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The Evidence Base for Transition Programmes for Adolescents with Sickle Cell Disease

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Abstract

Background: In the United Kingdom (UK), sickle cell disease (SCD) is one of the most common genetic disorders at birth and worldwide millions are affected with the disorder. Transitioning young people with chronic illness from paediatrics to adult care is a complex process and it needs to be a planned and individualized process.

Objective: To review the existing literature on transition programmes for adolescents with SCD in the UK.

Methods: Online databases were used to search for studies using the key words: 'sickle', 'adolescent', 'transition', 'England', 'UK'.

Results: There are no studies that evaluate the efficacy of transition services for people with SCD in the UK. A multidisciplinary approach with the involvement of patients and parents is essential is important to the success of the transition programmes. This study encountered a number of obstacles in describing the evidence base for SCD transition programmes due to (i) limited well-designed research studies and (ii) the lack of evaluation of existing guidelines using clinical indicators. This is despite the fact that other aspects of SCD management have benefited from well-designed studies and randomised-control trials.

Conclusion: In view of the increasing number of young people with SCD surviving to adulthood, there is a need to strengthen transition services to enable them to become independent adults. More good quality studies are necessary to create an evidence-base to inform ways to deliver better care in the UK.

Keywords: Sickle cell disease; Anemia; Adolescence; Adults; Transition; Pediatrics

Introduction

Sickle cell disease (SCD) is an autosomally inherited disease resulting in the production of abnormal haemoglobin S (HbS). It is caused by a point mutation at position 6 of the beta-globin allele due to the substitution of glutamic acid with valine. As a result affected haemoglobin molecules polymerize on deoxygenation [1]. The resulting damage to the red blood cells and the vascular endothelium leads to a haemolytic anaemia and vaso-occlusion, which is responsible for the acute and chronic complications of SCD (Figure 1).

SCD is prevalent in Afro-Caribbean, African, and Middle-Eastern and Mediterranean populations. It affects an estimated 12 - 15,000 people in the United Kingdom (UK), 70% of whom have HbSS [2]. The estimated median survival age for SCD patients in the United States (US) in the 1970s was 14 years [3] but advances in the management have seen increases in survival, with median survival now in the 5th decade [4]. SCD is therefore no longer only a disease of childhood, and transition planning from pediatric care (PC) to adult centred care (ACC) is now mandatory.

Transition is defined as 'the purposeful planned movement of adolescents and young adults with chronic physical and medical conditions from child-centered to adult-oriented healthcare systems' [5]. Transitioning in managing adolescent SCD is needed, given the significant differences between PC and ACC. PC is characterized by substantial parent involvement in decision-making, with little active participation by the patient, while ACC is associated with patient self-management and autonomous decision-making [6]. SCD is a lifelong condition thus, successfully transitioning adolescents into ACC is important to ensure the continued engagement of the individual with health services and in turn, better patient outcomes. Identifying the characteristics of efficacious transition programmes is also important as research from the US finds an increased risk of death among adolescents with SCD soon after moving to ACC [7,8]. Additionally, adolescents with SCD have a unique set of needs stemming from the interaction between adolescence and their medical condition, for example delayed growth and sexual maturity [9], for which special consideration in an adolescent-focused setting may be more appropriate.

The Department of Health also acknowledges the need to improve existing services for adolescents with SCD to enable independence in the management of their condition, enhancing the role of the expert patient [10]. While there is significant research into the psychosocial aspects of transitioning i.e. the concerns of adolescents and care-givers, there is little evidence assessing the efficacy of existing transitioning programmes [11,12]. This purpose of this review is to assess the evidence-base guiding the transitioning of patients with SCD from PC to ACC in the UK.

