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Review

Postoperative blood salvage versus allogeneic blood transfusion in total knee and hip arthroplasty: a literature review

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Summary. *Background and aim of the work:* We aimed to compare Postoperative Blood Salvage (PBS) with Allogeneic Blood Transfusion (ABT) in patients undergoing Total Hip and Knee Arthroplasty (THA, TKA). *Methods:* A bibliographic research was carried out in order to review the literature dedicated to postoperative blood salvage in major orthopaedic surgery, excluding papers dealing exclusively with preoperative autologous donation, intraoperative blood salvage and ABT. PBS and ABT were compared according to complications, costs and duration of hospitalization. PBS effectiveness in reducing ABT was also assessed. *Results:* PBS system is useful for reducing the complication rate and the length of hospital stay if compared to ABT. Costs for the reinfusion of unwashed shed blood, washed blood, and allogeneic transfusion are controversial among the different authors. Several papers demonstrate that PBS significantly reduces the need of postoperative ABT in both THA and TKA, while there is low evidence that PBS does not affect the risk of surgical wound complications. To reduce potential risks related to PBS, including non-hemolytic febrile reaction, the reinfusion of saved blood should begin within 4-6 hours after the start of collection through the wound drainage. *Conclusions:* According to literature, PBS appears to be a valid alternative to ABT, which is the standard treatment for postoperative anemia in THA and TKA. Contraindications to PBS must be ruled out before recommending it to patients undergoing major orthopaedic procedures. (www.actabiomedica.it)

Key words: blood transfusion, reinfusion, blood salvage, orthopedic surgery, arthroplasty, THA, TKA, postoperative, allogeneic, autologous

Introduction

Total hip arthroplasty (THA) and total knee arthroplasty (TKA) are commonly performed in orthopaedic operating theaters as a consequence of the growing age of the population. It has been estimated that every year about 1.000.000 patients undergo THA and 800.000 patients undergo TKA worldwide (1,2). In Italy, THAs and TKAs amount to about 57.000 and 45.000 per year, respectively (3).

During these procedures, bleeding inevitably occurs and might persist for some hours during the postoperative period with possible clinical implications (4). It has been reported that the mean volume of blood loss in the intra-operative period can exceed 500 ml for THA and 350 ml for TKA, while the average blood loss in the post-operative period can reach 750 ml after THA and 800 ml after TKA (4,5).

According to Rao et al., 36,7% of patients operated of THA receive an ***Allogeneic Blood Transfusion***

(ABT) with an average of 1,4 transfused units for each patient; in TKA 19,2% of the patients need an ABT with an average of 1,6 units per patient (6).

Even if blood transfusions have never been safe as today and check-up examinations are carried out on each blood bag, transfusion remains a procedure not totally exempt from risks (7). Among the most frequent causes of death for ABT is the acute hemolytic reaction occurring after the administration of AB0 incompatible units. This incompatibility is often the consequence of identification errors made during the taking of a blood sample from a patient or during the transfusion (8). Unlike the infectious complications, that have rarely occurred during the last decade, a trend in decrease for these errors has not been observed (9, 10).

There is also the danger of a global blood shortage. The worldwide requirement, even if estimates change from country to country, is about 7.500.000 liters of blood per year. By 2030 it has been estimated that there will be a lack of 4.000.000 units (about 2.000.000 liters) in the United States. It's essential to remember that blood is the result of charitable contribution and not of trade: we have the task to utilize it well and not waste it (11).

All these reasons have pushed and promoted the research on blood sparing surgery. This topic involves surgical techniques, diagnostic devices, pre and postoperative procedures that can help in reducing ABT. Back in the 60s, the surgeon Denton Cooley performed one of the first open-hearth operations without the use of blood. During the 70s, when hepatitis cases among transfused patients increased, the search of alternatives to transfusions began to take place (12). Anyway the history of the medicine without blood is inevitably connected to the events of Jehovah's Witnesses that refuse transfusions because they consider a sin the other people's blood insertion in own body (13).

