257 217

Int. J. Oral Maxillofac. Surg. 1999; 28: 137–142
Printed in Denmark . All rights reserved

Copyright © Munksgaard 1999

International Journal of
Oral & Maxillofacial Surgery
ISSN 0901-5027

Medicine

Multimodal strategy for reduction of homologous transfusions in cranio-maxillofacial surgery

R. G. Rohling[1], P. E. Haers[1], A. P. Zimmermann[1], U. Schanz[2], R. Marquetand[1], H. F. Sailer[1]
[1]Department of Cranio-Maxillofacial Surgery and [2]Department of Internal Medicine (Hematology), University Hospital Zurich, Switzerland

R. G. Rohling, P. E. Haers, A. P. Zimmermann, U. Schanz, R. Marquetand, H. F. Sailer: Multimodal strategy for reduction of homologous transfusions in cranio-maxillofacial surgery. Int. J. Oral Maxillofac. Surg. 1999; 28: 137–142.
© Munksgaard, 1999

Abstract. The transfusion of homologous blood carries well-known risks that have prompted efforts to develop alternative techniques. Such measures are of particular interest to patients undergoing elective procedures. A total of 204 patients, out of 1470 patients who consecutively underwent major cranio-maxillofacial procedures under general anesthesia over a two-year period, were enrolled in a prospective protocol to reduce homologous transfusion requirements when a blood loss in excess of 500 ml was anticipated. The data were compared with the results of a retrospective control group (n=2890) covering major procedures during the previous four years, when blood-saving measures were applied occasionally, but not based on a global strategy. Techniques for the reduction of homologous transfusions were acute normovolemic hemodilution, controlled moderate hypotension, cell saver and predeposit autologous blood. In addition, preoperative administration of human recombinant erythropoietin was introduced during the last year of the study. These techniques were applied individually or in combination, depending on contraindications specific for each technique, using invasive monitoring in order to maintain intraoperative hemodynamic stability. The goal of this study was to examine the extent to which homologous transfusions may be reduced with the systematic application of transfusion-sparing techniques. Of 204 patients qualifying for the transfusion-sparing protocol, 30 received homologous transfusions. In comparison to the control group, utilization of transfusion-sparing techniques had doubled. The overall reduction in the use of homologous transfusions was highly significant. When acute normovolemic hemodilution, controlled moderate hypotension and the cell saver were used in combination, a greater reduction in homologous transfusions was achieved than with the use of either a single modality or combination of any two. No transfusions were required in patients pretreated with erythropoietin.

Key words: cranio-maxillofacial surgery; homologous blood reduction; acute normovolemic hemodilution; controlled moderate hypotension; cell saver; erythropoietin.

Accepted for publication 3 October 1998

Current methods for the reduction of the number and frequency of homologous red cell transfusions have become an established part of anaesthetic practice. The routine availability of acute normovolemic hemodilution during the induction of anesthesia, controlled moderate hypotension, the cell saver for intra- and postoperative autotransfusion and predeposit autologous blood donation, has created opportunities to transform sporadic efforts into a coherent strategy. As a promising new adjunct, human recombinant erythropoietin offers the added benefit of elev-

Table 1. Contraindications and complications of blood-saving measures

Method	Contraindications	Complications
Acute normovolemic hemodilution (ANH)	Anemia, hypovolemia, significant cardiovascular disease, severe respiratory insufficiency, systemic infections, sepsis, fever of unknown origin, coagulation disorders, protein malnutrition	Tissue hypoxia
Controlled moderate hypotension	Cerebrovascular insufficiency, coronary and/or valvular heart disease, increased intracranial pressure, impaired pulmonary, hepatic or renal function, anemia	Irreversible ischemias
Cell Saver	Infected wounds, tumor ablative surgery (except with intraoperative irradiation of blood)	Clotting abnormalities
Predeposit autologous donation	see ANH	see ANH
Preoperative rh-Epo	Starting hematocrit 45%, thrombocytosis, hypertension	"Influenza-like syndrome"

ating the hematocrit in the preoperative period.

Homologous as well as autologous blood products are subject to common error, i.e. the release of incompatible blood and contamination with bacterial organisms due to inadequate preservation or improper handling during storage and transport. Risks inherent in homologous transfusions are the transmission of bacteria, viruses and protozoa, as well as alloimmunization and immunomodulation; transfusion-induced immunosuppression may present acutely with an increased rate of postoperative infection and may also contribute to a higher rate of tumor recurrence [3,7,12,15]. The advantages of reduction in homologous transfusions can be summarized as follows: reduction of posttransfusion hepatitis and of HIV transmission as well as of infectious agents carried by leukocytes (e.g. cytomegalovirus), improved immune defenses with a lower rate of infection and tumor recurrence, reduction of HLA-alloimmunization by allogenic leukocytes, reduction of platelet refractoriness and transplant rejection, and a decrease in logistic difficulties, especially in cases of rare blood groups.

The present study was undertaken to evaluate the possibility to eliminate or reduce intra- and postoperative homologous transfusions with the systematic use of currently available transfusion reduction methods during extensive maxillofacial surgical procedures.

Material and methods

Over a two-year period (1994–1996), all patients with an anticipated blood loss of at least 500 ml were included in the study. Informed consent was obtained in detail and patients enrolled in a rigorous protocol of transfusion reduction methods based on the contraindications specific for each technique (Table 1). All patients received antibiotic prophylaxis with clindamycine or cefuroxim. In addition, a single dose of netilmicin was given to all cell saver patients 30 minutes before retransfusing the cell saver blood. All patients got a standardized, predominantly intravenous general anesthesia. In addition to routine monitoring, electrocardiogram, pulse oximetry, continuous capnometry and temperature monitoring, the arterial pressure was recorded directly. A central venous line was placed when indicated. Urine volume was determined hourly.

When not contraindicated (Table 1), acute normovolemic hemodilution (ANH) was instituted following induction of anesthesia by phlebotomy of an average of 9 ml/kg whole blood depending on current hematocrit values and physical status. This quantity allows on average 450 ml to 700 ml blood to be retransfused to the patient at the end of the operation without lowering the hematocrit below a safe level. At the same time, an equivalent volume of hydroxyethyl starch was infused to maintain normovolemia. Whole blood was collected and stored in 500 ml bags containing 50 ml CPDA-1 as a stabilizer.

In order to elevate the operative field above the heart, patients were placed in a reverse Trendelenburg position. Controlled moderate hypotension (CMH) was induced intraoperatively by lowering blood pressure pharmacologically to a mean arterial pressure (MAP) of approximately 60 mmHg using a vasodilatator. In conjunction with appropriate intraoperative analgosedation, blood pressure was regulated with a variable infusion of phentolamine. In patients with preexisting hypertension, MAP was reduced by no more than 20% of baseline.

When not contraindicated (Table 1), extravasated blood from the operative field was collected in a cell saver (CS) reservoir, followed by separation of erythrocytes from plasma and irrigation fluid in a washing centrifuge (Compact-A, Dideco™, Mirandola, Italy).

During the second year of the study, predeposit autologous blood donation in elective surgery cases was replaced by pretreatment with recombinant human erythropoietin (rh-Epo). A subcutaneous rh-Epo dosing schedule of 200 IU/kg twice a week was instituted three weeks prior to surgery, and continued until a hematocrit of 50% was reached. Iron was supplemented in every case.

