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Original article

Economic analysis of blood product transfusions according to the treatment of acute myeloid leukemia in the elderly

Étude économique de la transfusion de produits sanguins en fonction du traitement de la leucémie aiguë myéloïde du sujet âgé

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Abstract

Background. – Blood transfusion requirement represents one of the most significant cost driver associated with acute myeloid leukemia (AML). Low-intensity treatments (low-dose cytarabine, hypomethylating agents) have the potential to reduce transfusion dependence, and improve health-related quality of life.
Patients and methods. – We assessed the cost-effectiveness of treatment types regarding blood product transfusions in a cohort of 214 AML patients aged ≥ 70 years.
Results. – Analyzes did not indicate any significant overall survival (OS) advantage of intensive chemotherapy comparatively to low-intensity treatment. The difference was significant when compared to best supportive care (BSC) ($P < 0.0001$). Blood products transfusion cost per patient was 1.3 times lower with low-intensity therapy and 2.7 times lower with BSC than with intensive chemotherapy. Mean transfusion cost per patient according to OS varied from 2.4 to 1.3 times less with low-intensity treatment comparatively to intensive chemotherapy for patients having OS ≤ 13.3 months. Costs varied from 3.5 to 2.6 times less with BSC comparatively to intensive chemotherapy. In contrast, mean transfusion costs were comparable among treatments for patients with OS > 13.3 months.
Conclusion. – Low-intensity treatments represent a cost-effective alternative to BSC and require a reduced number of transfused blood products comparatively to intensive chemotherapy, while OS was not significantly different.

Keywords: Acute myeloid leukemia; Therapy; Blood transfusion; Cost-effectiveness; Prognosis

Résumé

Objectif. – Les transfusions sanguines représentent un coût important dans le traitement des leucémies aiguës myéloïdes (LAM). Les traitements de faible intensité (aracytine à faible dose, agents hypométhylants) peuvent réduire la dépendance transfusionnelle et améliorer la qualité de vie des patients.
Patients et méthodes. – Nous avons étudié, en function du type de traitement administré pour la LAM, le rapport coût-efficacité des transfusions de produits sanguins sur une cohorte de 214 patients âgés de 70 ans et plus.
Résultats. – Les analyses n'ont montré aucun avantage significatif en termes de survie globale entre la chimiothérapie intensive et les traitements de faible intensité. Par contre, la différence était significative comparée à un traitement uniquement par des soins de support ($p < 0{,}0001$). Le coût des transfusions sanguines par patient était respectivement 1,3 et 2,7 fois plus faible avec les traitements de faible intensité et les traitements uniquement par soins de support par rapport aux traitements basés sur la chimiothérapie intensive. Le coût moyen des transfusions par patient en function de la survie était 2,4 à 1,3 fois moins important avec les traitements de faible intensité par rapport à la chimiothérapie intensive pour les

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patients avec une survie globale ≤ 13,3 mois. Les coûts étaient 3,5 à 2,6 fois moins importants avec un traitement uniquement par soins de support par rapport à un traitement par la chimiothérapie intensive. Par contre, le coût moyen des transfusions était comparable quel que soit le traitement pour les patients avec une survie globale > 13,3 mois.
Conclusion. – Les traitements de faible intensité représentent sur le plan coût-efficacité une alternative au traitement reposant uniquement sur des soins de support et permettent une économie notable en termes de transfusions sanguines par rapport à un traitement par la chimiothérapie intensive, alors que la survie globale n'est pas significativement différente.

Mots clés : Leucémie aiguë myéloïde ; Traitement ; Transfusion sanguine ; Coût-efficacité ; Pronostic

1. Introduction

Acute myeloid leukemia (AML) is a malignancy that is characterized by infiltration of bone marrow (BM) by abnormal hematopoietic progenitors that disrupt normal production of erythroid, myeloid, and/or megakaryocytic cell lines. A review of surveillance, epidemiology and end results (SEER) shows that AML is primarily a disease of the elderly [1]. The incidence in Europe is about 3.7 per 100,000 [2]. Although the outcome of younger patients with AML has improved because of intensive chemotherapy with advanced supportive care and introduction of hematopoietic stem cell transplantation, the benefit associated with intensive chemotherapy, mostly a combination of intermediate-dose cytarabine and an anthracycline, in older patient remains debated [3]. Life expectancy in elderly patients is a function of age, disability and co-morbidity, performance score, along with leukemia characteristics such as genetic alterations or white blood cell count at diagnosis [4,5]. A recent analysis has suggested that intensive chemotherapy delivered to patient ≥ 70 years with AML, may not be beneficial to most and could be harmful to some [6]. No validated algorithm has been established so far to determine a patient's eligibility for intensive remission induction therapy. However, these patients are often referred to as 'unfit' or not suitable candidates for intensive induction therapy. In these patients, low-dose cytarabine (LD-AraC) has been demonstrated to be more beneficial than best supportive care (BSC) and hydroxyurea [7]. Furthermore, the recent availability of new drugs that may have an improved side effect profile and in some cases bioavailability may offer future improvement for this patient population. The efficacy of hypomethylating agents has been studied in older AML patients with mixed results [8,9]. Recent randomized trials testing hypomethylating agents, azacitidine or decitabine, compared with low-dose cytarabine found improved CR rates and better survival with hypomethylating agents [10,11]. Actually, in daily practice, the final decision to treat intensively or not is made by the treating hematologist on a case by case basis according to patient's age, cytogenetics, performance score, concomitant diseases, and type of AML (*de novo* or secondary).

Treatment of AML typically includes BSC, which consists mainly of red blood cell transfusions and platelet transfusions. Transfusion dependence is associated with significant clinical, economic and quality of life burden in patients with myelodysplastic syndrome (MDS) [12] or AML [13,14]. Most patients with AML are transfusion dependent, a characteristic that has been associated with significantly shorter overall survival [13]. Novel treatments with the capacity to reduce transfusion dependence and prolong survival duration have the potential to reduce costs and improve health-related quality of life [14]. The present study assesses the cost-effectiveness of intensive chemotherapy versus BSC versus alternative therapies (hypomethylating agents, LD-AraC, or other investigational drugs) in elderly patients aged 70 years or older regarding blood product transfusions from a French payer perspective. Intensive chemotherapy and BSC were the comparators in this analysis, since they continue to represent the most commonly used treatment for elderly AML according to the defined status of patients considered as 'fit' or 'unfit' for intensive chemotherapy.

2. Patients and methods

2.1. Patients

In total, 214 patients aged 70 years or older (median: 75 years; range: 70–93 years) with newly diagnosed AML were seen in the Department of Hematology at Lyon-University Hospital from 2000 to 2014. Patients fit criteria of the recognized French-American-British classification [15]. Diagnosis of AML was based on smears of bone marrow aspirates. AML was defined by the presence of ≥20% myeloblasts in the marrow or peripheral blood [16]. Any type of AML (*de novo* or secondary) was considered. All clinical trials, in which patients were included, were reviewed and approved by the institutional review board and were conducted in accordance with the Declaration of Helsinki. All participants to clinical trials gave their written informed consent. Before 2007, most of patients considered 'fit' by the local physician received an intensive treatment approach. However, no specific criteria for defining such patients were used. Beginning in 2007, most patients received a non-intensive option.

2.2. Treatment

On entry, all 68 patients receiving intensive chemotherapy were treated by a combination of intermediate-dose cytarabine and an anthracycline. One patient with acute promyelocytic leukemia (APL) also received all-*trans* retinoic acid (ATRA). Patients achieving CR were given consolidation chemotherapy according to the protocol design in which they were included in. The second study group comprised 70 patients who were