- Sickle cell anaemia or HbSS: homozygous state, which is also the commonest form of SCD and it frequently represents a moderate to severe phenotype.
- HbS/β^0 thalassaemia: heterozygote state, usually difficult to differentiate from sickle cell anaemia phenotype due to severity of clinical symptoms.
- HbSC (HbS and HbC): heterozygote state, usually less severe clinical manifestations than HbSS and HbS/β^0 thalassaemia.
- HbS/β^+ thalassaemia: clinical symptoms can vary among ethnic groups, but frequently mild to moderate.
- HbS/HPFH (HbS with hereditary persistence of foetal Hb): vaso-occlusive complications are less frequent or absent due to high HbF levels.
- HbSE (HbS and HbE): in general, patients are asymptomatic or present with very mild phenotype.

Figure 1: Examples of sickle cell disease (SCD) genotypes.

Methods

The databases used in the literature review were Medline, PubMed, Embase and PsychInfo. The key search terms included: 'sickle', 'adolescent', 'transition', 'England', 'UK'. Studies were included if they were: (i) from journals (ii) UK-based transition programmes for SCD (iii) attempted to evaluate the programme (iv) in English. The search was limited to articles published between 1990 and 2012.

Articles were excluded from the review if (i) they were opinion pieces (ii) the abstract of the paper was unavailable in English (iii) papers were not analytical studies. A paucity of data was observed when these search terms and inclusion criteria were applied. The search was therefore expanded to include descriptive studies of transitioning in other high-income countries in chronic diseases not limited to SCD. The inclusion of studies from other countries was deemed acceptable as Anie et al. [13], combined data from the US and UK in the same study, on the premise that difficulties in transitioning adolescents with SCD are not specific to a single country.

Results

There was an overall lack of research evaluating the efficacy of transition programmes for adolescents with SCD in the UK. This lack of an evidence base to guide SCD transition is evident in the fact that NHS recommendations for transitioning adolescents is based on Category C/Level IV evidence, described as "evidence from expert committee reports and/or clinical experience of respected authorities; indicates absence of directly applicable studies of good quality" [4]. It must be acknowledged that there are excellent models of transition schemes within the NHS [14], but current practices have not been evaluated for clinical efficacy. It appears that current research into transitioning in SCD is focused on qualitative studies that explore patients' and doctors' perspectives and the psychosocial challenges associated with the disease and its management during adolescence [6,15].

It is observed that few studies assessed clinical indicators but did so sub-optimally. For example, Wojciechowski et al. [9] attempted to evaluate the efficacy of a transitioning programme using the percentage of adolescents attending their first ACC appointment as a measure. Hankin et al. showed that 74% of adolescents who participated in a pilot transition programme attended their first ACC appointment compared with 33% in the control group (who were not offered the transition programme). This study found that attendance at the first ACC appointment is not an optimum indicator of successful transition; patients may still be lost to long-term follow-up after attending the first appointment. Furthermore, many studies provided no baseline data in order to make comparisons between these indicators pre- and post-intervention.

Several publications discussed the patterns of psychosocial difficulties reported by adolescents with SCD during transition. These include anxiety regarding the termination of the relationship between paediatric healthcare professionals and developing a new relationship with an adult clinician [8,16]. This can develop into reluctance to accept and participate in ACC [17]. Part of this anxiety may be attributed to the absence of adequate prior preparation of adolescents to address future expectations when they finally arrived in the ACC. This is exemplified by one study where 65.3% of the adolescent study participants report having never discussed transitioning with their providers even though almost half felt it was an important issue [18]. Bryant et al. [19] explained that moving an adolescent to ACC requires an adjustment process. There may be some initial fear and anxiety, followed by an acceptance that moving to ACC is unavoidable and finally, welcoming the responsibility of being in control of their condition and being treated like adults [19]. A successful transition programme aims to prepare the adolescent for ending the relationship with paediatric services, while encouraging them to be more receptive to ACC providers. This is particularly important as studies suggest that certain issues pertinent to the adolescence period for example, alcohol use, contraception and genetic counselling, are often poorly managed in PC [11]. Fostering the acceptance of adult healthcare providers in adolescents could enable an improvement in the management of these challenging areas in the adult setting.