Autologous blood transfusion, described about 100 years ago for the first time, is one of the therapies that is part of this alternative medicine (14). Pre-surgical autologous donation, intraoperative blood salvage and postoperative blood salvage (PBS) are procedures that have been introduced in the clinical practice with the aim of reducing the recourse to ABT.

The *pre-operative autologous donation* is an autonomous blood transfusion technique where the patient, during the weeks previous to the surgical operation, donates blood to himself. Blood is gathered in appropriate bags, it is conserved in fixed-temperature refrigerators (blood banks) and will be transfused to the patient, if it will be necessary, during or after the surgical operation (15.) To realize preoperative autologous donation, the patient should have a hemoglobin level of at least 11 g/dl and be in physical conditions to permit the donation. The last preoperative donation should precede the operation of 72 hours at least to ensure the patient's return to a normovolemic state (15). In addition to these limits, pre-surgical autologous donation has to deal with blood storage problems and the unexpected delays of the surgical operations that can invalidate autologous blood for use. This procedure is also expensive, both in economic terms and in time terms, for hospital staff but for patients too (4). Patients must often employ two or three half days before the operation to go to the blood bank, they must be exposed to screening for the bloodletting and go back home (16). Another aspect to consider is that the majority of patients addressing to THA and TKA operations are aged and anemic: for this reason the pre-surgical donation of a quantity of blood that results sufficient to satisfy their need during the operation is not always possible (5). The pre-operative auto-donated blood is often transfused like whole blood and this causes, especially in elderly patients, a major risk of circulatory overload (17). Moreover, approximately 50% of patients that have given their blood in the preoperative phase are anemic the day of the operation, increasing for this reason the risk to receive a postoperative ABT (18). We also have to considered and reflect about the wastefulness of blood taken in preoperative phase. For about 40-70% of patients that subject themselves to this technique, just a part of the pre-donated blood is actually reinfused. In addition, this blood is safe just for a certain period of time and it's not suitable to be transfused to other patients (16, 19). The result is that about 28 to 45% of the pre-donated blood is not used (17). The pre-donated blood, being gathered with other blood bags till the moment of the possible transfusion for the operation, is not totally exempt from risks of error in the assignment to the wrong patient. For

this reason it has the same AB0 incompatibility risk of the ABT (17,18). In the end, the pre-surgical autologous donation, like the ABT, is not accepted by Jehovah's Witnesses because it doesn't use a closed-circuit system (13).

Intra and post-operative salvages consist in a set of procedures and devices aimed to salvage blood that normally would be lost during and after the surgical operation.

Intraoperative salvage consists in the gathering of blood loss flowing from cut blood vessels in the tissues involved by the surgical procedure and the following transfusion, prior filtering and washing by centrifugation. This procedure takes place by a specific machinery, composed by an adjustable and continuous vacuum source, a peristaltic pump and a centrifuge. To realize the intra-operative salvage it's necessary that the expected volume of lost blood in the intra-operative period is 800 ml at least, the surgical site has not to be infected and malignant cells have not to be present (15). With this procedure satisfying results have been realized but it also has been proved how much it is expensive and not always accessible (5). Intra-operative salvage is also a complex procedure that needs an approach of a well-qualified team (19).

The *Postoperative Blood Salvage* (***PBS***) consists in the gathering of hematic loss versed from the drains of the surgical wound and their infusion, prior sedimentation, filtration and eventually washing with saline solution. The blood is spontaneously defibrinated in contact with tissue before the runoff from the drains. The system works in aspiration or just for gravity. Normally the system is composed by: a collection chamber, a housing for the autotransfusion unit, the reinfusion bag, a reinfusion set. The sedimentation permits to reinfuse concentrated red blood cells, reducing the reinfusion of hemolysis products, that stay in the supernatant. The filtration is guaranteed through two filters, one for macro-aggregates of 120 μm inserted in the collection chamber and the other for micro-aggregates of 40 μm inserted directly in the bag. A device for the washing can be present depending on blood is reinfused washed or unwashed. Also in this case it is dissuaded to reinfuse blood salvaged by an infected wound (15).