Hemoglobin, hematocrit, electrolytes and arterial blood gases were determined at intervals geared to the intraoperative situation. During ongoing blood loss, crystalloid and/or colloid solutions were administered while hematocrit was closely monitored. In healthy adults, the lower limit for intervention was a hematocrit of 20%, unless superseded by clinical judgement. Retransfusion of autologous whole blood harvested during ANH took place in reverse order, i. e. patients first received the second bag, followed by processing and retransfusion of any cell saver units. The first unit of ANH whole blood was administered as needed at the end of surgery. Homologous or predeposit autologous blood was utilized only in cases of unusually large fluid turn-over or a hematocrit below the transfusion threshold.

Intraoperative blood loss was calculated by subtracting the total volume of irrigation expended during surgery from the combined volume of whole blood stored in the cell saver reservoir, if so equipped. Blood-soaked drapes and sponges were collected, weighed and added to the first figure. This estimate was entered in the anesthesia record at the end of surgery.

A total of 204 patients, out of 1470 patients operated on in the period 1994–1996, were enrolled in the prospective protocol. In all cases involved, blood loss in excess of 500 ml was anticipated and homologous transfusion reduction methods (TRM) were ap-

Table 2. Scope of surgical procedures in study group

Surgical category	Study group
Orthognathic	43.6%
Reconstructive	17.2%
Oncologic	15.7%
Traumatologic	13.2%
Preprosthetic	7.8%
Craniofacial	2.5%

Table 3. Demographic and clinical data of patients enrolled in study group

Patients characteristics	Mean±SD; range
n (male/female)	204 (98/106)
Age (years)	32.6±16.1; 8–71
Weight (kg)	65.5±13.2; 18–112
Height (cm)	170.5±10.3; 122–195
ASA I/II/III (*n*)	131/61/12
Length of procedure (hours)	6.6±2.6; 2–20
Hematocrit preop (%)	39.7±5.1; 25–52
Hematocrit intraop (%)	29.3±3.9; 15–47
Blood loss intraop (ml)	1163±740; 500–6000
Blood pressure intraop (mmHg)	MAP: 69±6; 50–110 SAP: 100±8; 70–150 DAP: 55±6; 40–90
Temperature intraop (°C, rectally)	36.1±0.6; 34.3–38.5

ASA=American Society of Anesthesiology Classification of general health; MAP=Mean arterial pressure; SAP=systolic arterial pressure; DAP=diastolic arterial pressure.

Table 4. Comparison of use of homologous transfusion reduction methods (TRM) and homologous transfusions (HT) in control and study groups

	Patients (*n*)	TRM (*n*, %)	HT recipients (*n*, %)	HT (units)	HT/operation
Control Group					
Total	2890	176 (6.1%)	334 (11.6%)	1655	0.57
Study Group					
Total	1470	204* (13.9%)*	30* (2.0%)	141*	0.1

* $P<0.001$.

plied prospectively. Surgical bleeding of this magnitude is frequently encountered in bimaxillary orthognathic procedures, major oncologic, traumatologic, reconstructive or preprosthetic procedures (Table 2). These data were compared to retrospective data from 2980 patients operated on previously (1990 – 1994). The number of homologous units transfused was counted and any efforts to reduce homologous transfusions were noted from the anesthesia records.

The statistical significance of differences in the quantity of homologous blood was tested with the Mann Whitney U-test. A value of $P<0.05$ was considered statistically significant.

Results

Table 3 lists patient age, gender, height, weight, pre- and intraoperative hematocrit, blood loss during surgery, intraoperative body temperature and blood pressure, length of procedure and risk classification. The procedures performed in these 204 cases were orthognathic surgery (43.6%), reconstructive surgery (17.2%), oncologic surgery (15.7%), traumatology (13.2%), preprosthetic surgery (7.8%) and craniofacial surgery (2.5%). These procedures in which blood-saving measures were applied (according to the criterion of expected blood loss exceeding 500 ml), constitute 13.9% of the whole group ($n=1470$). This is significantly more than in the control group ($n=2890$), in which similar measures were applied in only 176 cases (6.1%) (Table 4). In none of the cases which were not selected for the blood-saving measures, were homologous blood transfusions necessary.

In 30 of the 204 procedures, additional homologous transfusions were indicated. In 26 of these, massively infected surgical wounds or malignancy prohibited the use of the cell saver. In 7 of these 30 cases, the preoperative hematocrit was too low to perform acute normovolemic hemodilution safely. Compared to the control group, there was a reduction in the percentage of recipients of homologous blood (2.0% *versus* 11.6% in the control group), which was significant ($P<0.001$). The increase in the use of blood-saving measures, together with the corresponding reduction in homologous transfusions, is illustrated in Figure 1.

Controlled moderate hypotension (CMH) was employed in all 204 patients, with an average MAP of 69±6 mmHg. It was possible to eliminate sustained episodes of relative intraoperative hypertension (average mean systolic pressure: 100±8 mmHg) in all cases. Following introduction of the study protocol, those patients in whom other techniques were contraindicated and therefore were restricted to the use of CMH alone, were also the ones requiring the most homologous transfusions (43.7%; see Table 5). In combination with either CS or ANH, only 33.3% and 13.7%, respectively, received additional homologous transfusions. Thus, use of triple and quadruple combinations resulted in the lowest percentage of patients requiring donor blood. No homologous transfusions were needed when rh-Epo was used in addition to ANH, CMH and CS. Predeposit autologous blood donations (PBD) were taken in 64/204 cases and retransfused in 28/64 (44%), whereas in the control group, all 159 PBD patients received the autologous transfusions. Only 50 of these 159 patients had the

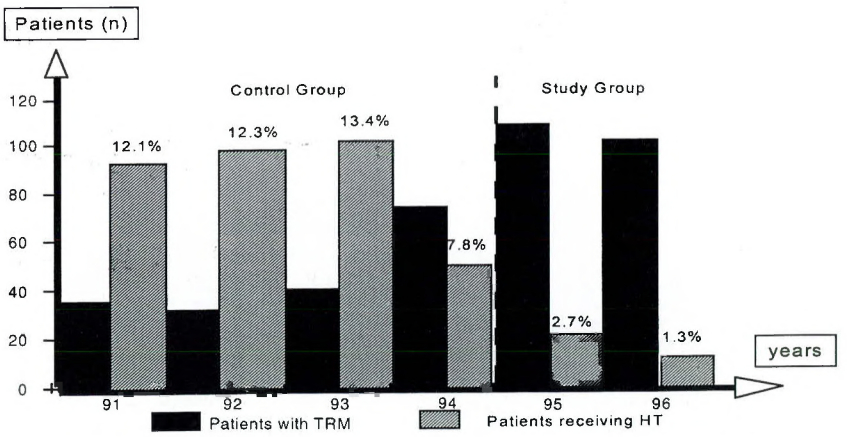


Fig. 1. Reduction of homologous transfusions (HT) with increasing use of homologous transfusion reduction methods (TRM).