Increasing attention is being focused on patient readiness [6,20]. Transition readiness is described as the "decisions and actions taken by the adolescent, family and healthcare providers to prepare, implement and complete the transition to adult centred care" [6]. Central to patient readiness is patient education and information. A directly proportional relationship is identified between information provision and patient compliance such that, adolescents with SCD who are well-informed about SCD exhibit better management of their condition and adjust more easily to ACC than those with less knowledge [21]. McPherson et al. [19] also suggest that information on the actual process of transition, such as future insurance coverage and navigating the adult medical system, should be delivered. SCD and transition education also exerts an effect on patient self-efficacy, another cornerstone of patient readiness. Self-efficacy is described as the degree to which patients believe they have control over their disease [14]; this encompasses patient's perceived competence and resourcefulness in managing their own disease [9]. Demographic

variables such as age, educational grade and gender are found to exert little influence on self-efficacy [13]; it is evident that education is responsible for generating high levels of self-efficacy in a significant proportion of adolescents, especially in the daily management if SCD such as adherence of medication regimens and appointments.

Developing self-efficacy involves the assimilation of information by the adolescent and requires behaviour modification to enable the adolescent to assume responsibility for the management of their SCD. Time is required to learn and adopt the necessary behaviours hence it is suggested that transitioning is well-planned and timely, i.e. introduced several years before the anticipated transfer to ACC, with on-going evaluation to assess adolescent's self-efficacy and capacity for self-management [2,18]. Introducing the concept of transitioning close to the required time of transfer is found to result in feelings of abandonment and abrupt transfers [19], which result in adolescents being ill-prepared for ACC. Reviewing existing transition programmes finds that transition is often introduced around the age of 13. In one US programme, SCD patients aged 12 are given a folder containing checklists of skills required for the self-management of their disease, educational materials and appointment tracking cards [22]. In another UK programme, adolescents with SCD are introduced to the concept between the ages of 12 and 13 [2] with on-going education and reassessment in the following years, aiming to increase patient's readiness for ACC in the late teenage years (Figure 2). These examples reinforce the notion that transitioning must begin early with regular progress reviews (Figure 3).

