Clinical efficacy of plasma-reduced platelet concentrates from multicomponent (MC) collection: a non-randomized prospective study in onco-haematological paediatric patients

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Abstract

Background and objectives. Platelet transfusions are currently used to prevent haemorrhagic events in onco-haematological patients. Recently, platelet concentrates from multicomponent collection have been introduced in several blood collection facilities. Moreover, plasma-reduced platelet concentrates (PC) have been proposed with the aim of reducing platelet transfusion-related reactions, but there is some concern about the real effectiveness of such products given the higher degree of platelet activation subsequent to the higher concentration of platelets. We performed a prospective, non randomized study to investigate the in-vivo efficacy of PC from a random donor (R-PC), plateletpheresis (A-PC) and plasma-reduced PC (PR-PC) from multicomponent collection.

Material and methods. Post transfusion platelet count increase was checked by Corrected Count Increment (CCI) at +1 hour and +24 hours. Patients were monitored for the onset of side effects such as changes in arterial blood pressure, pulse rate, body temperature and for reactions such as urticaria/rash, chills, fever, etc. Platelet-specific antibody search was carried out using an immunofluorescence method (PSIFT) in patients with unsatisfactory platelet count increment.

Results. Sixty-six onco-haematological patients received a total of 221 platelet transfusions and some

Introduzione

La trasfusione di piastre (plt) è di importanza capitale nella cura di pazienti sottoposti a chemioterapia ad alte dosi o a trapianto di cellule staminali emopoietiche (TCSE) per malattie emato-oncologiche, sia per prevenire che per trattare episodi di sanguinamento1-4. Attualmente, sono disponibili concentrati piastinici (CP) di differenti caratteristiche: a) CP da singolo donatore (S-CP) ottenuti per separazione da unità di sangue intero (450 ± 10% mL) o per centrifugazione a basso numero di giri o riunendo più buffy-coat5, b) CP da aferesi (A-CP), utilizzando diverse apparecchiature, la maggior parte delle quali sono in grado di ottenere CP leuco-pletti6-7 e c) CP sempre da aferesi, impiegando la raccolta multicomponente (MC) che consente la contestuale raccolta di più emocomponenti [CP e concentrati eritrocitari (CE); CP e plasma; CE e plasma; doppia raccolta di CE]8. Semplicemente modificando il programma di raccolta MC, siamo stati in grado di ottenere CP a plasma ridotto (PR-CP, emocomponente noto anche come "plt secche"), con la raccolta di 3,0x1011 plt in un piccolo volume (45-80 mL) di plasma.


Abbiamo, quindi, programmato uno studio prospettico, non-randomizzato, in pazienti destinati a ricevere CP per prevenire e/o trattare episodi emorragici al fine di: i)
patients received different type of PCs. Patients who were given R-PC underwent a total of 92 platelet transfusion events, while those who were given A-PC and PR-PC underwent a total of 58 and 71 platelet transfusion events, respectively. We did not find significant differences in post transfusion CCI either at +1 hour or +24 hours, in any of the three groups. Overall, patients received premedication in 116 platelet transfusion events and did not in 105 events. A total of nine moderate side effects were observed in transfused patients: six in individuals who received random donor PC and three reactions in patients who were given PR-PC from multicomponent collection. PSIFT results were negative when carried out in the nine patients who showed an unsatisfactory CCI on at least two occasions.

Conclusions. Plasma-reduced PC from multicomponent collection permitted a satisfactory post transfusion platelet increment, similar to that observed in patients who were given random donor PC and platelepheresis.

Key words: plasma-reduced platelet concentrates, clinical efficacy, platelet transfusion, side effects, multicomponent collection, platelepheresis

Introduction

Platelet transfusion is of paramount importance in supporting patients undergoing high-dose chemotherapy and/or haematopoietic stem cell transplantation for haematological diseases, as both prophylaxis and treatment for bleeding. Several types of platelet concentrates (PC) are presently available: a) random-PC (R-PC) obtained from the separation of standard (450 ± 10 % mL) whole blood units, using either the soft-spin method or the buffy-coat technique, b) apheresis-PC (A-PC) obtained by using different devices, most of which presently allow a WBC-reduced product to be collected and c) the recently introduced multicomponent collection (MC), which allows for the collection of different haemocomponents (PC and RBC, PC and plasma, plasma and RBC, double RBC-donation) using appropriate devices. By simply modifying the collection program, this latter modality also allows us to collect plasma-reduced PC (PR-PC, otherwise known as dry-platelets), yielding more than 3.0x10\(^11\) platelets in a reduced plasma volume (45-80 mL). PR-PC can be resuspended with a storage solution and can either be used to accertare se i PR-CP permettono una ridotta incidenza di reazioni trasfusionali e ii) stabilirne l'efficacia in vivo.