Table 5. Effect of homologous transfusion reduction methods (TRM) on homologous transfusions (HT)

	Control group Patients (*n*) with TRM		Study group Patients (*n*) with TRM	
TRM	no HT	with HT	no HT	with HT
Single modality	22	16 (71.4%)	16	7 (43.7%)
CMH	43	12 (27.9%)	0	0
ANH	56	12 (21.4%)	0	0
CS				
Dual modality	13	4 (30.7%)	0	0
ANH+CS	13	2 (15.4%)	3	1 (33.3%)
CS+CMH	19	1 (5.2%)	138	19 (13.7%)
ANH+CMH				
Triple combination	10	1 (10%)	37	3 (8.1%)
ANH+CS+CMH	0	0	8	0
rh-Epo+ANH+CMH				
Quadruple combination				
rh-Epo+CS+ANH+CMH	0	0	2	0
Total	176	48 (27.3%)	204	30 (15%)

benefit of transfusion reduction methods, of whom homologous transfusions became necessary in seven. Of patients in whom no special measures to reduce the transfusion requirements were employed, twelve required additional homologous blood. Combined blood-saving measures were not used frequently in the control group; only ten patients received a triple combination of CMH, CS, and ANH during that period (Table 5).

In comparison to the control group, the overall consumption of homologous transfusions in the study group was reduced by 83%.

Discussion

A correct estimate of intraoperative blood loss in maxillofacial procedures is difficult. A study using radioactively labeled erythrocytes showed that, in 8 of 13 patients, the estimated blood loss and true loss of erythrocyte mass differed by 56–70% and estimates were usually too low[22]. In large maxillofacial procedures, the quantity of blood entering the suction apparatus only provides a rough approximation of the true blood loss[10]. Therefore, supervision of fluid status for maintenance of normovolemia and hemodynamic stability is of vital importance.

There are several studies concluding that bimaxillary osteotomies entail a greater blood loss than most other procedures within the scope of maxillofacial surgery [6,14]. In a series by SAMMAN et al.[21], 78 of 291 patients (27%) undergoing bimaxillary osteotomies received homologous transfusions. When these outcomes are contrasted with the present data, the impact of systematically applied transfusion reduction methods in patients enrolled in our prospective study is apparent: only two in 71 patients (2.9%) with bimaxillary osteotomies required homologous blood.

In a discussion of individual techniques for the reduction of homologous transfusion, acute normovolemic hemodilution (ANH) has emerged as a safe, cost-effective and simple basic tool in the conservation of homologous blood[16]. For the specialty of maxillofacial surgery, BONNET et al.[1] found that ANH results in improved skin flap viability. PELLON et al.[18] serially assessed facial tissue density using radiotelemetry in 16 patients treated with ANH and 16 non-hemodiluted controls. During the first postoperative week, no adverse influence on facial edema was noted.

The primary goal of ANH is the storage of autologous whole blood which is promptly substituted with crystalloid and colloid solutions. Its immediate effect is a reduction in hematocrit which translates into loss of relatively erythrocyte-poor blood intraoperatively. The major advantage of this technique is the ability to retransfuse autologous whole blood with high-quality erythrocytes and fully functional clotting factors. The main risk inherent in phlebotomy is tissue hypoxia in cases of poor cardiovascular compensation. Hence, patient safety is contingent upon the recognition of contraindications as well as individualized invasive monitoring. A decision crucial to the technique is the extent of hemodilution, which is principally determined by pre-existing medical illness. There is no consensus in the literature regarding the intra- and postoperative transfusion threshold: in ASA I and ASA II patients (i.e. with no or mild/moderate systemic disorder, respectively), values for the critical hematocrit vary from 18% to 21%, whereas for ASA III patients (with severe systemic disorder), a hematocrit of 24% is considered the lowest tolerable[19,23]. It is generally agreed that low hematocrit values are acceptable only when normovolemia is maintained. Continuous invasive monitoring and blood gas analyses at closely-spaced intervals play a crucial role in the maintenance of stable cardiopulmonary and hematological parameters. In this study, ANH was performed in 185 of 204 procedures. The absolute transfusion threshold was a hematocrit of 20% for healthy subjects. No postoperative complications attributable to excessively low hematocrits were noted.

Controlled moderate hypotension (CMH) targets hemodynamics in relation to the rate of surgical bleeding. In an early study comparing maxillofacial surgical patients with normotensive and hypotensive management during general anesthesia (average MAP: 98 *versus* 73 mmHg), SCHABERG et al.[22] proved that lowering the blood pressure reduces blood loss. Studies by CHAN et al.[2] and WASHBURN et al.[25] claim a significant reduction in homologous transfusions with a lower MAP. A meta-analysis on the efficacy of controlled hypotension as a single measure showed that blood loss was reduced by 50±18% on average, and homologous transfusions by 59±20%[17]. By contrast, VON BORMANN et al.[24] were not able to detect a comparable transfusion-sparing effect. From the standpoint of safety for patients due to undergo CMH, a careful search for possible contraindications should be an integral part of the pre-anesthetic workup. For the prevention of organ hypoperfusion, especially when combined with ANH, continuous invasive cardiopulmonary monitoring is mandatory. The recommendation of some authors[24] to abstain from a combination of ANH with controlled hypotension due to concern about myocardial oxygen delivery appears overstated. In our study, 138 of 204 patients toler-

ated a combination of both techniques with no adverse consequences. However, MAP was lowered to no less than 60 mmHg.

The cell saver as a single measure does not reliably prevent the need for homologous transfusions when blood loss is high. Rather, it should be viewed as part of a coordinated concept in the preservation of homologous blood. The erythrocyte suspension generated from salvaged blood is of high quality. This avoids the retransfusion of undesirable ingredients of the autotransfusate since metabolites of the clotting cascade and free hemoglobin are reduced to clinically insignificant levels[9]. In the specialty of maxillofacial surgery, high bacterial counts in the surgical field currently represent a relative, if not absolute, contraindication to its use[5]. In a prospective study by Locher & Sailer[13] on pyrexia associated with use of the cell saver in 18 maxillofacial surgical patients, a rise in body temperature between 0.5 and 3°C was noted on the first postoperative day. By contrast, no cases of postoperative hyperthermia occurred in the present study. However, blood cultures taken fifteen and 120 minutes after retransfusion in patients with transoral cell saving showed the presence of the same microorganisms which were detected in blood cultures of the cell saver suspension and there was a significant increase of cytokines at these time intervals[20]. The bacterial contamination in transoral cell-saving has also been reported by others[11]. The impact on the dissemination of bacterial organisms, systemic cytokine levels and clinical implications are currently under investigation so that no final recommendations on the cell saver in maxillofacial surgery can be made at this time. These recommendations will probably depend on the modality of cell-saving (transoral *versus* transcoronal) and the indication of the intervention. Only 42 of 204 patients were transfused with the erythrocyte suspension generated by the cell saver. Its sparing use reflects contraindications to the retransfusion of erythrocytes in a population of patients dominated by trauma victims with massively infected wounds, and in the presence of tumor.

When the triple combination of TRM (ANH, CMH, CS) was complemented by preoperative administration of rh-Epo in place of predeposit autologous blood (PBD), homologous transfusions were no longer necessary. It is our impression that patients find the application of rh-Epo more agreeable and less exhausting in comparison with the PBD. A higher preoperative hematocrit increases the safety and efficacy of ANH. The use of rh-Epo may obviate the need for PBD and its risks. At the present time, the routine use of rh-Epo as an adjunct to ANH is hampered by its relatively high cost.

