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Blood transfusion therapy in cancer patients: Modern aspects (literature review)

Relevance: *Anemia is a common syndrome in cancer patients, and blood transfusion is the most common treatment for anemia. Anemia and blood transfusion are associated with worse clinical outcomes. The efficacy and safety of different blood transfusion strategies are unclear.*

The study aimed to analyze current blood transfusion strategies in oncology.

Results: *In most clinical situations, a restrictive strategy showed efficacy and safety. However, low perioperative hemoglobin level is associated with increased mortality and complication rates. Several clinical trials demonstrated the benefits of liberal strategy; it may be due to comorbidities and low compensatory ability.*

Conclusion: *Anemia in cancer patients is associated with worse clinical outcomes. Current blood transfusion strategies in oncology follow a restrictive approach based on the likelihood of blood transfusion complications. Oncology patients represent a challenging population that requires a personalized approach to perioperative anemia management.*

Keywords: *anemia, blood transfusion in oncology, restrictive blood transfusion strategy, liberal blood transfusion strategy.*

Introduction: Anemia is a widespread syndrome in patients with malignant neoplasms. The Russian Society of Clinical Oncology reports this syndrome in approximately 40% of patients with solid neoplasms, while anemia incidence reaches 80% in patients with neoplasms of the hematopoietic system [1]. Anemia development in cancer patients may also be associated with radiation or chemotherapy. Surgical treatment widely used in oncological practice also leads to anemia development due to acute blood loss during volumetric surgical interventions.

The World Health Organization (WHO) classifies anemia severity by the hemoglobin level depending on gender, age, and some other factors [2]. The hemoglobin level of 129-110 g/l in men (over 15 years old) refers to mild anemia, 109-80 g/l – moderate anemia, and below 80 g/l – severe anemia. Standard hemoglobin levels for females (over 15 years old and outside pregnancy) are 119-110 g/l – mild anemia, 109-80 g/l – moderate anemia, below 80 g/l – severe anemia. The national literature offers anemia severity gradation different from the WHO classification [3].

Materials and Methods: The literature search was made in PubMed/Medline, Cochrane Library databases for 2002-2019 by the keywords "blood transfusion in oncology," "transfusion strategy," "restrictive and liberal transfusion strategy," "anemia," and "cancer." This review includes original scientific articles on the research topic.

Results: Donor red blood cell transfusion plays a leading role in treating anemia in patients with malignancies, irrespective of the anemia genesis. An analysis of anemia treatment in cancer patients in Europe shows both a high frequency of blood transfusions and high hemoglobin values during transfusions [4, 5]. The literature questions the appropriateness and emphasizes the high incidence of complications associated with this treatment method. The European Society of Medical Oncologists (ESMO) cancer patients' anemia treatment guidelines prescribe a restrictive approach to donor red cell transfusions: hemoglo-

bin 70-80 g/l; if clinical symptoms suggest severe anemia, a higher hemoglobin level in transfusion is possible [6]. However, the risks of transfusion-related complications are indicated.

In 1999, the New England Journal of Medicine published the results of the multicenter randomized clinical trial TRICC, one of the first trials to usher in an era of restrictive approaches in transfusion medicine [7]. This study involving more than 800 patients demonstrated a significant reduction in mortality in the group of patients with a restrictive transfusion strategy. The restrictive strategy consisted of lowering target and threshold hemoglobin levels and reducing the number of donor red cell doses transfused. Worth noting that the restrictive transfusion strategy also had economic benefits in addition to improved clinical outcomes. This study initiated many studies comparing transfusion strategies in different clinical areas: neurosurgery and cardiac surgery, intensive care and perioperative medicine, cardiology, and geriatrics. Oncology practice is no exception: the studies assessed both various clinical outcomes and the tumor recurrence rate. However, perioperative anemia is an independent risk factor for adverse outcomes: increased 30-day mortality, the incidence of acute kidney injury, and infectious complications [8]. Perioperative anemia occurs in 25-75% of patients operated for malignant neoplasms [9]. Anemia is also associated with an increased incidence of adverse outcomes in cancer patients, but several features exist. Low hemoglobin increases the hypoxia-inducible factor (HIF-1) and interleukin-6 production, probably contributing to the neoplastic process [10]. Another factor increasing the risks associated with anemia in cancer patients is their much lower tolerance for anemia and very limited ability to compensate for anemia compared to the general surgical patient population [11] due to a frequent presence of concomitant respiratory and cardiovascular diseases.

As mentioned above, blood transfusion can be accompanied by complications that are directly related to the method (hemolytic reactions, acute lung transfusion damage, etc.) or deteriorate the long-term results.

In a meta-analysis including over 6000 patients, Wang T. et al. showed a significant impairment of outcomes (including increased mortality) in patients after lung cancer surgery with blood transfusion. The authors also noted a significant increase in the number of donor red cell doses [11]. Another systematic review and meta-analysis of blood transfusion in patients operated for colorectal cancer showed reduced clinical outcomes after blood transfusion, including increased mortality [12]. Similar results were reported based on an analysis of clinical outcomes in more than 4000 patients with colorectal cancer: blood transfusion was associated with higher mortality regardless of the initial anemia severity [13].