Pazienti e metodi

Pazienti

Abbiamo valutato pazienti pediatrici emato-oncologici, non selezionati, candidati a chemo-terapia o a TCSE, trattati con CP fra marzo 2001 e giugno 2002. L'inclusione nel protocollo di studio aveva ottenuto l'autorizzazione dei genitori. I pazienti che avevano sofferto precedentemente di reazioni trasfusionali venivano premedicati con steroidi o anti-istaminici.

Preparazione e trasfusioni dei CP

I CP erano stati ottenuti da donatori volontari, seguendo la normativa italiana sulla donazione di sangue. Partendo da unità di 450 mL di sangue intero raccolto in sacche triple (MacoPharma, Tourcoing, Francia), con CPD, venivano preparati S-CP con il metodo della centrifugazione lenta. Questi CP erano conservati a temperatura controllata di +22 °C e mantenuti in agitazione continua (8-10 gpm) sino alla loro utilizzazione. Ai fini statistici, abbiamo considerato che ogni S-CP contenesse 0,6 x 10\(^11\) plt, in diretto rapporto con i controlli di qualità che eseguimmo di routine (contenteno medio 0,65 ± 0,15x10\(^11\) plt, Perseghin et al., osservazioni non pubblicate). Per la raccolta di A-CP, veniva utilizzato il separatore cellulare Cobe Spectra LRS turbo (Gambro BCT, Lakewood, CO, USA), la procedura durava 90', e si otteneva una concentrazione finale di plt pari a circa 1.400x10\(^3\)/µL. Se del caso (per esempio, per riceventi a basso peso), l'A-CP veniva suddiviso in 2 unità.

Per la preparazione di PR-CP è stato impiegato il separatore Cobe Trima LRS (Gambro BCT), modificandone il programma per ottenere una raccolta di plt in un volume ridotto di plasma (non oltre 90 mL), con concentrazione finale di plt sino a 4.000 x 10\(^9\)/L. Dopo 1 h di riposo a temperatura ambiente, veniva aggiunta, in proporzione 2:1 rispetto al plasma, la soluzione T-SOL (Baxter, Deerfield, IL, USA), seguendo le indicazioni del produttore; poi si procedeva alla raccolta di un campione per i conteggi. Su tutti i CP (A-CP e PR-CP) veniva eseguito il conteggio piastrinico e quello dei leucociti (GB), quantunque il separatore avvertisse con un messaggio se il numero di GB contaminanti risultava superiore a 1 x 10\(^6\).
fresh or may be frozen as a long-term supply. A lower incidence of non-haemolytic transfusion-related side-effects using PR-PC versus R-PC or A-PC, has been reported, whilst a possible, higher degree of platelet activation observed in PR-PC obtained from MC collection as compared to A-PC could jeopardize efficacy in the clinical setting. However, few reports have been published to date on the in-vivo efficacy of different platelet concentrates within the paediatric onco-haematological setting. We therefore planned a prospective, non-randomized study in patients scheduled to receive PC transfusion to prevent or treat bleeding episodes i) to ascertain if PR-PC transfusion allows a reduced incidence of transfusion-related side-effects and ii) to assess the in-vivo efficacy of PR-PC transfusion.

**Patients and methods**

**Patients**

We evaluated unselected paediatric onco-haematological patients scheduled for chemotherapy or haematopoietic stem cell transplantation, who required PC transfusions between March 2001 and June 2002. Parents’ authorization was obtained for inclusion in the study protocol. Patients who had previously showed post-transfusion reactions were premedicated with steroids and/or anti-histamines.

**PC preparation and transfusion**

PCs were obtained from volunteer donors and in accordance with Italian legal requirements for blood donation. R-PCs were prepared using the soft-spin method from 450 mL whole blood unit collected in triple bag (MacoPharma, Tourcoing, France), anticoagulated with CDP. R-PCs were stored at controlled-temperature (+22 °C) while undergoing 8-10 rpm flat agitation until use. For statistical evaluation we assumed that each R-PC contained $0.6 \times 10^{11}$ platelets, according to our routinely performed quality-controls (mean R-PC content: $0.65 \pm 0.15 \times 10^{11}$; Perseghin et al., unpublished observations).

