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THE SINGLE-UNIT TRANSFUSION IN THE BLED-OUT OBSTETRIC PATIENT

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THE HISTORICAL PRACTICE OF SINGLE-UNIT TRANSFUSION

The first reported blood transfusion took place in Rome in 1492. Pope Innocent VIII suffered an apoplectic stroke, became weak and lapsed into coma. His physicians advised a blood transfusion in hopes that it would help their patient. Employing the crude methods of the day, the Pope failed to benefit from this intervention and died by the end of that year. Since then, many advances have been made, blood groups have been discovered and transfusion practices refined. Presently, blood is part of the everyday armamentarium used by physicians to treat countless diseases and conditions.

In their 2005 retrospective analysis evaluating the role of single-unit red blood cell transfusion, Ma and colleagues noted that, in the 1960s, single units were deemed insufficient to correct anemia and, therefore, useless[1]. These investigators also retold a clinical maxim from that time, i.e. the patient whose transfusion requirements could be met with one unit of red blood cells was no more in need of a transfusion than the donor who gave 500 ml of blood. Although the origins of this maxim are unclear, the prevailing attitude in the medical community was rather obvious. In the years following the 1962 Joint Blood Council call for scrutiny of blood transfusion practices in hospitals having a predominance of single-unit transfusions, one study found that 60–70% of these interventions were not indicated[2]; in addition, two studies found that all of the single-unit transfusions assessed were unnecessary or questionable[3,4], and yet another study found this practice questionable in 38% of assessed cases[5]. The very existence of these investigations documents the widespread practice of single-unit transfusions and the scrutiny to which they were subjected during the 1960s.

The debate on the usefulness of single-unit red blood cell transfusions continued with vigor in the following decades. In 1985, Grindon and associates[6] condemned the scrutiny of single-unit transfusions advocated in 1962 by the Joint Blood Council, stating that the 'administration of one unit of blood more often reflects appropriate use than misuse'. One year later, in 1986, an observational study reported that most single-unit transfusions were administered during surgery and that the indications for 62% of these were questionable[7]. Very shortly thereafter, however, a case report published in the *Journal of the American Medical Association* demonstrated that a single-unit transfusion increased the hematocrit to a safe level, especially in patients with low body mass index[8].

EVENTS LEADING TO ALTERATION OF BLOOD TRANSFUSION PRACTICES

The conflicting opinions were so numerous that the US government decided to address this issue. However, this effort only provided tangential guidelines rather than ending the debate. In 1988, the National Institutes of Health (NIH) formulated a Consensus Conference Statement, entitled 'Perioperative Red Cell Transfusion'. This document recommended the threshold of hemoglobin concentration for transfusion to be lowered from 10 g/dl to a value between 7 and 10 g/dl, depending on the clinical assessment, laboratory data, and volemia of individual patients. At the same time, it was

deemed advisable that the number of units of blood administered should be kept to a minimum, mostly to reduce the number of transmitted infections[9].

The safety concerns expressed by the NIH were amplified by additional reports associating allogenic blood transfusions with infections, transfusion-related and allergic reactions as well as adverse immunomodulatory effects[10,11]. A review published in the *British Medical Journal* in 1990[12] sought to bring an end to single-unit transfusions. Simply stated, this article opined that the single-unit transfusion significantly increased the risks of viral infection while, at the same time, offered little or no therapeutic benefit. In the immediate aftermath of this publication, a study conducted in 1992 in a West African city, also published in the *British Medical Journal*, estimated the risk of HIV infection to be between 5.4 and 10.6 per 100 units of blood administered, a substantial threat even in cases of single-unit transfusions in developing countries[13].