For what concerns THA and TKA, where there is a severe hematic loss rather than in the intra-operative period especially in the post-operative one, the technique of the PBS can be preferred, and especially for those patients unsuitable to the pre-surgical autologous donation and for those patients that, for religious motivations and not, refuse the ABT or autologous transfusions that don't use a closed-circuit system.

Objective

Aim of this study is to review the literature comparing Postoperative Blood Salvage (PBS) with Allogeneic Blood Transfusion (ABT) in patients undergoing THA and TKA.

Materials and methods

We performed a bibliographic research through the consultation of the following databases: PubMed, Cochrane and Google Scholar. The keywords used were the following: "autologous blood transfusion", "orthopedics", "orthopedic surgery", "postoperative blood salvage", "shed blood reinfusion".

We included in the study the articles dealing with PBS in major orthopaedic procedures (THA and TKA), published in English, Italian, French and Spanish language, from 1-1st-1991 to 1-31st-2016. Articles that treat exclusively the preoperative autologous donation, the intraoperative blood salvage and the ABT were excluded.

From the 26 articles included in the research the PBS and the ABT were considered, comparing complications, costs, length of stay, efficacy of the PBS in decreasing the amount of ABT. About the PBS technique we also examined contraindications, time and volume limits, and mean volume of blood reinfused.

Results

Comparing the results obtained from 7 articles about the *complications* of the PBS and ABT, we can say that the PBS system results safer in terms of complications respect to the ABT: in particular the PBS totally nullifies the risk of HIV/HCV transmission

and AB0 incompatibility reaction, and it also decreases the risk of deep venous thrombosis (DVT)/pulmonary embolism (PE) and infections in general. The only complication that can occur more frequently in the PBS is the non-hemolytic febrile reaction (6, 17, 18, 20-23) (Table 1).

We selected 4 papers dealing with *costs* of initial investment and recovery or donation operation in terms of equipment and materials costs. Rao et al., evaluating all these variables, assert that the unwashed shed blood reinfusion is the less expensive method, the washed shed blood reinfusion comes after and in the end we find the ABT to be the most expensive method (Table 2) (6). On the other hand Tiò et al. and So-Osman et al. report increased costs for PBS (21, 24).

About the efficacy of the *PBS* to *decrease* the *necessity to* resort to the *ABT*, it emerges that in THA after the PBS the percentage of the patients that must resort to the ABT is 15%, against 33% of the patients without PBS (5, 23, 25-28) (Table 3 a). For the TKA only 10% of the patients after PBS must resort to the ABT against 34% of the patients without PBS (5, 22, 23, 25, 27, 29-33) (Table 3 b). So we can conclude with strong evidence ($p<0,001$; Confidence Interval 95%) that the PBS decreases significantly the recourse to the ABT. In contrast, So-Osman et al. found that PBS did not reduce erythrocyte use (24).

In relation to the *hospital length of stay*, only 7 out of the examined articles treat this theme but just one for the THA (28) (Table 4 a) and two for the TKA (29, 32) (Table 4 b) show a statistically significant difference. According to these authors, the mean length of stay of the patients with PBS is shorter than that of the patients without PBS. Unfortunately it is not possible to obtain a statistically significant cumulative result of these studies because not all the authors report the standard deviation necessary for the analysis.

Comparing the data retrieved from 3 articles for THA and 2 for TKA it is also emerged, even if with low evidence ($p>0,05$; Confidence Interval 95%) that the PBS system doesn't affect the risk of *wound complications*: in THA patients the incidence of wound complications with the PBS system is 3% whereas that with simple drain is 4% (26, 28, 34) (Table 5 a); in TKA patients the percentage of wound complications

Table 1. Comparison of complications between the PBS and the ABT. The only *complication* which is more frequent in PBS vs ABT is non haemolytic febrile reaction

	ABT	PBS
Nonhemolytic febrile reaction	0,02-2% (6,18)	2-22% (6)
Infections	4,6-15,3% (6,20)	2-4% (6,20)
DVT/PE	2% (6,20)	1% (20)
HIV transmission	1 in 1,4 X 1.000.000 to 1 in 2,4 X 1.000.000 (17)	0
HCV transmission	1 in 872.000 to 1 in 1,7 X 1.000.000 (17)	0
AB0 incompatibility reaction	hemolysis: 1 in 60.000 (17) death: 1 in 600.000 (17,18)	0 0