A-PCs were collected by means of a Cobe Spectra LRS Turbo cell separator (Gambro BCT, Lakewood, CO, USA) through a 90-min procedure with a final platelet concentration of about $1,400 \times 10^9 / \mu L$. When appropriate (i.e. in the case of a low-weight recipient), the A-PC unit was divided in two split units. PR-PCs were obtained by...
using the Cobe Trima LRS device (Gambro BCT),
the software program was modified to allow for the
collection of platelets in a reduced plasma volume
(up to 90 mL), with a platelet concentration up to
4,000x10^9/L. After 1h-rest at room temperature, T-SOL
(Baxter, Deerfield, IL, USA) was added to PR-PC in a
2:1 ratio, following the manufacturer's indications and
then the unit was sampled for counting, as reported
above. All A-PCs and PR-PCs were sampled for total
platelet content and WBC count even though both cell
separators displayed a warning message if more than 1
x 10^6 leucocytes contaminated the yield. All PCs were
transfused within 48h from collection. CCI was calculated
as previously reported10.

**Laboratory tests for PC assessment**

Peripheral blood counts in patients and quality controls
(platelet content and WBC count) on PCs were performed
using an SE 9500 RET automatic instrument (Sysmex Inc.,
Long Grove, IL, USA). WBC contamination was assessed
using the micro-droplet fluorochromatic assay15.

**Transfusion policy**

PCs were given prophylactically when patient's platelet
count was below 10x 10^9/L, following our internal guidelines
for platelet transfusion, or for higher values in presence of
bleeding episodes. We managed to give each patient a
platelet dose of 0.6 x 10^11/kg/bw, regardless of the PC
source. Patients received ABO compatible PC, without any
randomization. PCs were released for transfusion
depending on their availability in the inventory and on
patients characteristics (mostly patient's weight). Thus, a
given patient might received different types of PCs during
the study period. Patients who have had previously
experienced non-haemolytic transfusion-related side effects
(i.e. after R-PC) on at least two occasions were scheduled
to receive a different type of PC (A-PC or PR-PC). Low-
weight children were more likely to receive R-PC. In the
event of unsatisfactory CCI a platelet antibody search was
performed, as reported below. All patients received
leucocyte-poor PCs: A-PCs and RC-PCs were obtained by
means of cell separator equipped with the Leukoreduction
System (LRS), while R-PC underwent bedside filtration
(Purecell PL, Pall Medical, Milano, Italy) carried out by
trained nurses according to institutional protocols.

**Platelet antibody immunofluorescence test**

volte e si aggiungevano 25 µL di glicerolo al 75%.
Una goccia di questa sospensione veniva distesa su
un vetrino e letta al microscopio a fluorescenza.
L'intensità della fluorescenza delle piastrine,
paragonata a controlli positivi e negativi, veniva
valutata come negativa, debolmente positiva o
positiva.

**Efficacia dei CP e valutazione della tossicità**

Il personale infermieristico rilevava e registrava le
pulsazioni cardiache, la pressione arteriosa e la temperatura
e ogni possibile reazione sfavorevole alla trasfusione di
CP. Il conteggio delle plt veniva eseguito sia prima che
dopo 1 h dalla trasfusione in tutti i pazienti (compresi gli
ambulatoriali), mentre un ulteriore conteggio veniva
eseguito il giorno successivo soltanto nei pazienti
ricoverati. Abbiamo, quindi, valutato le possibili correlazioni
fra caratteristiche dei riceventi (peso, conteggio pre-
trasfusione, febbre, TCSE) e la conta piastrinica post-
trasfusionale.

**Analisi statistica**

Queste analisi sono state condotte con uno specifico
software (Statsoft Inc, Tulsa, OK, USA). I dati sono mostrati
come mediana e range, mentre le variabili continue sono
presentate come media (±DS). Sono stati utilizzati, se del
caso, sia test parametrici che non parametrici. I valori di
p < 0,05 sono stati giudicati significativi.