It has become apparent from the prospective study that PBD plays a subordinate but not an negligible role, at least as long as rh-Epo does not become routine practice. The systematic use of TRM adequately compensated for surgical bleeding in the majority of cases. However, at 44%, the rate of retransfusion of predeposit autologous blood remains high. Under no circumstance should PBD be viewed as a substitute for established intraoperative transfusion reduction methods; the outcome would be a needlessly high rate of homologous transfusions. The use of predeposit autologous blood demands the same scrutiny as homologous transfusions and should be relegated to instances when the potential of ANH, CMH and CS has been fully exploited.

Since the introduction of a multimodal blood-saving strategy, none of the patients operated on in the absence of transfusion-sparing measures required homologous transfusions. This indicates that patients likely to incur a high blood loss were appropriately selected for TRM. The present study leaves no doubt that the consistent multimodal use of transfusion-sparing techniques is highly effective. One of our principal findings was that the most significant reductions in homologous transfusions are achieved by the combination of different methods, a contention validated by several recent reports[4,8]. This study documents the dramatic impact of a rigorously applied protocol for the conservation of homologous transfusions in major cranio-maxillofacial surgery. Competent perioperative surveillance of hemodynamic and hematological data, acceptance of a moderately low hematocrit and appropriate criteria for administration of homologous products are fundamental requirements for the safe and effective execution of a transfusion-sparing protocol.

References

1. Bonnet M, Julia J, Mathieu-Daudé J, du Cailar J. Intéret de l'hémodilution en chirurgie maxillofaciale sur l'oedème traumatique postopératoire et sur la vitalité des lambeaux. Ann Fr Anaesth Réanim 1986: **5**: 243–8.
2. Chan W, Smith DE, Ware WH. Effects of hypotensive anesthesia in anterior maxillary osteotomy. J Oral Surg 1980: **38**: 504–8.
3. Dodd R. The risk of transfusion-transmitted infection. N Engl J Med 1992: **327**: 419–21.
4. Haberkern M, Dangel P. Normovolemic hemodilution and intra-operative autotransfusion in children: experience with 30 cases of spinal fusion. Eur J Pediatr Surg 1991: **1**: 30–5.
5. Hansen E, Taeger K. Intraoperative Autotransfusion mit Blutbestrahlung bei Tumoroperationen: Grundlage und Praxis. Anästhesiol Intensivmed 1996: **6**: 306–12.
6. Hegtvedt A, Collins M, White R, Turvey T. Minimizing the risk of transfusion in orthognathic surgery: use of predeposited autologous blood. Int J Adult Orthod Orthognath Surg 1987: **4**: 185–92.
7. Houbiers JG, van de Velde CJ, van de Watering LM, et al. Transfusion of red cells is associated with increased incidence of bacterial infection after colorectal surgery. A prospective study. Transfusion 1997: **37**: 126–34.
8. Hur S, Huizenga B, Major M. Acute normovolemic hemodilution combined with hypotensive anesthesia and other techniques to avoid homologous transfusion in spinal fusion surgery. Spine 1992: **17**: 867–73.
9. Jacobi K, Walter A, Kuhn R, Dworak O, Neidhardt B, Rügheimer E. Möglichkeiten und Grenzen der intraoperativen maschinellen Autotransfusion (MAT) bei radikalen Prostatektomien. Anaesthesist 1997: **46**: 101–7.
10. Kelly JF, Terry BC. Blood volume changes in the surgical treatment of oral-facial deformities: a preliminary report. J Oral Surg 1973: **31**: 90–4.
11. Kerscher A, Schubert S, Gernhuber J. The cell saver in orthognathic surgery – a microbiological problem? Int J Oral Maxillofac Surg 1997: **26** (Suppl 1): 62.
12. Linden J, Paul B, Dressler K. A report of 104 transfusion errors in New York State. Transfusion 1992: **32**: 601–6.
13. Locher MC, Sailer HF. The use of the cell saver in transoral maxillofacial surgery: a preliminary report. J Craniomaxillofac Surg 1992: **20**: 14–7.
14. Moenning JE, Bussard DA, Lapp TH, Garrison BT. Average blood loss and the risk of requiring perioperative blood transfusion in 506 orthognathic surgical procedures. J Oral Maxillofac Surg 1995: **53**: 880–3.
15. Murphy PJ, Connery C, Hicks GL. Homologous blood transfusion as a risk factor for infection after coronary bypass grafting. J Thorac Cardiovasc Surg 1992: **104**: 1092–5.
16. Olsfanger D, Jedeikin R, Metser U, Nusbacher J, Gepstein R. Acute

normovolaemic haemodilution and idiopathic scoliosis surgery: effects on homologous blood requirements. Anaesth Intensive Care 1993: **21**: 429–31.
17. Pasch T. Indikationen, Effektivität und Grenzen der kontrollierten Hypotension. Klinische Anästhesiologie und Intensivtherapie. In: Ahnefeld FW, Bergmann H, Kilian J, Kubanek B, Weissauer W, eds.: Fremdblutsparende Methoden. Berlin: Springer-Verlag, 1993: 89–95.
18. Peillon D, Dubost J, Bienvenu J, et al. Acute normovolaemic hemodilution does not reduce the inflammatory process induced by facial surgery. Can J Anaesth 1995: **42:** 305–9.
19. Robertie PG, Gravlee GP. Safe limits of isovolemic hemodilution and recommendations for erythrocyte transfusion. Int Anaesthesiol Clin 1990: **28**: 197–204.
20. Rohling R, Schanz U, Zimmermann A, Brüesch M, Kohn D, Sailer HF. Retransfusion von Cell Saver-Blut bei kieferchirurgischen Eingriffen und Zytokinspiegel-Verläufe. Schweiz Med Wochenschr 1998: **128** (Suppl 104): 11.
21. Samman N, Cheung L, Tong AC, Tideman H. Blood loss and transfusion requirements in orthognathic surgery. J Oral Maxillofac Surg 1996: **54**: 21–4.
22. Schaberg S, Kelly J, Terry B, Posner M, Anderson E. Blood loss and hypotensive anesthesia in oral-facial corrective surgery. J Oral Surg 1976: **34**: 147–56.
23. Stehling L, Zauder HL. Acute normovolemic hemodilution. Transfusion 1991: **31**: 857–68.
24. von Bormann B, Friedrich M. Hämodilution. Klinische Anästhesiologie und Intensivtherapie. In: Ahnefeld FW, Bergmann H, Kilian J, Kubanek B, Weissauer W, eds.: Fremdblutsparende Methoden. Berlin: Springer-Verlag, 1993: 161–71.
25. Washburn MC, Hyer RL. Deliberate hypotension for elective major maxillofacial surgery: a balanced halothane and morphine technique. J Maxillofac Surg 1982: **10**: 50–5.