Table 2. Costs of unwashed shed blood reinfusion vs washed shed blood reinfusion vs ABT (6). Comparing the *costs* of initial investment and recovery or donation operation in terms of equipment and materials we find the unwashed shed blood reinfusion to be the less expensive method, the washed shed blood reinfusion comes after and in the end the ABT to be the most expensive method (6)

Costs ($)	Unwashed shed blood reinfusion		Washed shed blood reinfusion		ABT	
	TKA	THA	TKA	THA	TKA	THA
Mean unit cost	475	1167	759	1827	766	2609
Fixed cost per unit	389	954	684	1674	510	2354
Variable cost per unit	86	214	75	153	255	255

Table 3. *PBS decreases* significantly the recourse to the *ABT* (p<0,001; CI 95%): in THA after the PBS the percentage of the patients that must resort to the ABT is 15%, against 33% of the patients without PBS (3 a); for the TKA only 10% of the patients after PBS must resort to the ABT against 34% of the patients without PBS (3 b)

Author	Number of patients	Patients without PBS	Patients with PBS	ABT without PBS	ABT with PBS
a) post THA					
Smith (21)	158	52% (82/158)	48% (76/158)	21% (17/82)	8% (6/76)
Slagis (22)	50	52% (26/50)	48% (24/50)	50% (13/26)	43% (10/24)
Mirza (23)	218	50% (109/218)	50% (109/218)	30,3% (33/109)	9,2% (10/109)
Atay (5)	36	53% (19/36)	47% (17/36)	79% (15/19)	53% (9/17)
Total sample	462	51% (236/462)	49% (226/462)	33% (78/236)	15% (34/226)
b) post TKA					
Munoz (24)	581	34% (199/581)	66% (382/581)	30,6% (61/199)	8,4% (32/382)
Kourtzis (25)	119	49% (58/119)	51% (61/119)	86,2% (50/58)	8,1% (5/61)
Slagis (22)	30	50% (15/30)	50% (15/30)	33% (5/15)	28% (4/15)
Boese (26)	404	50% (202/404)	50% (202/404)	13,4% (27/202)	11,4% (23/202)
Atay (5)	41	51% (21/41)	49% (20/41)	38% (8/21)	5% (1/20)
Munoz (27)	300	33% (100/300)	66% (200/300)	48% (48/100)	11% (22/200)
Cheng (28)	60	57% (34/60)	43% (26/60)	40% (14/34)	15,8% (4/26)
Total sample	1.535	41% (629/1.535)	59% (906/1.535)	34% (214/629)	10% (91/906)

Table 4. In relation to the *hospital length of stay*, only 6 out of 21 examined articles treat this theme but just one for the THA (a) and two for the TKA (b) show a statistically significant difference. According to these authors, the mean length of stay of the patients with PBS is shorter than that of the patients without PBS. Unfortunately it is not possible to obtain a statistically significative cumulative result of these studies because not all the authors report the standard deviation necessary for the analysis

Author	Patients without PBS	Patients with PBS	Length of stay without PBS (days)	Length of stay with PBS (days)	Statistical significance (p≤0,05)
a) PBS (THA)					
Smith (26)	52% (82/158)	48% (76/158)	6,98	6,4	NO
Monte Del Trujillo (34)	44% (48/108)	56% (60/108)	11,6	10,1	NO
Mirza (28)	50% (109/218)	50% (109/218)	9	7	YES
b) PBS (TKA)					
Munoz (29)	34% (199/581)	66% (382/581)	13	11	YES
Shenolikar (35)	50% (50/100)	50% (50/100)	16,7	15,6	NO
Munoz (32)	33% (100/300)	67% (200/300)	16	13	YES

with PBS is of 3% against 7% of the simple drain (32, 35) (Table 5 b).