**Risultati**

Sessantasei pazienti (27 sotto chemioterapia e 39
sottoposti a TCSE), oggetto di questo studio, hanno
complessivamente ricevuto 221 trasfusioni di CP (92 RP-
CP, 58 A-CP e 71 S-CP) come mostrato in tabella I. La
contaminazione in GB è sempre stata inferiore a 1x10^6 nei
CP ottenuti impiegando i due tipi di separatori utilizzati. La
concentrazione plt mediana è stata di 2,830 x 10^9/L (range
2,010-3,980) nei RP-CP (prima dell'aggiunta di T-SOL) e di
1,470 x 10^9/L (range 1,065-1,920) per A-CP. I pazienti che
hanno ricevuto S-CP erano di peso corporeo minore,
se paragonati a quelli degli altri due gruppi (Tabella
II). Questi dati riflettevano soprattutto la disponibilità
dei prodotti al momento piuttosto che le
caratteristiche di non-randomizzazione dello studio.
La conta pre-trasfusionale delle plt era leggermente
Platelet-specific antibody testing was carried out with the immunofluorescence method (PSIFT). Briefly, 100 mL of patient's serum was incubated for 30 minutes at laboratory temperature with 100 mL of platelet suspensions (3-5 x 10^11 /L) from 6 group O donors. After 4 washes with phosphate buffered solution containing EDTA and Bovine Serum Albumin, 100 mL of goat anti-human IgG conjugated with FITC (Sigma Inc, St. Louis, MO,USA) was added and left to incubate for 30 minutes at laboratory room temperature in the dark. Platelets were washed 4 times and 25 mL of 75% glycerol was added. A drop of the suspension was then placed on a slide for examination with a fluorescence microscope. Fluorescence intensity and distribution displayed by platelets compared with positive and negative controls, was scored as negative, weakly positive, and positive.

**PC efficacy and toxicity assessment**

Vital signs (heart rate, arterial blood pressure, body temperature) and possible side effects were recorded più bassa nei pazienti che avevano ricevuto A-CP piuttosto che in quelli che avevano ricevuto S-CP o RP-CP (14 ± 8 x 10^9/L contro 16 ± 9 x 10^9/L e 19±10^9/L, rispettivamente; p = 0,023). Il CCI a 1 h e a 24 h non differiva nei tre gruppi (Tabella II). Inoltre, l'incremento di plt non era differente nei pazienti trapiantato rispetto a quelli sottoposti a chemioterapia: era, infatti, di 13 ± 11 contro 12 ± 7 (p = ns) a 1 h e di 9±10 contro 8 ± 7 (p = ns) a 24 h, rispettivamente. Tuttavia, una piccola differenza si è potuta osservare nel CCI a 1 h nei pazienti febbrili (>38 °C) se paragonati a pazienti senza febbre: 8 ± 7 contro 13 ± 11 (p = 0,043), ma tale differenza non si riscontrava a 24 h.

A 27 malati, riceventi complessivamente 116 CP (4,3 paziente), era stata somministrata una premedicazione (con anti-istaminici o idrocortisone) perché avevano sofferto, in precedenza, di reazioni trasfusionali, mentre 39 pazienti, riceventi un totale di 105 CP (2,7/paziente), non erano stati premedicati (Tabella II).

A 9 malati, con CCI insoddisfacente (<7,5 a 1 h) rilevato almeno due volte, sono stati eseguiti complessivamente 10 PSIFT, tutti con esito negativo. Il mancato incremento di
by nurses. Platelet count was checked pre- and post-transfusion (+1 hour) in all patients (including out-patients) while an additional platelet count was performed the following day in hospitalized patients only. Thus, we investigated the possible correlation between patients' characteristics (weight, pre-transfusion platelet count, fever, haematopoietic stem cell transplantation) and post transfusion platelet count.

**Statistics**

Statistical analysis was performed by means of a computer specific software (Statsoft Inc, Tulsa, OK, USA). Data are shown as median and range, while continuous variables are presented as mean ± SD. Both parametric and non-parametric tests were used, when appropriate; p values <0.05 were considered as significant.