Address:
R. G. Rohling, MD and P. E. Haers, MD, DDS
Department of Cranio-Maxillofacial Surgery
University Hospital Zurich
Rämistr. 100
8091 Zurich
Switzerland

Int. J. Oral Maxillofac. Surg. 1999; 28: 137–142
Printed in Denmark . All rights reserved

Copyright © Munksgaard 1999

International Journal of
Oral & Maxillofacial Surgery
ISSN 0901-5027

Medicine

Multimodal strategy for reduction of homologous transfusions in cranio-maxillofacial surgery

R. G. Rohling[1], P. E. Haers[1], A. P. Zimmermann[1], U. Schanz[2], R. Marquetand[1], H. F. Sailer[1]
[1]Department of Cranio-Maxillofacial Surgery and [2]Department of Internal Medicine (Hematology), University Hospital Zurich, Switzerland

R. G. Rohling, P. E. Haers, A. P. Zimmermann, U. Schanz, R. Marquetand, H. F. Sailer: Multimodal strategy for reduction of homologous transfusions in cranio-maxillofacial surgery. Int. J. Oral Maxillofac. Surg. 1999; 28: 137–142.
© Munksgaard, 1999

Abstract. The transfusion of homologous blood carries well-known risks that have prompted efforts to develop alternative techniques. Such measures are of particular interest to patients undergoing elective procedures. A total of 204 patients, out of 1470 patients who consecutively underwent major cranio-maxillofacial procedures under general anesthesia over a two-year period, were enrolled in a prospective protocol to reduce homologous transfusion requirements when a blood loss in excess of 500 ml was anticipated. The data were compared with the results of a retrospective control group (n=2890) covering major procedures during the previous four years, when blood-saving measures were applied occasionally, but not based on a global strategy. Techniques for the reduction of homologous transfusions were acute normovolemic hemodilution, controlled moderate hypotension, cell saver and predeposit autologous blood. In addition, preoperative administration of human recombinant erythropoietin was introduced during the last year of the study. These techniques were applied individually or in combination, depending on contraindications specific for each technique, using invasive monitoring in order to maintain intraoperative hemodynamic stability. The goal of this study was to examine the extent to which homologous transfusions may be reduced with the systematic application of transfusion-sparing techniques. Of 204 patients qualifying for the transfusion-sparing protocol, 30 received homologous transfusions. In comparison to the control group, utilization of transfusion-sparing techniques had doubled. The overall reduction in the use of homologous transfusions was highly significant. When acute normovolemic hemodilution, controlled moderate hypotension and the cell saver were used in combination, a greater reduction in homologous transfusions was achieved than with the use of either a single modality or combination of any two. No transfusions were required in patients pretreated with erythropoietin.

Key words: cranio-maxillofacial surgery; homologous blood reduction; acute normovolemic hemodilution; controlled moderate hypotension; cell saver; erythropoietin.

Accepted for publication 3 October 1998

Current methods for the reduction of the number and frequency of homologous red cell transfusions have become an established part of anaesthetic practice. The routine availability of acute normovolemic hemodilution during the induction of anesthesia, controlled moderate hypotension, the cell saver for intra- and postoperative autotransfusion and predeposit autologous blood donation, has created opportunities to transform sporadic efforts into a coherent strategy. As a promising new adjunct, human recombinant erythropoietin offers the added benefit of elev-

Table 1. Contraindications and complications of blood-saving measures

Method	Contraindications	Complications
Acute normovolemic hemodilution (ANH)	Anemia, hypovolemia, significant cardiovascular disease, severe respiratory insufficiency, systemic infections, sepsis, fever of unknown origin, coagulation disorders, protein malnutrition	Tissue hypoxia
Controlled moderate hypotension	Cerebrovascular insufficiency, coronary and/or valvular heart disease, increased intracranial pressure, impaired pulmonary, hepatic or renal function, anemia	Irreversible ischemias
Cell Saver	Infected wounds, tumor ablative surgery (except with intraoperative irradiation of blood)	Clotting abnormalities
Predeposit autologous donation	see ANH	see ANH
Preoperative rh-Epo	Starting hematocrit 45%, thrombocytosis, hypertension	"Influenza-like syndrome"

ating the hematocrit in the preoperative period.

Homologous as well as autologous blood products are subject to common error, i.e. the release of incompatible blood and contamination with bacterial organisms due to inadequate preservation or improper handling during storage and transport. Risks inherent in homologous transfusions are the transmission of bacteria, viruses and protozoa, as well as alloimmunization and immunomodulation; transfusion-induced immunosuppression may present acutely with an increased rate of postoperative infection and may also contribute to a higher rate of tumor recurrence [3,7,12,15]. The advantages of reduction in homologous transfusions can be summarized as follows: reduction of posttransfusion hepatitis and of HIV transmission as well as of infectious agents carried by leukocytes (e.g. cytomegalovirus), improved immune defenses with a lower rate of infection and tumor recurrence, reduction of HLA-alloimmunization by allogenic leukocytes, reduction of platelet refractoriness and transplant rejection, and a decrease in logistic difficulties, especially in cases of rare blood groups.

The present study was undertaken to evaluate the possibility to eliminate or reduce intra- and postoperative homologous transfusions with the systematic use of currently available transfusion reduction methods during extensive maxillofacial surgical procedures.

Material and methods

Over a two-year period (1994–1996), all patients with an anticipated blood loss of at least 500 ml were included in the study. Informed consent was obtained in detail and patients enrolled in a rigorous protocol of transfusion reduction methods based on the contraindications specific for each technique (Table 1). All patients received antibiotic prophylaxis with clindamycine or cefuroxim. In addition, a single dose of netilmicin was given to all cell saver patients 30 minutes before retransfusing the cell saver blood. All patients got a standardized, predominantly intravenous general anesthesia. In addition to routine monitoring, electrocardiogram, pulse oximetry, continuous capnometry and temperature monitoring, the arterial pressure was recorded directly. A central venous line was placed when indicated. Urine volume was determined hourly.

When not contraindicated (Table 1), acute normovolemic hemodilution (ANH) was instituted following induction of anesthesia by phlebotomy of an average of 9 ml/kg whole blood depending on current hematocrit values and physical status. This quantity allows on average 450 ml to 700 ml blood to be retransfused to the patient at the end of the operation without lowering the hematocrit below a safe level. At the same time, an equivalent volume of hydroxyethyl starch was infused to maintain normovolemia. Whole blood was collected and stored in 500 ml bags containing 50 ml CPDA-1 as a stabilizer.

In order to elevate the operative field above the heart, patients were placed in a reverse Trendelenburg position. Controlled moderate hypotension (CMH) was induced intraoperatively by lowering blood pressure pharmacologically to a mean arterial pressure (MAP) of approximately 60 mmHg using a vasodilatator. In conjunction with appropriate intraoperative analgosedation, blood pressure was regulated with a variable infusion of phentolamine. In patients with preexisting hypertension, MAP was reduced by no more than 20% of baseline.

When not contraindicated (Table 1), extravasated blood from the operative field was collected in a cell saver (CS) reservoir, followed by separation of erythrocytes from plasma and irrigation fluid in a washing centrifuge (Compact-A, Dideco™, Mirandola, Italy).

During the second year of the study, predeposit autologous blood donation in elective surgery cases was replaced by pretreatment with recombinant human erythropoietin (rh-Epo). A subcutaneous rh-Epo dosing schedule of 200 IU/kg twice a week was instituted three weeks prior to surgery, and continued until a hematocrit of 50% was reached. Iron was supplemented in every case.

