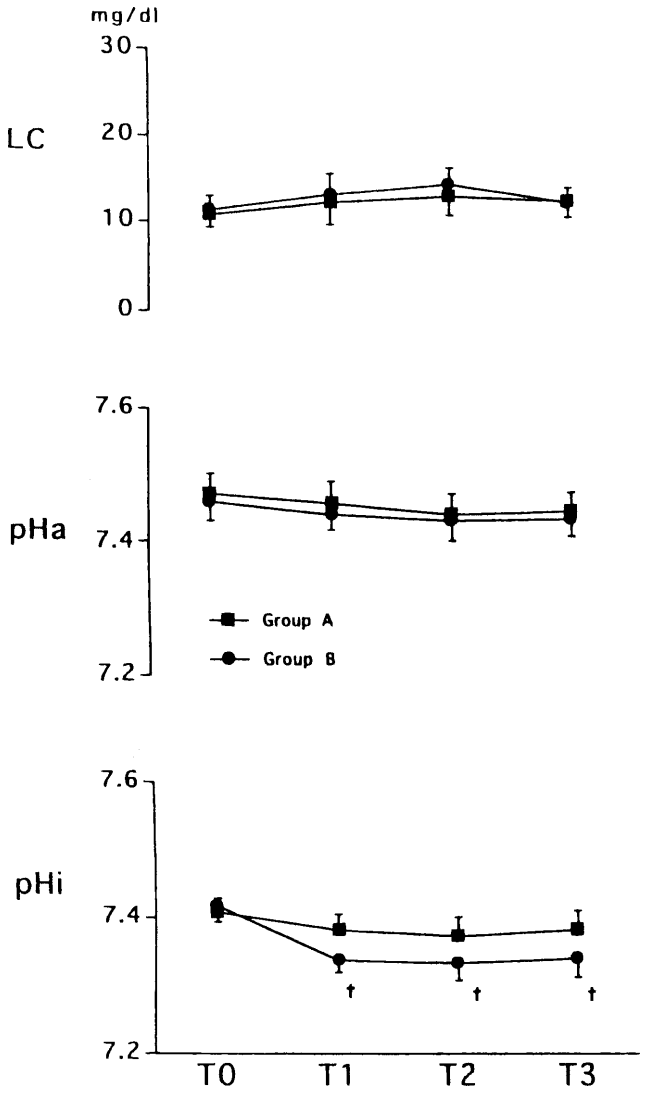

Fig. 5. Time courses of changes in lactate (*LC*), arterial blood pH (*pHa*), and gastric intramucosal pH (*pHi*) (mean ± SD; $n = 10$, for each value) [64]. *Group A*: controlled hypotension with mild hemodilution. *Group B*: controlled hypotension with moderate hemodilution. *T0*, Before hemodilution; *T1*, after hemodilution; *T2*, 80 min after start of hypotension; *T3*, 60 min after recovery from hypotension; *T4*, 1st postoperative day. $^{\dagger}P < 0.05$ *vs* T0 (from Fukusaki et al. [64])

combination for more than 120 min impaired hepatic function (Fig. 3) [66]. The combination damaged renal tubular cells, as shown by an increase in urinary *N*-acetyl-β-D-glucosaminidase. However, the damage seemed to be minimal from a clinical viewpoint, because blood urea nitrogen and serum creatinine were within the normal range after surgery (Fig. 4) [65]. ANH in itself might impair oxygenation in gastric mucosa in terms of gastric intramucosal pH study, whereas the combination of ANH with controlled hypotension would not enhance the impairment of splanchnic oxygen supply in adult (Fig. 5) [64] or elderly [67] patients. The impairment of tissue oxygenation in gastric mucosa during ANH seemed to have no clinical importance, because there were no gastroenterologic problems after surgery.

Cerebral and myocardial tissue oxygenation is maintained during use of the combined method because PGE_1-induced hypotension can preserve cerebral blood flow, CO_2 reactivity [68], coronary blood flow, and myocardial oxygen supply [39]. There were no neurological problems and no significant ischemic ST-T changes in the electrocardiogram during and after surgery.

The combination of acute hemodilution using synthetic plasma volume expanders and controlled hypotension induced by SNP, NTG, or PGE_1 may cause further deterioration of hemostatic disturbances, i.e., inhibition of platelet aggregation, reduction in platelet adhesiveness, and structural alterations in fibrin clots. SNP and NTG, in clinically relevant dosages, have been

Table 2. Recommended techniques for the combination of acute normovolemic hemodilution and controlled hypotension