**Results**

For 66 patients undergoing chemotherapy (27) or Haematopoietic Stem Cell (HSC) transplantation (39) a total of 221 platelet transfusions (92 R-PC, 58 A-PC, 71 PR-PC) were registered in the study (Table I). The total WBC content was lower than 1x10^6 for all PC products obtained using the two cell separators. Median platelet concentration was 2,850 x 10^9 /L (range 2,010-3,980) in PR-PC (before the addition of T-SOL) and 1,470 x 10^9 /L (range 1,065-1,920) in A-PC. Patients who were given R-PC had a lower body-weight compared to the other two groups (Table II): these findings were due mainly to inventory disponibility and to the non-randomized nature of the study. Pre-transfusion platelet count was slightly lower in patients belonging to the A-PC group compared to R-PC and PR-PC patients (14 ± 8x10^9/L vs 16 ± 9x10^9/L and 19 ± 10^9/L, respectively, p = 0.023). CCI at +1 hour and at +24 hours did not differ in the three groups of patients (Table II). Moreover, platelet...
increase was no different in transplanted patients compared to those who received chemotherapy: CCI was 13 ± 11 vs 12 ± 7 (p = ns) at +1 hour and 9 ± 10 vs 8 ± 7 (p = ns) at +24 hours, respectively. However, a slight difference was observed in CCI at +1 hour in patients with fever (T >38 °C) compared to afebrile patients: 8 ± 7 vs 13 ± 11 (p = 0.043), although no difference was observed at +24 hours. Twenty-seven patients who underwent a total of 116 platelet transfusions (4.3/patient) were given pre-transfusion medication (anti-histamines and/or hydrocortisone), due to previous transfusion-related side-effects, while 39 patients who underwent a total of 105 platelet transfusions (2.7/patient) received no premedication (Table II). Nine patients, in whom an unsatisfactory CCI (<7.5 at +1 hour) was observed at least twice, underwent a total of 10 PSIFT antibody searches, with negative results. The failed platelet increase was thus attributed to concomitant therapy (antimycotic drugs) and/or pre-existing clinical conditions such as gastro-intestinal bleeding. These 9 patients were then given PC without any platelet crossmatch. From a clinical point of view, six platelet transfusion-related side-effects (asthenia, urticaria/rash, fever, chills, headache) were observed in 5 out of 47 (10 %) premedicated patients who received bedside filtered R-PC. One patient complained twice of fever and chills. Only three reactions (urticaria, chills) were observed in two non premedicated patients, who both received PR-PC. No side effects were reported in patients who were given A-PC (Table III). As a whole, 7 out 66 patients (11 %) complained of moderate platelet transfusion-related side effects, which were observed in 9 out 221 (4 %) platelet transfusions. No significant changes in arterial blood pressure and/or pulse rate was observed (data not shown).