Hemoglobin, hematocrit, electrolytes and arterial blood gases were determined at intervals geared to the intraoperative situation. During ongoing blood loss, crystalloid and/or colloid solutions were administered while hematocrit was closely monitored. In healthy adults, the lower limit for intervention was a hematocrit of 20%, unless superseded by clinical judgement. Retransfusion of autologous whole blood harvested during ANH took place in reverse order, i. e. patients first received the second bag, followed by processing and retransfusion of any cell saver units. The first unit of ANH whole blood was administered as needed at the end of surgery. Homologous or predeposit autologous blood was utilized only in cases of unusually large fluid turn-over or a hematocrit below the transfusion threshold.

Intraoperative blood loss was calculated by subtracting the total volume of irrigation expended during surgery from the combined volume of whole blood stored in the cell saver reservoir, if so equipped. Blood-soaked drapes and sponges were collected, weighed and added to the first figure. This estimate was entered in the anesthesia record at the end of surgery.

A total of 204 patients, out of 1470 patients operated on in the period 1994–1996, were enrolled in the prospective protocol. In all cases involved, blood loss in excess of 500 ml was anticipated and homologous transfusion reduction methods (TRM) were ap-

Table 2. Scope of surgical procedures in study group

Surgical category	Study group
Orthognathic	43.6%
Reconstructive	17.2%
Oncologic	15.7%
Traumatologic	13.2%
Preprosthetic	7.8%
Craniofacial	2.5%

Table 3. Demographic and clinical data of patients enrolled in study group

Patients characteristics	Mean±SD; range
n (male/female)	204 (98/106)
Age (years)	32.6±16.1; 8–71
Weight (kg)	65.5±13.2; 18–112
Height (cm)	170.5±10.3; 122–195
ASA I/II/III (*n*)	131/61/12
Length of procedure (hours)	6.6±2.6; 2–20
Hematocrit preop (%)	39.7±5.1; 25–52
Hematocrit intraop (%)	29.3±3.9; 15–47
Blood loss intraop (ml)	1163±740; 500–6000
Blood pressure intraop (mmHg)	MAP: 69±6; 50–110 SAP: 100±8; 70–150 DAP: 55±6; 40–90
Temperature intraop (°C, rectally)	36.1±0.6; 34.3–38.5

ASA=American Society of Anesthesiology Classification of general health; MAP=Mean arterial pressure; SAP=systolic arterial pressure; DAP=diastolic arterial pressure.

Table 4. Comparison of use of homologous transfusion reduction methods (TRM) and homologous transfusions (HT) in control and study groups

	Patients (*n*)	TRM (*n*, %)	HT recipients (*n*, %)	HT (units)	HT/operation
Control Group					
Total	2890	176 (6.1%)	334 (11.6%)	1655	0.57
Study Group					
Total	1470	204* (13.9%)*	30* (2.0%)	141*	0.1

* $P<0.001$.

plied prospectively. Surgical bleeding of this magnitude is frequently encountered in bimaxillary orthognathic procedures, major oncologic, traumatologic, reconstructive or preprosthetic procedures (Table 2). These data were compared to retrospective data from 2980 patients operated on previously (1990 – 1994). The number of homologous units transfused was counted and any efforts to reduce homologous transfusions were noted from the anesthesia records.

The statistical significance of differences in the quantity of homologous blood was tested with the Mann Whitney U-test. A value of $P<0.05$ was considered statistically significant.

Results

Table 3 lists patient age, gender, height, weight, pre- and intraoperative hematocrit, blood loss during surgery, intraoperative body temperature and blood pressure, length of procedure and risk classification. The procedures performed in these 204 cases were orthognathic surgery (43.6%), reconstructive surgery (17.2%), oncologic surgery (15.7%), traumatology (13.2%), preprosthetic surgery (7.8%) and craniofacial surgery (2.5%). These procedures in which blood-saving measures were applied (according to the criterion of expected blood loss exceeding 500 ml), constitute 13.9% of the whole group ($n=1470$). This is significantly more than in the control group ($n=2890$), in which similar measures were applied in only 176 cases (6.1%) (Table 4). In none of the cases which were not selected for the blood-saving measures, were homologous blood transfusions necessary.

In 30 of the 204 procedures, additional homologous transfusions were indicated. In 26 of these, massively infected surgical wounds or malignancy prohibited the use of the cell saver. In 7 of these 30 cases, the preoperative hematocrit was too low to perform acute normovolemic hemodilution safely. Compared to the control group, there was a reduction in the percentage of recipients of homologous blood (2.0% *versus* 11.6% in the control group), which was significant ($P<0.001$). The increase in the use of blood-saving measures, together with the corresponding reduction in homologous transfusions, is illustrated in Figure 1.

Controlled moderate hypotension (CMH) was employed in all 204 patients, with an average MAP of 69±6 mmHg. It was possible to eliminate sustained episodes of relative intraoperative hypertension (average mean systolic pressure: 100±8 mmHg) in all cases. Following introduction of the study protocol, those patients in whom other techniques were contraindicated and therefore were restricted to the use of CMH alone, were also the ones requiring the most homologous transfusions (43.7%; see Table 5). In combination with either CS or ANH, only 33.3% and 13.7%, respectively, received additional homologous transfusions. Thus, use of triple and quadruple combinations resulted in the lowest percentage of patients requiring donor blood. No homologous transfusions were needed when rh-Epo was used in addition to ANH, CMH and CS. Predeposit autologous blood donations (PBD) were taken in 64/204 cases and retransfused in 28/64 (44%), whereas in the control group, all 159 PBD patients received the autologous transfusions. Only 50 of these 159 patients had the

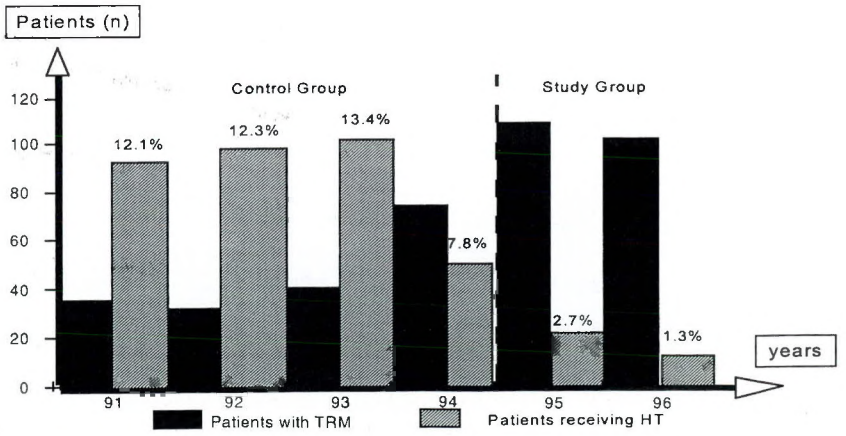


Fig. 1. Reduction of homologous transfusions (HT) with increasing use of homologous transfusion reduction methods (TRM).

