A feasibility study of allogeneic hematopoietic stem cell transplantation for severe thalassemic patients covered by Universal Coverage scheme

Background

Thalassemia is the most common gene-related hematological disease in Thailand. With a Thai population of 65 million, approximately 40% carry thalassemia traits and about 1% manifest the disease [1]. The incidence of new severe thalassemia (i.e. Hb Bart's hydrops fetalis, β-thalassemia major, and β-thalassemia/Hb E) is estimated at 4,253 patients per year [1]. Generally patients with severe thalassemia present with anemia at the first year of life. The provision of regular blood transfusion (BT) is standard practice for the treatment of severe thalassemia. Without ongoing BT, these individuals would have an expected life-span of only a few years. BT given over a long period of time can result in iron-overload causing heart failure and damage to other organs associated with high mortality. In order to reduce iron accumulation, iron chelating therapy (ICT) needs to be administered subcutaneously for 8 to 12 hours per day, 5 to 7 days per week. Effective provision of ICT is often compromised by poor compliance as the process itself can have a detrimental effect on quality of life (QoL), especially amongst children [2-3].

Currently, hematopoietic stem cell transplantation (HSCT) is the only curative treatment available to severe thalassemic patients. Hematopoietic stem cells are usually extracted from bone marrow, peripheral blood, and umbilical cord blood. An allogeneic HSCT patient can obtain stem cells from a healthy human leukocyte antigen (HLA)-matched donor, being either a patient's relative (i.e. related HSCT) or from non-related donors (i.e. unrelated HSCT). HLA is determined by conventional serologic typing for class I and II antigen. DNA typing with high-resolution sequence-specific oligonucleotide probes for class I and II loci is undertaken for patients with matched and mismatched HLA-related or mismatched HLA-unrelated donors. Sibling donors are considered ideal as they can inherit identical HLA genes, reducing the probability of graft rejection and other complications. The formula for calculating the chances of a particular person having an HLA-matched sibling is $1 - (0.75)^n$, where n denotes the total number of siblings [4]. The average Thai family has two children; therefore 25% of patients are likely to have an HLA-matched sibling donor [5], while 75% of these potential sibling-donors would themselves be without thalassemia. Thus the proportion of thalassemic patients that would have an HLA-matched sibling donor is approximately 19%. The remainder of the population must rely on unrelated

donors. At present there is one local stem cell databank in place at the Thai Red Cross Society for the identification of such donors which has inadequate donor pool, while reliance on foreign databases implies reduced donor availability and an increase in costs. As evident, HSCT is a resource-intense procedure requiring high financial expenditure especially at the first year of treatment. Moreover, patients receiving HSCT may experience poor quality of life due to its toxicity and complications. HSCT, however, is the only treatment to cure thalassemia at present, providing patients with longer life expectancy and potentially normal quality of life [5].

In Thailand, healthcare coverage for the provision of HSCT differs amongst the three health insurance schemes. HSCT is provided with full coverage to thalassemic patients who are government employees and their dependents enrolled under the Civil Servant Medical Benefit Scheme (9% of the Thai population) as well as employees enrolled under the Social Security Scheme (11% of the population). Provision of HSCT has not yet been included in the benefit package of the Universal Coverage (UC) scheme that applies to approximately 80% of the Thai population and is managed by the National Health Security Office (NHSO) [6].

An economic evaluation study of allogeneic HSCT for severe thalassemic patients in Thailand was conducted to compare the costs and health outcomes for related and unrelated HSCT compared with BT-ICT and evaluate the budget impact [7]. The study found that related HSCT was likely to be a cost-effective and affordable treatment for severe thalassemia patients aged less than 10 years in Thailand. The findings of cost-utility and budget impact analyses were also presented to the Subcommittee for Development of the Health Benefit Package and Service Delivery of the NHSO. Although that the results suggested that related HSCT for young children with severe thalassemia was the most cost-effective option in the Thai context, the current limited infrastructure implies that this will only be available to a minority of patients, proving to be a major obstacle to policy formulation and implementation. This is indicative of a broader problem that is particularly occurred in low and middle income countries, where life-saving and cost-effective technologies are becoming more readily accessible while the infrastructure and financial resources are not yet available to provide these on a large scale and in an equitable manner. There are immense challenges to rationing such services in deciding whether these should be