**Discussion**

The routine use of platelet transfusions, either as prophylaxis or treatment, has greatly reduced the incidence of severe/fatal haemorrhagic events in onco-haematological settings\(^1\)-\(^4\). Platelet transfusions are usually administered to patients as random donor PC, plateletpheresis or, more recently, as PC from multicomponent collections\(^8\),\(^16\),\(^17\). This latter product is given to patients as PR-PC, with the aim of reducing the incidence of plasma-protein and cytokines-related post-transfusion reactions\(^18\). Nevertheless, there is some concern about the clinical in-vitro efficacy of PR-PC, because it has been shown that the collection of PR-PC may induce a certain level of platelet activation, which in turn may enhance activated platelets removal by tissue macrophages\(^19\). Our prospective, non-randomized study, the research of anticorpi anti-platelet-specifici, effetttuata utilizzando la tecnica PSIFT, ha dato esito negativo in 9 pazienti che avevano avuto CCI 2000, misura che si è dimostrata efficace per prevenire l’incidenza di refrattarietà piastrinica 25,26. È stato precedentemente riportato che l’incidenza di anticorpi diretti contro glicoproteine piastrinico-specifiche in trasfusi con PC
study, performed in a pediatric onco-haematological unit, did not show any significant difference in terms of post-transfusion platelet increase, both at +1 h and +24 h, in the three groups studied who were given PCs from different origins. We have previously shown that platelets from PR-PC have a lower response to in-vitro agonists (collagen, ADP, thromboxane-A2 analog) and a higher percentage of P-selectin-expressing platelets compared to platelets from R-PC and A-PC\textsuperscript{12}. However, we did not find any significant difference in CCI in this present study. It should be pointed out that all PCs were transfused within 48 h from collection, so we could not ascertain possible consequences of PR-PC protracted storage (up to 5 days) on in-vitro efficacy. In a previous study\textsuperscript{13} carried out in 87 patients who underwent HSCT, +16-h CCI was 5.7 ± 8.3, and significant correlation was found with four factors: concomitant therapy with vancomycin, alloimmunization, CMV infections and the use of a cell separator for the preparation of platelet concentrates. It has been shown that levels of platelet activation can be influenced by the method of collection/processing and can increase during storage with possible detrimental effects on post-transfusion platelet increase\textsuperscript{20}. Furthermore, we did not find any differences in CCI between transplanted and untransplanted patients, although a lower platelet increase was observed in febrile (T >38 °C) patients compared to others. A previous study, performed only in paediatric transplanted patients, found different factors which affected platelet increase, namely vancomycin therapy, alloimmunization, platelet source and CMV infection\textsuperscript{13}. In the present study, the search for platelet specific antibodies, carried out using the PSIFT technique, gave negative results in the 9 patients who showed an unsatisfactory CCI. Eight of these nine patients were given stem cell transplantation (2 received autologous SC, 2 URD-SC, and 5 allo-SC) and the lower platelet increase was attributed to either concomitant antymycotic therapy (4 patients) and/or to gastro-intestinal bleeding (5 patients) or fever (6 patients). Moreover, it is well known that factors other than allo-immunization may influence the onset of platelet transfusion refractoriness. These factors include PC quality, leucocyte contamination, fever, splenomegaly, drug-related antibodies, DIC, etc.\textsuperscript{21}. No conclusion could be drawn as to the real incidence of platelet specific antibodies, since no basal platelet antibody screening was performed. Nevertheless, it is likely that in our patient series the real incidence was markedly lower than the 20-30% previously reported in HLA-immunized patients\textsuperscript{22-24}. Since the early ‘90s leucodepleted blood components have been era del 3,8%\textsuperscript{27}. Da un punto di vista clinico, abbiamo osservato un’incidenza globale di reazioni correlate alla trasfusione di CP veramente molto bassa: soltanto 7 riceventi (11%) hanno presentato 9 reazioni. È degno di nota il fatto che sei delle sopraccitate reazioni avevano interessato pazienti che erano stati trasfusi con S-CP ed erano stati premedicati con anti-istaminici e idrocortisone. Dato che tutti i nostri S-CP erano leucodepleti per filtrazione bed side, queste reazioni erano probabilmente dovute a citochine plasmatiche, quali IL-1, TNF-a e IL-6, rilasciate dai leucociti danneggiati durante la conservazione\textsuperscript{28}. Bisogna tener presente che la filtrazione bed side genera bradichinina, che agisce in soggetti in cura con ACE-inibitori. La bradichinina, un peptide a 9 amminoacidi con forti proprietà vasodilatatrici, può indurre, a sua volta, eritemi, ipotensione grave, dolori addominali, dispnea\textsuperscript{30}. Nessuno dei nostri pazienti, trasfusi con S-CP filtrati bed side, era in trattamento con ACE-inibitori. Si è dimostrato che la filtrazione bed side di emocomponenti, se eseguita da personale ben addestrato, è sovrapponibile a quella effettuata in laboratorio\textsuperscript{29}. La premedicazione non evita le reazioni e quanto da noi constatato è in accordo con quanto recentemente riportato da Wang et al\textsuperscript{31}. Questi Autori non hanno rilevato nessuna differenza fra pazienti premedicati e non premedicati, trasfusi con S-CP leucodepleti: l’incidenza delle reazioni era del 15,4% e del 15,2%, rispettivamente. Queste osservazioni, unite alle nostre, potrebbero incoraggiare i curanti a traslasciare la politica della premedicazione.

Le nostre conclusioni principali sono le seguenti: i) i PR-CP permettono un incremento soddisfacente nel numero delle plt, se paragonati a S-CP e ad A-CP; ii) si è osservata una bassa incidenza di reazioni post-trasfusionali, che intervengono soprattutto in pazienti trasfusi con S-CP sottoposti a filtrazione bed side e la premedicazione non evita la loro insorgenza e, infine, iii) nessuno dei nostri pazienti, che hanno avuto CCI insoddisfacenti, presentava positività alla ricerca di anticorpi anti-piastrinospecifici, forse in relazione alla nostra politica di leucodeplezione totale degli emocomponenti.