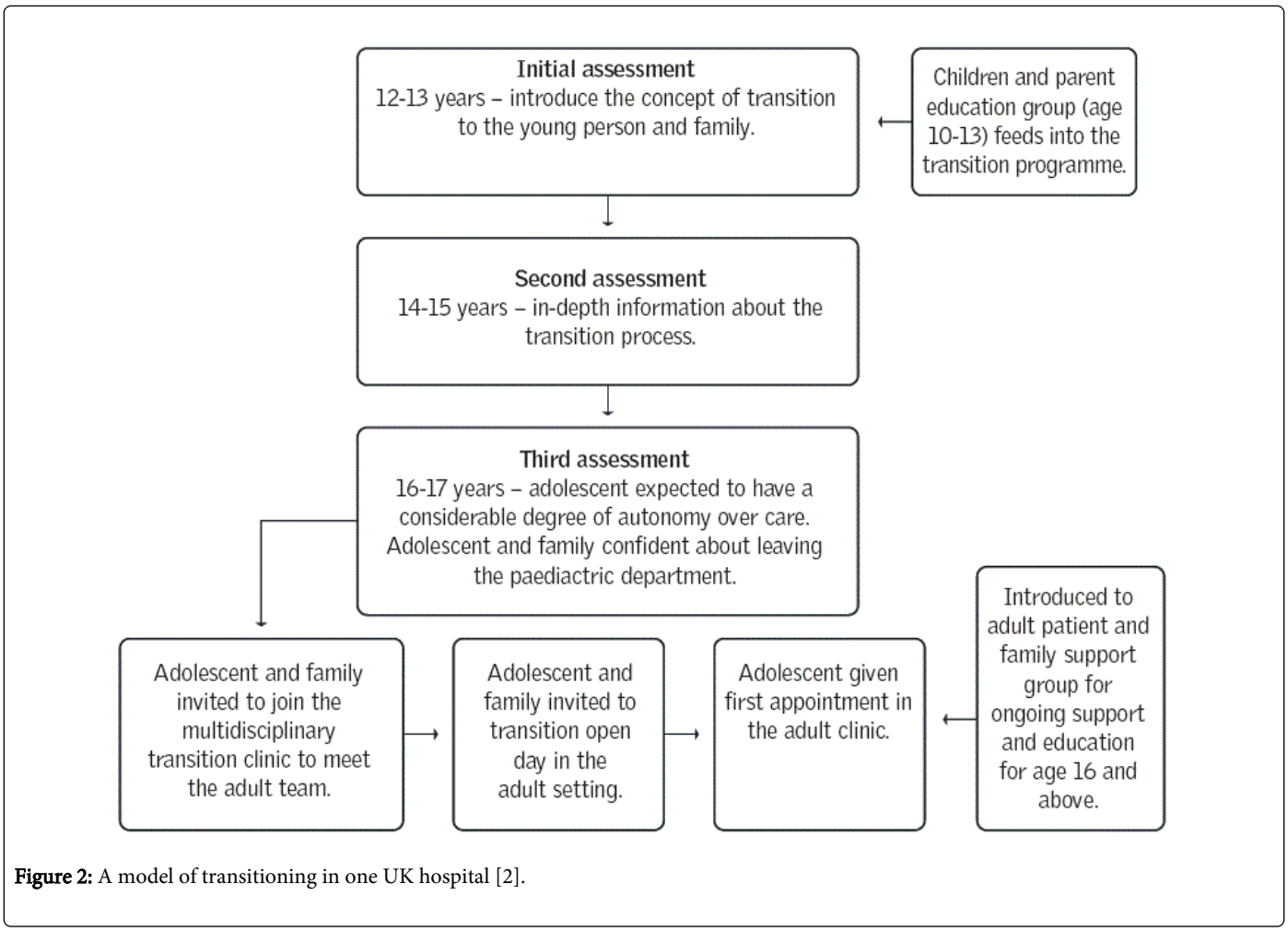

Figure 2: A model of transitioning in one UK hospital [2].

The role of parents in adolescents transitioning to ACC is complex. It is reported that parental awareness and attitudes on SCD influence their support of adolescents in becoming independent in managing their health [16,23]. In general, PC is characterized by parents having primary responsibility for disease-management and decision-making. This is especially true in SCD where neurocognitive difficulties are prevalent in the population making some patients even more reliant on parental input [23,24]. This shift of responsibility often poses challenges for parents, especially over-protective parents and parents of those with severe SCD [25]. It is therefore suggested that some attention be directed to parents of adolescents with SCD during the transition process [21]; this is to prepare them for becoming less involved in their child's care and to advise on ways of promoting independence in their children. It is noted that parent's participation in transition should be limited so as not to negate the purpose of transition programmes.

Several papers highlight the importance of specialist nurses in SCD transition programmes [6,19,25]. They are identified as the optimal healthcare professionals to initiate discussions regarding transition, given their position as provider of emotional support and SCD education [19]. Watson [26] also advocates for the use of nurse specialists in transitioning programmes, as the absence of a specialist healthcare professional responsible for coordinating transitioning was