The mean *volume of blood* saved and reinfused with the PBS resulted of 484 ml in a total sample of 143 patients operated of TKA reported by 5 authors (5, 27, 35-37) (Table 6 a) and of 324 ml for 401 patients operated of THA reported by 8 authors (5, 26-28, 34, 36, 37, 38) (Table 6 b).

Han and Shin with their studies underline that, to decrease potential risks included the non-hemolytic febrile reaction, the *reinfusion* of blood must begin *within 4-6 hours* by the start of the salvage (4). Also Faris et al. reported that when the PBS is completed within 6 hours or less the prevalence of febrile reaction is about 2%, but when 6 hours are passed the prevalence increases to 22% (39).

No author considered the perspective of the *maximum volume* to reinfuse. The data reported in Table 7 have been extrapolated from the technical file of Eurosets (40) but they have no statistical significance.

Table 5. Comparing the data retrieved from three articles for THA and the two for TKA it is also emerged (p>0,05; CI 95%) that the PBS system doesn't affect the risk of *wound complications*: in THA patients the incidence of wound complications with the PBS system is 3% whereas that with simple drain is 4% (a); in TKA patients the percentage of wound complications with PBS is of 3% against 7% of the simple drain (b)

Author	Number of patients	Patients without PBS	Patients with PBS	Wound complications (%) without PBS	Wound complications (%) with PBS
a) THA					
Smith (26)	158	52% (82/158)	48% (76/158)	6% (5/82)	4% (3/76)
Monte Del Trujillo (34)	108	44% (48/108)	56% (60/108)	4,2% (2/48)	0% (0/60)
Mirza (28)	218	50% (109/218)	50% (109/218)	2,7% (3/109)	3,7% (4/109)
Total sample	484	49% (239/484)	51% (245/484)	4% (10/239)	3% (7/245)
b) TKA					
Munoz (32)	300	33% (100/300)	67% (200/300)	1% (1/100)	0% (0/200)
Shenolikar (35)	100	50% (50/100)	50% (50/100)	18% (9/50)	14% (7/50)
Total sample	400	37% (150/400)	63% (250/400)	7% (10/150)	3% (7/250)

Table 6. The mean *volume of blood* saved and reinfused with the PBS was 484 ml in a total sample of 143 patients operated of TKA reported by 5 authors (a) and 324 ml for 401 patients operated of THA reported by 8 authors (6)

Author	Patients with PBS (N)	Mean volume of blood reinfused (ml)
a) TKA		
Kristensen (36)	13	920
Shenolikar (35)	50	349
Slagis (27)	15	883
Moonen (37)	45	378
Atay (5)	20	480
Total sample	143	484
b) THA		
Kristensen (36)	18	650
Grosvenor (38)	62	349
Slagis (27)	24	437
Moonen (37)	35	203
Atay (5)	17	413
Mirza (28)	109	300
Smith (26)	76	252
Monte del Trujillo (34)	60	336
Total sample	401	324

Table 7. Maximum volume to reinfuse with PBS (from Eurosets Experience) 40

Patient's weight (Kg)	Men (ml)	Women (ml)
50-60	650	550
61-70	750	650
71-80	850	750
81-90	950	850
91-100	1000	950
> 100	1000	1000

The absolute and systemic *contraindications to the PBS* with or without washing have not been considered by none of the authors included. However in the technical file of Eurosets (40) is asserted, although without statistical validity, that the absolute contraindications to the reinfusion are serious renal disease found out in the preoperative phase and the coagulopathy highlighted in the preoperative phase with usual functional tests (platelet count, bleeding time, prothrombin time). In literature situations where the reinfusion in patients affected by HCV and HIV caused a worsening of the disease are not mentioned (40). For what concerns the contraindications to the PBS without washing, just one author, among those selected, asserts that the reinfusion of unwashed shed blood is contraindicated in the patients affected by neoplasia, to avoid the dissemination of the tumor (metastasis). But the capacity of replication of neoplastic cells is nullified by the washing (41).