Methods	Procedures
Patients	Excluded: patients with untreated hypertension, ischemic heart disease, cerebral infarction, renal or hepatic dysfunction, or anemia (Hgb $< 11\,g\cdot dl^{-1}$). Age: <80 years
Infusion	Preoperative: LR (AR) with Glu, $15\,ml\cdot kg^{-1}\cdot 4\,h^{-1}$. Intraoperative: LR (AR), $6–8\,ml\cdot kg^{-1}\cdot h^{-1}$ Postoperative: LR (AR) with Glu, $2\,ml\cdot kg^{-1}\cdot h^{-1}$. Additional: LR (AR), 3 times blood loss
Anesthesia	Premedication: H2-blockade, atropine 0.5 mg, hydroxyzine $1\,mg\cdot kg^{-1}$. Anesthesia: N_2O-O_2-isoflurane or sevoflurane
Monitoring	Invasive arterial blood pressure, SpO_2, P_{ETCO_2} (35 mmHg), blood gases, body temperature, ECG
ANH	Mild ANH (predicted Hct 30%–32%) and moderate ANH (predicted Hct 22%–25%): drawing 400–1000 ml of blood and replacing it with same amount of 6% HES or 3% DXT
Controlled hypotension	Hypotensive drugs: PGE_1. MAP: 55–60 mmHg. Period: <120 min under normothermia
Blood transfusion	Autologous (fresh blood with ANH, shed blood with Cell Saver): intraoperative blood loss > 300 ml. Homologous transfusion trigger Hgb $< 7.0\,g\cdot dl^{-1}$

ANH, Acute normovolemic hemodilution; *LR*, lactated Ringer's solution; *AR*, acetated Ringer's solution; Glu, glucose; Hgb, hemoglobin; SpO_2, percutaneous oxygen saturation; P_{ETCO2}, end-tidal carbon dioxide tension; ECG, electrocardiogram; Hct, hematocrit; HES, hydroxyethyl starch; DXT, dextran; PGE_1, prostaglandin E_1; MAP, mean arterial blood pressure.

shown to alter hemostatic mechanisms and inhibit platelet function significantly [69,70], but TMP provides control of arterial pressure with preservation of platelet function [71]. Although it is known that PGE_1 may impair hemostatic function [72,73], the coagulation-fibrinolysis system shows no siginficant changes during PGE_1-induced hypotension at a clinical dosage [74,75]. Fukusaki et al. have concluded that ANH to a hematocrit of 22%–23% causes a slight coagulopathy, which is not enhanced when combined with PGE_1-induced hypotension, and the disturbance would have minor clinical significance [35].

Clinical application

The major advantage of the combination of ANH and controlled hypotension is that surgical blood loss can be reduced and autologous fresh blood containing rich coagulant factors can be obtained. Intraoperative blood loss with use of the combined method was significantly less than that with ANH alone, and there was no homologous transfusion requirement with the combined method (Fig. 1, Table 1) [35]. Thus, the combined method has the advantage that no predeposit of blood is required. However, patients with ischemic heart disease, untreated hypertension, cerebral infarction, hepatic dysfunction, renal dysfunction, coagulopathy, or anemia (hemoglobin $<11\,g\cdot dl^{-1}$) should not receive the combination treatment.

Anesthesia is maintained with 60% nitrous oxide in oxygen supplemented with isoflurane and fentanyl. Ventilation is controlled to maintain to end-tidal CO_2 tension at approximately 35 mmHg using vecuronium. Lactated Ringer's (LR) or acetated Ringer's (AR) solution containing 5% glucose is infused at $15\,ml\cdot kg^{-1}$ for a period of 4 h before surgery, and LR or AR solution is continued at a rate of 6 to $8\,ml\cdot kg^{-1}\cdot h^{-1}$ during surgery. Additional LR or AR is infused at three times the amount of blood loss. The rectal temperature is maintained at 36° to 37°C by a circulating water blanket and adjustment of room temperature.

After induction of anesthesia, mild or moderate ANH is produced by drawing 400–1000 ml of blood and replacing it with the same amount of colloid solution, i.e., 3% DXT or 6% HES. Controlled hypotension is started before surgery, during which MAP is maintained at 55 to 60 mmHg. The autologous blood is transfused when the intraoperative blood loss exceeds 300–400 ml or the controlled hypotension has finished, and the shed blood salvaged with a Cell Saver also is transfused after surgery. Homologous transfusion must be initiated if the hemoglobin value is reduced to $7.0\,g\cdot dl^{-1}$ or less during the perioperative period. Recommended techniques for the combined method are shown in Table 2.

Postoperative complications

In the combined method reported by Fukusaki et al., the hemoglobin concentration recovered to 91% of the preoperative value 4 weeks after surgery [76]. There were no significant differences in the recovery of the surgical wound, rehabilitation schedule, hospital stay, and the occurrence of thrombophlebitis compared with patients treated with controlled hypotension with nonhemodilutional autologous transfusion [76]. Brown et al. [77] reported six cases of ischemic optic neuropathy exhibiting postoperative vision loss after massive blood loss during surgery, in which unintentional hemodilution and uncontrolled hypotension occured. No patients had cardiac, neurologic, renal, or gastroenterologic problems postoperatively after undergoing treatment by the intentional combined method.

Summary

The combination of ANH with controlled hypotension is effective and safe under the conditions of hematocrit 22%–25%, MAP 55–60 mmHg, duration 120 min or less, and predicted blood loss about 1000 ml. The addition of mild hypothermia may be useful for the protection of organ function when the combined method is applied for more than 120 min.

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