RE-EMERGENCE OF CONSIDERATION OF THE SINGLE-UNIT TRANSFUSION

Not surprisingly, the 1990 *British Medical Journal* publication and others condemning single-unit red blood cell transfusion did not bring the debate to a halt. At the same time, the studies from the 1960s to the 1980s warned against administering single-unit red blood cell transfusions, and clinical guidelines suggested ever-lower thresholds for transfusion as a means to preserve blood resources and increase safety[14]. Whereas some physicians became convinced that single-unit blood transfusions had no place in the treatment of anemia, others came to believe, somewhat paradoxically, that individual units of blood should be given as needed, but only when the patient's hemoglobin concentration fell below a specified threshold, which varied across guidelines. As a counterplea to those who were opposed to single-unit transfusions and in favor of low, specified thresholds of hemoglobin concentration for transfusion, one 1992 study concluded that transfusion practices should be audited for undertransfusion as well as overtransfusion[15]. This suggestion, i.e. the possibility that patients could be undertransfused, was repeated in 1998 by a study that pointed out the dangers of lowering transfusion thresholds[16].

Shortly thereafter, the 1999 multicenter Transfusion in Critical Care (TRICC) trial randomized intensive-care patients to receive 'restricted' or 'liberal' red blood cell transfusions in order to analyze overall 30-day mortality rates in patients who might be undertransfused[17]. Patients received transfusions when their hemoglobin concentrations dropped below 7 g/dl in the restricted treatment group or 9 g/dl in the liberal treatment group. Mortality rates in this Canadian trial were similar in the two groups, but mortality was significantly lower among patients who were less acutely ill in the restricted treatment group.

A more recent study (2003) conducted to assess transfusion practices in a large Scottish hospital concluded that hospital clinicians administered transfusions when their patients' hemoglobin concentrations were between 7 and 9 g/dl[18]. Not only did the clinicians not follow the available TRICC trial protocol, which proposed transfusions only when hemoglobin concentrations fell below 7 g/dl, but the study's authors reported that the Scottish practices were consistent with the findings of other recently published studies[19-21]. In 2004, hoping to finally close the argument fuelled by the TRICC trial, a Canadian review reaffirmed the 1988 NIH recommendation regarding thresholds by stating, 'The quest for a universal transfusion trigger, i.e. one that would be applicable to patients of all ages under all circumstances, must be abandoned. All RBC (red blood cell) transfusions must be tailored to the patient's needs as it arises'[22]. This statement is of particular relevance to obstetricians, who commonly deal with anemic parturients and occasionally deal with bled-out postpartum mothers.

In 2005, Ma and collaborators[1] analyzed the results of single-unit transfusions for thresholds that began at 7 g/dl, and were raised to 9 g/dl by increments of 0.5 g/dl. These investigators demonstrated that, for most patients, the transfusion of one unit of red blood cells could raise the hemoglobin concentration sufficiently to avoid the need for a second unit. When the goal of red blood cell transfusion was to maintain the

hemoglobin concentration above a threshold considered as safe, they concluded, 'the single-unit transfusions may not only be appropriate, but preferable.' Unfortunately, the circumstances leading to compliance with the premises of using a threshold level before administering a transfusion do not apply in all parts of the world and are particularly restrictive in terms of bled-out parturients in the developing world.

SINGLE-UNIT TRANSFUSIONS IN THE BLED-OUT PATIENT OF THE DEVELOPING WORLD

The only subgroup analyzed in the 2005 study by Ma and collaborators[1] consisted of orthopedic patients, and the authors did not mention whether their analysis included pregnant women who experienced postpartum hemorrhage or were anemic. In 1992, the World Health Organization (WHO) published a tabulation of its 1990 estimates of the global death burden from all forms of anemia. Women of reproductive age were determined to be at greater risk of mortality from anemia than other groups of individuals[23]. Figure 1 shows the case fatality rate in relation to maternal anemia.

Anemia during pregnancy increases the risk of death, as it may lead to rapid cardiac decompensation, even without the additional stress of a true postpartum hemorrhage. Under such circumstances, the loss of less than 500 ml of blood could represent a fatal insult in a severely anemic woman. When the hemoglobin concentration is < 8 g/l, compensatory mechanisms fail, lactic acid accumulates and patients become breathless at rest. Cardiac failure may occur when the hemoglobin concentration is < 4 g/l, especially with twin pregnancies or with splenomegaly.