Another justification of a restrictive approach to donor red cell transfusions in patients with malignancies is that blood transfusion may increase the tumor relapse rate [14-16], possibly due to immunosuppression in response to blood transfusion. Despite much research in this area, there is no unequivocal opinion and clear position on the relationship between donor red cell transfusions and tumor relapse.

A prospective randomized clinical trial published in Anesthesiology involved 198 ICU cancer patients after major abdominal surgery [17]. Patients were randomized into groups with liberal (transfusion of hemoglobin levels below 90g/l) and restrictive (transfusion of hemoglobin levels below 70g/l) transfusion strategies. The number of postoperative complications was significantly lower in the liberal strategy group. However, some leading experts criticized that study. Another randomized trial of 2017 demonstrating the advantages of liberal transfusion included 300 cancer patients treated in ICU for septic shock [18]. The randomization was similar to the previous study. The liberal strategy group showed a higher survival rate at 28 and 90 days. This study results go against similar studies in patients with sepsis and septic shock in the general population and international guidelines for treating sepsis [19, 20]. The advantages of a liberal strategy in cancer patients can be explained by a frequent presence of comorbid cardiac disease. This group of patients requires higher hemoglobin values for increased oxygen delivery. Their ability to compensate for anemia (primarily by increasing cardiac output) is severely reduced, and they are at high risk of rapid heart failure decompensation. These findings were confirmed by many studies [21, 22].

The Republic of Kazakhstan's current legislation is dominated by the modern restrictive approach to the administration of erythrocyte-containing media transfusions [23]. The specifics of blood transfusions in cancer patients and with cardiac or other comorbidities are not emphasized. However, there is a possibility of an individual approach via oxygen consumption monitoring.

Conclusions: Anemia in cancer patients is associated with worse clinical outcomes. Current blood transfusion strategies in oncology follow a restrictive approach based on the likelihood of blood transfusion complications. On-

cology patients represent a challenging population that requires a personalized approach to perioperative anemia management.

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ТҰЖЫРЫМ

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Онкологиялық науқастардағы қан құю терапиясының заманауи аспектілері

Өзектілігі. Онкологиялық науқастарда анемия кең таралған синдром болып табылады, соған қарамастан, қан құю осы синдромды емдеуде әлі де жетекші орын алады. Анемия да, қан құю да клиникалық нәтижелердің нашарлауымен байланысты. Онкологиялық науқастарда әртүрлі қан құю стратегиялардың қауіпсіздігі мен тиімділігі мәселесі ашық күйінде қалып отыр.

Зерттеудің мақсаты: онкологиялық тәжірибеде қан құюға заманауи тәсілдерді шолу.

Нәтижелері: Көптеген клиникалық жағдайларда шектеулі қан құю стратегиясы тиімділік пен қауіпсіздікті көрсетті, алайда периперациондық кезеңдегі гемоглобиннің төмен көрсеткіштері онкологиялық науқастардағы өлім-жітім мен асқинулардың жоғарылауымен байланысты. Бірқатар зерттеулер онкологиядағы анағұрлым либералды қан құю тәсілдің қажеттілігін тікелей көрсетеді, бұл ауыр ілеспелі аурулармен және анемияны өтеу мүмкіндіктерінің шектеулі болуымен байланысты болуы мүмкін.

Тұжырымдар. Онкологиялық пациенттердегі қан аздық клиникалық нәтижелердің нашарлауымен байланысты, бірақ онкологиядағы гемотрансфузиялық терапияның заманауи стратегиялары гемотрансфузиялық асқинулардың ықтималдығын ескере отырып, шектеуші тәсілге сәйкес келеді. Онкологиялық науқастар пациенттердің күрделі санын білдіреді және периперациондық анемияны түзетуде дербестендірілген тәсілдерді талап етеді.

Түйінді сөздер: анемия, онкологияда қан құю, рестриктивті гемотрансфузиялық стратегиялар, либералды гемотрансфузиялық стратегиялар.

АННОТАЦИЯ

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Гемотрансфузионная терапия у онкологических больных: современные аспекты

Актуальность: Анемия у онкологических больных является широко распространенным синдромом, при этом гемотрансфузия все еще занимает ведущее место в лечении данного синдрома. Как анемия, так и гемотрансфузия ассоциированы с ухудшением клинических исходов.

Вопрос безопасности и эффективности различных гемотрансфузионных стратегий у онкологических пациентов остается открытым.

Цель: обзор современных подходов к гемотрансфузиям в онкологической практике.

Результаты: в большинстве клинических ситуаций ограничительная гемотрансфузионная стратегия показала эффективность и безопасность, однако низкие показатели гемоглобина в периперационном периоде ассоциированы с повышением летальности и осложнений у онкологических больных. Ряд исследований напрямую указывают на необходимость более либерального трансфузионного подхода в онкологии, что может быть связано с тяжелой сопутствующими заболеваниями и ограниченными возможностями компенсации анемии.

Выводы: Анемия у онкологических пациентов ассоциирована с ухудшением клинических исходов, но современные стратегии гемотрансфузионной терапии в онкологии соответствуют рестриктивному подходу с учетом вероятности гемотрансфузионных осложнений. Онкологические пациенты представляют сложную категорию пациентов и требуют персонализированных подходов в коррекции периперационной анемии.

Ключевые слова: анемия, гемотрансфузии в онкологии, рестриктивная стратегия гемотрансфузии, либеральная стратегия гемотрансфузии.