Table 5. Effect of homologous transfusion reduction methods (TRM) on homologous transfusions (HT)

	Control group Patients (*n*) with TRM		Study group Patients (*n*) with TRM	
TRM	no HT	with HT	no HT	with HT
Single modality	22	16 (71.4%)	16	7 (43.7%)
CMH	43	12 (27.9%)	0	0
ANH	56	12 (21.4%)	0	0
CS				
Dual modality	13	4 (30.7%)	0	0
ANH+CS	13	2 (15.4%)	3	1 (33.3%)
CS+CMH	19	1 (5.2%)	138	19 (13.7%)
ANH+CMH				
Triple combination	10	1 (10%)	37	3 (8.1%)
ANH+CS+CMH	0	0	8	0
rh-Epo+ANH+CMH				
Quadruple combination				
rh-Epo+CS+ANH+CMH	0	0	2	0
Total	176	48 (27.3%)	204	30 (15%)

benefit of transfusion reduction methods, of whom homologous transfusions became necessary in seven. Of patients in whom no special measures to reduce the transfusion requirements were employed, twelve required additional homologous blood. Combined blood-saving measures were not used frequently in the control group; only ten patients received a triple combination of CMH, CS, and ANH during that period (Table 5).

In comparison to the control group, the overall consumption of homologous transfusions in the study group was reduced by 83%.

Discussion

A correct estimate of intraoperative blood loss in maxillofacial procedures is difficult. A study using radioactively labeled erythrocytes showed that, in 8 of 13 patients, the estimated blood loss and true loss of erythrocyte mass differed by 56–70% and estimates were usually too low[22]. In large maxillofacial procedures, the quantity of blood entering the suction apparatus only provides a rough approximation of the true blood loss[10]. Therefore, supervision of fluid status for maintenance of normovolemia and hemodynamic stability is of vital importance.

There are several studies concluding that bimaxillary osteotomies entail a greater blood loss than most other procedures within the scope of maxillofacial surgery [6,14]. In a series by SAMMAN et al.[21], 78 of 291 patients (27%) undergoing bimaxillary osteotomies received homologous transfusions. When these outcomes are contrasted with the present data, the impact of systematically applied transfusion reduction methods in patients enrolled in our prospective study is apparent: only two in 71 patients (2.9%) with bimaxillary osteotomies required homologous blood.

In a discussion of individual techniques for the reduction of homologous transfusion, acute normovolemic hemodilution (ANH) has emerged as a safe, cost-effective and simple basic tool in the conservation of homologous blood[16]. For the specialty of maxillofacial surgery, BONNET et al.[1] found that ANH results in improved skin flap viability. PEILLON et al.[18] serially assessed facial tissue density using radiotelemetry in 16 patients treated with ANH and 16 non-hemodiluted controls. During the first postoperative week, no adverse influence on facial edema was noted.

The primary goal of ANH is the storage of autologous whole blood which is promptly substituted with crystalloid and colloid solutions. Its immediate effect is a reduction in hematocrit which translates into loss of relatively erythrocyte-poor blood intraoperatively. The major advantage of this technique is the ability to retransfuse autologous whole blood with high-quality erythrocytes and fully functional clotting factors. The main risk inherent in phlebotomy is tissue hypoxia in cases of poor cardiovascular compensation. Hence, patient safety is contingent upon the recognition of contraindications as well as individualized invasive monitoring. A decision crucial to the technique is the extent of hemodilution, which is principally determined by pre-existing medical illness. There is no consensus in the literature regarding the intra- and postoperative transfusion threshold: in ASA I and ASA II patients (i.e. with no or mild/moderate systemic disorder, respectively), values for the critical hematocrit vary from 18% to 21%, whereas for ASA III patients (with severe systemic disorder), a hematocrit of 24% is considered the lowest tolerable[19,23]. It is generally agreed that low hematocrit values are acceptable only when normovolemia is maintained. Continuous invasive monitoring and blood gas analyses at closely-spaced intervals play a crucial role in the maintenance of stable cardiopulmonary and hematological parameters. In this study, ANH was performed in 185 of 204 procedures. The absolute transfusion threshold was a hematocrit of 20% for healthy subjects. No postoperative complications attributable to excessively low hematocrits were noted.

Controlled moderate hypotension (CMH) targets hemodynamics in relation to the rate of surgical bleeding. In an early study comparing maxillofacial surgical patients with normotensive and hypotensive management during general anesthesia (average MAP: 98 *versus* 73 mmHg), SCHABERG et al.[22] proved that lowering the blood pressure reduces blood loss. Studies by CHAN et al.[2] and WASHBURN et al.[25] claim a significant reduction in homologous transfusions with a lower MAP. A meta-analysis on the efficacy of controlled hypotension as a single measure showed that blood loss was reduced by 50±18% on average, and homologous transfusions by 59±20%[17]. By contrast, VON BORMANN et al.[24] were not able to detect a comparable transfusion-sparing effect. From the standpoint of safety for patients due to undergo CMH, a careful search for possible contraindications should be an integral part of the pre-anesthetic workup. For the prevention of organ hypoperfusion, especially when combined with ANH, continuous invasive cardiopulmonary monitoring is mandatory. The recommendation of some authors[24] to abstain from a combination of ANH with controlled hypotension due to concern about myocardial oxygen delivery appears overstated. In our study, 138 of 204 patients toler-

ated a combination of both techniques with no adverse consequences. However, MAP was lowered to no less than 60 mmHg.

The cell saver as a single measure does not reliably prevent the need for homologous transfusions when blood loss is high. Rather, it should be viewed as part of a coordinated concept in the preservation of homologous blood. The erythrocyte suspension generated from salvaged blood is of high quality. This avoids the retransfusion of undesirable ingredients of the autotransfusate since metabolites of the clotting cascade and free hemoglobin are reduced to clinically insignificant levels[9]. In the specialty of maxillofacial surgery, high bacterial counts in the surgical field currently represent a relative, if not absolute, contraindication to its use[5]. In a prospective study by LOCHER & SAILER[13] on pyrexia associated with use of the cell saver in 18 maxillofacial surgical patients, a rise in body temperature between 0.5 and 3°C was noted on the first postoperative day. By contrast, no cases of postoperative hyperthermia occurred in the present study. However, blood cultures taken fifteen and 120 minutes after retransfusion in patients with transoral cell saving showed the presence of the same microorganisms which were detected in blood cultures of the cell saver suspension and there was a significant increase of cytokines at these time intervals[20]. The bacterial contamination in transoral cell-saving has also been reported by others[11]. The impact on the dissemination of bacterial organisms, systemic cytokine levels and clinical implications are currently under investigation so that no final recommendations on the cell saver in maxillofacial surgery can be made at this time. These recommendations will probably depend on the modality of cell-saving (transoral *versus* transcoronal) and the indication of the intervention. Only 42 of 204 patients were transfused with the erythrocyte suspension generated by the cell saver. Its sparing use reflects contraindications to the retransfusion of erythrocytes in a population of patients dominated by trauma victims with massively infected wounds, and in the presence of tumor.

When the triple combination of TRM (ANH, CMH, CS) was complemented by preoperative administration of rh-Epo in place of predeposit autologous blood (PBD), homologous transfusions were no longer necessary. It is our impression that patients find the application of rh-Epo more agreeable and less exhausting in comparison with the PBD. A higher preoperative hematocrit increases the safety and efficacy of ANH. The use of rh-Epo may obviate the need for PBD and its risks. At the present time, the routine use of rh-Epo as an adjunct to ANH is hampered by its relatively high cost.