**Riassunto**

**Premesse e obiettivi.** Le trasfusioni di piastrine vengono generalmente impiegate per trattare e/o prevenire episodi emorragici in pazienti oncoematologici. Del tutto recentemente, in molti servizi
assigned to onco-haematological patients at our hospital and universal pre-storage WBC reduction has been performed since the middle of 2000, which has proved to be effective in preventing HLA-alloimmunization and subsequent platelet transfusion refractoriness25,26. It has also been previously reported that the incidence of platelet specific antibodies against platelet glycoproteins in patients receiving chronic platelet support was 3.8%27. From a clinical point of view, we observed a very low overall incidence of platelet transfusion-related reactions: only seven patients (11%) reported a total of 9 reactions. It is worth emphasizing that six of the above reported reactions occurred in patients given R-PCs and who were premedicated with antihistamines and/or hydrocortisone. Since all our R-PCs were leucocyte reduced by means of bedside filtration, these reactions were more likely due to plasma cytokines, such as IL-1, TNF-α and IL-6, released from damaged WBCs during the storage period28. It should be kept in mind that bedside filtration may induce bradykinin generation, more frequently in patients who are given ACE-inhibitors. Bradykinin, a nonapeptide with strong vasodilatatory properties, may in turn induce side-effects such as flushing, severe hypotension, abdominal pain, dyspnoea30. None of our patients who received bedside filtered R-PC was on ACE-inhibitors treatment. It has been demonstrated that blood component bedside filtration performed by well-trained nursing staff is comparable to that performed in the laboratory29. Premedication did not avoid the onset of platelet transfusion-related reactions and our findings are in keeping with those recently reported by Wang et al.31. These Authors did not find any difference between premedicated and non premedicated patients given single-donor WBC-reduced platelet concentrates: the incidence of transfusion-related reactions was 15.4% and 15.2%, respectively. These observations together with our findings could encourage attending physicians to abandon what appears to be an useless premedication policy. In conclusion, our main findings were as follows: i) PR-PC allowed for a satisfactory platelet increase when compared with R-PC and A-PC; ii) a low incidence of platelet transfusion-related side effects was observed, occurring mostly in patients who were given bedside filtered R-PC and that premedication did not fully avoid the onset of reactions; and finally, iii) none of our patients who showed an unsatisfactory CCI had a positive platelet-specific antibody search, probably due to our universal WBC depletion policy.

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transfusionali si sono iniziati a preparare concentrati piastrinici (CP) con il sistema di raccolta multicomponente (MC). Inoltre, è stato proposto di preparare CP a plasma ridotto (PR-CP) con lo scopo di diminuire le reazioni, pur esistendo alcune perplessità circa la reale efficacia di questo prodotto, se si considera la consistente attivazione piastrinica correlata all'aumentata concentrazione dei trombociti. Abbiamo condotto uno studio prospettico, non randomizzato, per valutare l'efficacia in vivo dei CP da singolo donatore (S-CP), di quelli da aferesi (A-CP) e di quelli PR-CP ottenuti con la raccolta MC.

Materiali e metodi. L'incremento post-trasfusionale nel numero delle plt è stato valutato con il CCI (Corrected Count Increment) dopo 1 h e dopo 24 h dalla trasfusione. I pazienti sono stati monitorati per l'insorgenza di effetti collaterali, quali le variazioni nella pressione arteriosa, nel numero delle pulsazioni, nella temperatura corporea o per reazioni, quali orticaria, brividi, febbre ecc. Nei pazienti con CCI insoddisfacente sono stati ricercati gli anticorpi specifici antipiastrine in immunofluorescenza (PSIFT).

Risultati. Sessantasei pazienti onco-ematologici hanno ricevuto complessivamente 221 trasfusioni di plt e alcuni di essi sono stati trasfusi con tipi diversi di CP. Novantadue sono state le trasfusioni di S-CP, 58 quelle di A-CP e 71 quelle di PR-CP. Non abbiamo riscontrato differenze significative nel CCI a 1 h e a 24 h tra questi tre tipi di emocomponenti. Centosedici trasfusioni sono state precedute da pre-medicazione, non utilizzata nelle rimanenti 105. Nove sono state le lievi reazioni nei pazienti trasfusi: 6 in soggetti che avevano ricevuto S-CP e 3 in pazienti che avevano ricevuto PR-CP. Lo PSIFT è risultato negativo in questi 9 riceventi, che, in almeno due occasioni, avevano dimostrato un CCI deludente.

Conclusioni. I PR-CP da raccolta MC permettono validi CCI, sovrapponibili a quelli che si ottengono con S-CP e/o A-CP.

Parole chiave. Concentrati piastrinici e plasma ridotto, efficacia clinica, trasfusioni piastriniche, raccolta multicomponente, reazioni trasfusionali

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In-vivo efficacy of plasma-reduced platelets

References