allocated based on a "first come first serve", "severity of disease", "fair inning", “choicism” or a "health maximization" [8]. As a result, the Subcommittee has not reached a consensus and provided any policy recommendations to the NHSO. This situation reiterates that economic analysis alone is insufficient in providing practical decision recommendations to policy makers where such pertinent equity concerns are present. There is an urgent need to carefully consider social, ethical and moral dimensions of this health technology beyond its immediate economic benefits. The objectives of this study will be to investigate the feasibility and develop the policy decision choices for implementation of HSCT provision for severe thalassemic patients covered by UC scheme.

Method

Study design

Firstly, the quantitative study will be conducted in hospitals currently providing HSCT services in Thailand including four university hospitals (i.e., Ramathibodi, Siriraj, King Chulalongkorn Memorial, and Phramongkutklao). The survey aims to assess the current service capacity, past and present service provision including characteristics of patients undertaking HSCT (both with and without severe thalassemia), plan and future development of HSCT provision. An additional survey includes other university hospitals including Prince of Songkla University, Chiang Mai University, and Khon Kaen University throughout the country to ask whether and why, when, and how they are about to establish HSCT units.

Secondly, the qualitative interviews will be performed with the hospital directors or his/her deputies in public currently providing HSCT services. The interviews aim to determine the attitude, policy directions, and problems they are currently facing in running the HSCT units.

Thirdly, in-depth interviews will be carried out with caregivers of severe ex-thalassemic patients with undertaking HSCT. These interviews aim to assess attitudes and experience (including supports and difficulties they were facing during HSCT) toward HSCT.

Study population

The study populations will be the specialists of HSCT unit, director of those hospitals, caregivers of severe ex-thalassemic patients with post-HSCT.

Data collection tools and procedures

1. Providers

The study will be conducted using self-administered questionnaire for professionals from the HSCT unit and individual in-depth interview method with hospital directors or his/her deputies in public. A structured questionnaire will be used to appraise five elements: (i) current capacity (e.g., human resources, infrastructure, the total number of HSCT patients); (ii) The eligible criteria (i.e. medical criteria and non-medical criteria) will be used to provide HSCT for severe thalassemic patients; (iii) factors and limitations that are needed to be considered for the implementation of HSCT for severe thalassemic patients covered by UC scheme in the viewpoint of both specialists and directors; (iv) the proposed policy options for the adoption of HSCT in Thailand; and (v) interventions that could support to implement HSCT in Thai healthcare settings.

2. Patients' caregivers

The study will explore the entry point of receiving HSCT, understanding and attitude related to HSCT for severe thalassemic patients in the viewpoint of caregivers of severe ex-thalassemic patients with post-HSCT in four university hospitals. In-depth interview method will be used to collect the data from 20 subjects from selected active HSCT units. Moreover, the socioeconomic status of interviewees will be collected.

Data analysis

According to the data collection, the study will analyse the feasibility of supply sides for expanded HSCT services for severe thalassemic patients covered by UC scheme. Moreover, the study will raise the ethical concern of patients and family caregivers due to the provision of HSCT. Then, the study will suggest the policy decision choices of expanded HSCT service for severe thalassemic patients.

Ethical considerations

This research protocol and the interview questions will be reviewed and approved not only by the co-researcher of each studied setting but also the ethics committee of each studied setting. All participants will be fully informed and their consents will be sought by researchers.

Expected outcomes

The results of this study could be informed decision makers of NHSO to develop the policy when providing HSCT for severe thalassemic patients covered by UC scheme. From providers' interviews, the results could present the current capacity and the limitation of HSCT services in Thailand. The information could be used to evaluate the feasibility of the expanded HSCT in Thailand. Moreover, from the interview of patients' caregivers, this information can be used for decision makers to consider the ethical concerns.

Study plan

Activity in year 2011	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct
1. literature reviews								
2. the first expert meeting to develop conceptual framework								
3. the second expert meeting to develop proposal								
4. submission the study proposal to the ethical committee for approval								
5. data collection								
6. data analysis								
7. the third expert meeting to present preliminary result								
8. Results' presentation to the NHSO								
9. developed final research report								

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