It has become apparent from the prospective study that PBD plays a subordinate but not an negligible role, at least as long as rh-Epo does not become routine practice. The systematic use of TRM adequately compensated for surgical bleeding in the majority of cases. However, at 44%, the rate of retransfusion of predeposit autologous blood remains high. Under no circumstance should PBD be viewed as a substitute for established intraoperative transfusion reduction methods; the outcome would be a needlessly high rate of homologous transfusions. The use of predeposit autologous blood demands the same scrutiny as homologous transfusions and should be relegated to instances when the potential of ANH, CMH and CS has been fully exploited.

Since the introduction of a multimodal blood-saving strategy, none of the patients operated on in the absence of transfusion-sparing measures required homologous transfusions. This indicates that patients likely to incur a high blood loss were appropriately selected for TRM. The present study leaves no doubt that the consistent multimodal use of transfusion-sparing techniques is highly effective. One of our principal findings was that the most significant reductions in homologous transfusions are achieved by the combination of different methods, a contention validated by several recent reports[4,8]. This study documents the dramatic impact of a rigorously applied protocol for the conservation of homologous transfusions in major cranio-maxillofacial surgery. Competent perioperative surveillance of hemodynamic and hematological data, acceptance of a moderately low hematocrit and appropriate criteria for administration of homologous products are fundamental requirements for the safe and effective execution of a transfusion-sparing protocol.

References

1. BONNET M, JULIA J, MATHIEU-DAUDÉ J, DU CAILAR J. Intéret de l'hémodilution en chirurgie maxillofaciale sur l'oedème traumatique postopératoire et sur la vitalité des lambeaux. Ann Fr Anaesth Réanim 1986: **5**: 243–8.
2. CHAN W, SMITH DE, WARE WH. Effects of hypotensive anesthesia in anterior maxillary osteotomy. J Oral Surg 1980: **38**: 504–8.
3. DODD R. The risk of transfusion-transmitted infection. N Engl J Med 1992: **327**: 419–21.
4. HABERKERN M, DANGEL P. Normovolemic hemodilution and intra-operative autotransfusion in children: experience with 30 cases of spinal fusion. Eur J Pediatr Surg 1991: **1**: 30–5.
5. HANSEN E, TAEGER K. Intraoperative Autotransfusion mit Blutbestrahlung bei Tumoroperationen: Grundlage und Praxis. Anästhesiol Intensivmed 1996: **6**: 306–12.
6. HEGTVEDT A, COLLINS M, WHITE R, TURVEY T. Minimizing the risk of transfusion in orthognathic surgery: use of predeposited autologous blood. Int J Adult Orthod Orthognath Surg 1987: **4**: 185–92.
7. HOUBIERS JG, VAN DE VELDE CJ, VAN DE WATERING LM, et al. Transfusion of red cells is associated with increased incidence of bacterial infection after colorectal surgery. A prospective study. Transfusion 1997: **37**: 126–34.
8. HUR S, HUIZENGA B, MAJOR M. Acute normovolemic hemodilution combined with hypotensive anesthesia and other techniques to avoid homologous transfusion in spinal fusion surgery. Spine 1992: **17**: 867–73.
9. JACOBI K, WALTER A, KUHN R, DWORAK O, NEIDHARDT B, RÜGHEIMER E. Möglichkeiten und Grenzen der intraoperativen maschinellen Autotransfusion (MAT) bei radikalen Prostatektomien. Anaesthesist 1997: **46**: 101–7.
10. KELLY JF, TERRY BC. Blood volume changes in the surgical treatment of oral-facial deformities: a preliminary report. J Oral Surg 1973: **31**: 90–4.
11. KERSCHER A, SCHUBERT S, GERNHUBER J. The cell saver in orthognathic surgery – a microbiological problem? Int J Oral Maxillofac Surg 1997: **26** (Suppl 1): 62.
12. LINDEN J, PAUL B, DRESSLER K. A report of 104 transfusion errors in New York State. Transfusion 1992: **32**: 601–6.
13. LOCHER MC, SAILER HF. The use of the cell saver in transoral maxillofacial surgery: a preliminary report. J Craniomaxillofac Surg 1992: **20**: 14–7.
14. MOENNING JE, BUSSARD DA, LAPP TH, GARRISON BT. Average blood loss and the risk of requiring perioperative blood transfusion in 506 orthognathic surgical procedures. J Oral Maxillofac Surg 1995: **53**: 880–3.
15. MURPHY PJ, CONNERY C, HICKS GL. Homologous blood transfusion as a risk factor for infection after coronary bypass grafting. J Thorac Cardiovasc Surg 1992: **104**: 1092–5.
16. OLSFANGER D, JEDEIKIN R, METSER U, NUSBACHER J, GEPSTEIN R. Acute

normovolaemic haemodilution and idiopathic scoliosis surgery: effects on homologous blood requirements. Anaesth Intensive Care 1993: **21**: 429–31.
17. Pasch T. Indikationen, Effektivität und Grenzen der kontrollierten Hypotension. Klinische Anästhesiologie und Intensivtherapie. In: Ahnefeld FW, Bergmann H, Kilian J, Kubanek B, Weissauer W, eds.: Fremdblutsparende Methoden. Berlin: Springer-Verlag, 1993: 89–95.
18. Peillon D, Dubost J, Bienvenu J, et al. Acute normovolaemic hemodilution does not reduce the inflammatory process induced by facial surgery. Can J Anaesth 1995: **42:** 305–9.
19. Robertie PG, Gravlee GP. Safe limits of isovolemic hemodilution and recommendations for erythrocyte transfusion. Int Anaesthesiol Clin 1990: **28**: 197–204.
20. Rohling R, Schanz U, Zimmermann A, Brüesch M, Kohn D, Sailer HF. Retransfusion von Cell Saver-Blut bei kieferchirurgischen Eingriffen und Zytokinspiegel-Verläufe. Schweiz Med Wochenschr 1998: **128** (Suppl 104): 11.
21. Samman N, Cheung L, Tong AC, Tideman H. Blood loss and transfusion requirements in orthognathic surgery. J Oral Maxillofac Surg 1996: **54**: 21–4.
22. Schaberg S, Kelly J, Terry B, Posner M, Anderson E. Blood loss and hypotensive anesthesia in oral-facial corrective surgery. J Oral Surg 1976: **34**: 147–56.
23. Stehling L, Zauder HL. Acute normovolemic hemodilution. Transfusion 1991: **31**: 857–68.
24. von Bormann B, Friedrich M. Hämodilution. Klinische Anästhesiologie und Intensivtherapie. In: Ahnefeld FW, Bergmann H, Kilian J, Kubanek B, Weissauer W, eds.: Fremdblutsparende Methoden. Berlin: Springer-Verlag, 1993: 161–71.
25. Washburn MC, Hyer RL. Deliberate hypotension for elective major maxillofacial surgery: a balanced halothane and morphine technique. J Maxillofac Surg 1982: **10**: 50–5.

Address:
R. G. Rohling, MD and P. E. Haers, MD, DDS
Department of Cranio-Maxillofacial Surgery
University Hospital Zurich
Rämistr. 100
8091 Zurich
Switzerland