Discussion

In the patients operated of THA and TKA there is a continuous bleeding from the operating site. This bleed often involves the necessity to resort to allogeneic or autologous blood transfusions. There is often a

tendency to consider inevitable the recourse to ABT when there are efficient alternatives: the most suitable in the THA and TKA operations is the autologous transfusion with the technique of the PBS, the benefits and disadvantages of which have been shown in this paper.

From this review of the scientific literature it's emerged that the PBS is safer than ABT both for the patients, exposed to minor risk of complications, and for the health care staff that, having to do with a closed-circuit system, is less exposed to biological risk and to the transmission of pathogens.

Naturally the PBS doesn't assure the patient to not receive any ABT but it's emerged that the percentage of patients which must receive an ABT with the PBS is significantly lower than that of the patients without PBS. The risk of adverse events caused by the ABT that concern the heaviest complications, in other words the virus transmission and the reaction from AB0 incompatibility, is directly proportional to the number of transfused allogeneic bags (18). So the patients with the PBS result anyway less exposed to these risks.

Another aspect connected to the possible complications of the ABT concerns the costs. The paper by Rao et al. considers the complications of emo-transfusions, once again more frequent after ABT than PBS, but not the related costs connected to the management of the complications (6). Moreover in calculating the mean unit cost it must be considered that with only one kit for PBS it is possible to recover and transfuse a greater quantity of blood than that there is in a bag of allogeneic blood. Infact to calculate the mean cost of one unit of salvaged blood, total costs associated to the PBS have been divided for the number of transfused units (6).

From the comparison of the results of the papers reviewed, PBS reveals to be related to a lower risk of adverse events and wound complications.

Also the length of stay in hospital resulted shorter with PBS rather than that without PBS in different studies with statistical significance; some articles, as a counterpart, report conflicting results but without an appropriate statistical consistence. In the reviewed samples, patients without PBS were more subjected to ABT respect to those with PBS, but in the analyzed articles patients subjected to only PBS, to only ABT, to both PBS and ABT and to no transfusion therapy, were not properly compared. Therefore this missing information would be useful to better understand what of the different methods mainly influences the length of stay and the costs.

The main complications of the PBS, which must be promptly recognized and managed to be reduced, are air embolism, dilutional coagulopathy, hypervolemia, bacteremia, hemoglobinuria and anticoagulant overdose (15) (Table 8).

Other aspects would be worthy of further investigation, like the maximum volume to reinfuse, beyond to which the hypervolemia risk is elevated, and the absolute and systemic contraindications to PBS.

For what concerns the limits in terms of time, we can say that if the reinfusion of salvaged blood begins within 4-6 hours from the start of PBS, the complications connected to this method of autologous transfusion are reduced to the minimum (4, 39).

Table 8. PBS complications and precautions (15)

Complication	Preventive actions
Air embolism	Use a blood pomp with an in-line air sensor
Dilutional coagulopathy	Monitor patient's clotting factors and hemoglobin
Hypervolemia	Carefully monitor fluid administration
Bacteremia	Do not recover blood from contaminated surgical sites
Hemoglobinuria	Keep suction a slow as possible Wash blood with correct amount of normal saline
Anticoagulant Overdose	Deliver anticoagulant at raccomandeted rate Verify correct minimum volume in direct reinfusion devices

The review articles included in our literature revision do not fully treat all the parameters that we have considered and therefore were included with the other articles for a broader comparison of the various outcomes.

The recent Meta-Analysis of RCT by van Bodegom-Vos et al. shows that in the last years cell salvage is not effective anymore in reducing the exposure to ABT (25). This difference could be explained by an increased tendency to bleed in the increasing number of operated patients under antiplatelet drugs.

Anyway alternative strategies with tranexamic acid or other local hemostatic agents should be considered to reduce the bleeding risk.

Conclusions

On the basis of the reviewed articles we can conclude that PBS seems to be an adequate alternative to ABT in THA and TKA. Anyway PBS, both exclusive and accompanied to ABT, results safer respect to the ABT alone. Health care staff as well results exposed to minor risks using the PBS. The recourse to PBS can contribute to decrease the length of stay and costs. For this reasons this method of blood salvage should be considered in all those cases that are not mentioned in the contraindications.

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