Based on available evidence, the single-unit transfusion should remain a viable therapeutic option in selected obstetric patients, especially in the developing world, where many women finish their pregnancies in moderate or severe anemic states. Depending on a variety of circumstances, such patients may die within a relatively short time after a postpartum

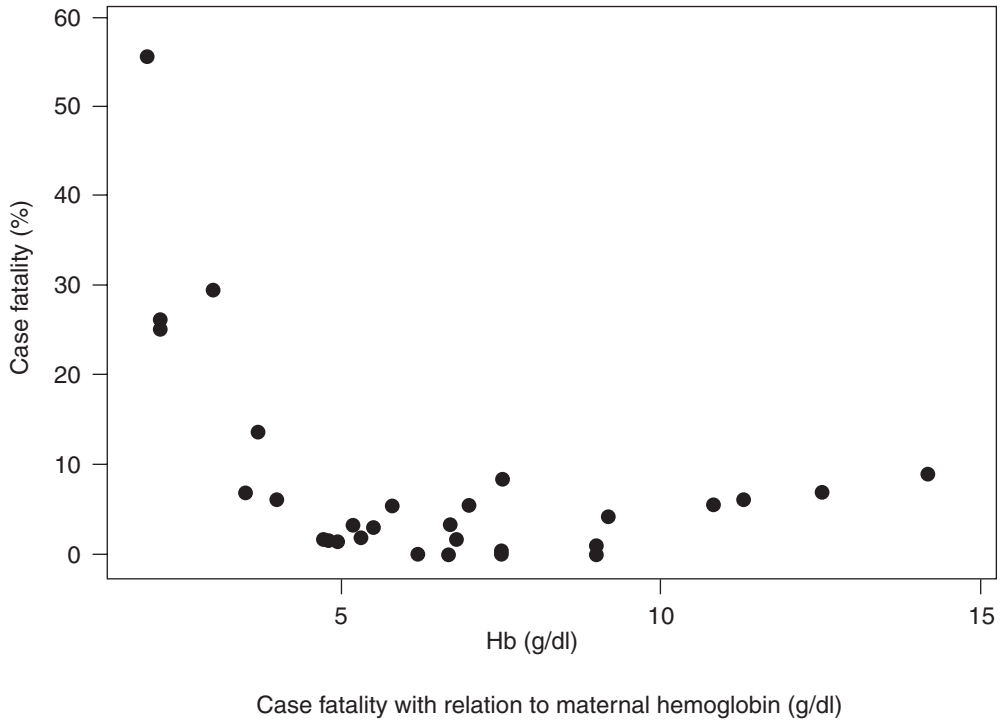

Figure 1 An analysis of anemia and pregnancy-related maternal mortality. Modified from Brabin BJ, Hakimi M, Pelletier D. *J Nutr* 2001;131:604S–14S

hemorrhage. If they do survive and if they are fortunate enough to be transported to a place where transfusion is available along with other resuscitative measures, a single-unit transfusion may make the difference between whether or not the woman can be considered sufficiently well to return home for aftercare.

Clearly, each case must be evaluated on its own merit. Sometimes, care-givers will be sufficiently satisfied with the effect of one unit that they may hold off a second planned transfusion, especially if they think that the patient has sufficiently recovered from the insult of postpartum hemorrhage. It is unlikely, however, that the effect of single-unit transfusion in women who have sustained postpartum hemorrhage will ever be examined in a randomized, controlled trial. In addition, it is highly unlikely that such a trial, if ever proposed to most western world institutional review boards, would be considered ethical.

SUMMARY

In summary, numerous studies have shown that single-unit transfusion can ameliorate symptoms of chronic anemia. Its value in obstetric emergencies when the anemia is acute has never been tested. In countries where resources are poor and the majority of women have anemia at the onset of their pregnancies, even the slightest deviation from normality during labor and delivery may lead to excessive obstetric hemorrhage that can put a woman's life at risk. In these cases, after stabilizing the patient with whatever resuscitative measures are available, transfer to a suitable center would be ideal. There, blood should be given, preferably typed and cross-matched and screened for infections. Unfortunately, such an eventuality is rare in the developing world, and patients, if they survive, arrive at the referral center in a moribund state. Some of these women, especially those who are younger and have stopped bleeding, may benefit from a single unit of blood along with other appropriate therapeutic measures. If, in the opinion of the clinician, this appears to be a reasonable course of action, then the single unit should not be denied simply in order to comply with what presently appears to be an outdated dictum[24].

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