found to be a significant barrier to service development for adolescents with chronic illnesses in one Australian hospital. The incorporation of the psychology team is also encouraged. Depression and anxiety exert negative effects on transitioning adolescents confidence with care, a criterion for good self-management and a hallmark of ACC [13]. Additionally, adolescents with SCD are at high-risk of cognitive impairment, given the 10% risk of cerebrovascular events i.e. stokes and silent infarcts, in patients under 16 [2]. Cerebrovascular events, particularly in the frontal lobe, cause diminished executive functioning such as planning, organisation and memory, affecting the learning of skills for self-management. For this reason, Wills et al. [23] recommend the inclusion of annual neuropsychological assessment in adolescents with SCD. They were able to identify patients with neurocognitive problems, and developed formal plans for their transfer to ACC. They established special liaison services for those with educational and behavioural difficulties. An evaluation of this programme reports a decline in missed appointments and high patient approval [23]. However the challenge is the cost required in replicating this program as it relied on donor support. Nevertheless this highlights the need for psychosocial support in many SCD transition programmes in line with other chronic diseases such as renal failure and cystic fibrosis [26].

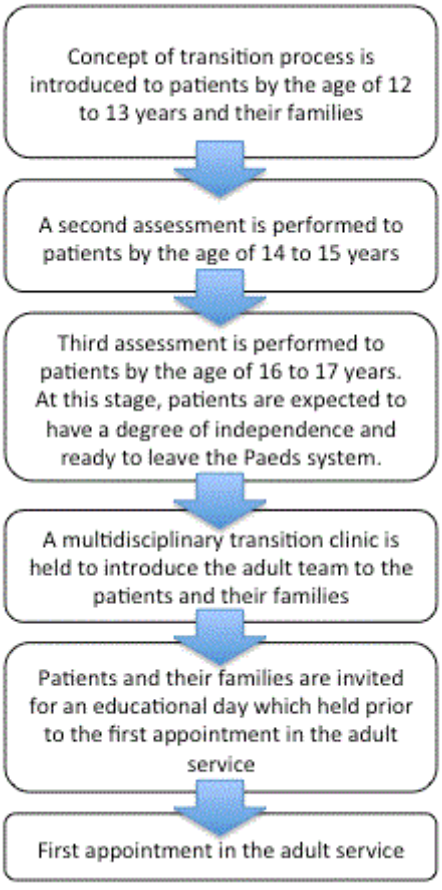

Figure 3: SCD transition process at evelina children hospital – Guy's and St Thomas NHS trust.

IA review of a London-based transition programme reports that a support group for SCD patients at university was valued by the participants [14]. Conversely, another study reports little success in starting peer-support groups, with only 17% of the adolescents with SCD showing interest in group meetings [22]. Peer-support groups have been shown to raise self-esteem, reduce social isolation and encourage information sharing [12,27].

The appropriate timing for the transfer to ACC is debatable and while some suggest that it should coincide with relevant life events, such as leaving school, to reinforce the adolescent's adult status [9,28,29], others believe that believe it should occur during a period of stability with no major changes in medical circumstances to avoid overwhelming patients [11]. In most studies, transition occurred between the ages of 18 and 21 [19,25]. But this appears to be due to health-system constraints. Studies suggest that transitioning should be flexible and determined by the adolescent's readiness, not by age [11,20] and while it would be ideal for patients to remain in PC until ready to move to ACC, questions arise as to the feasibility of such a programme.

The Importance of Establishing Evidence- Based SCD Transitioning

Evidence-based medicine (EBM) is defined as, "the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients" [19]. It is a multi-faceted process involving the production of evidence, the production and dissemination of evidence-based clinical guidelines, the implementation of these guidelines and finally, the evaluation of the guidelines using clinical outcomes [30]. Sackett et al. [29] find that EBM aims to integrate clinical expertise with clinical evidence from systematic research and note that neither one alone is sufficient. In other words, while the expert opinion currently forming the basis of current transitioning programmes in SCD is of value, their reliability would be greatly enhanced by evaluation using clinical indicators. This study finds that the obstacles in generating an evidence-base for SCD transitioning lie in (i) limited research and well-designed studies, and (ii) the lack of evaluation of existing guidelines using clinical indicators. Other areas in paediatric SCD management have benefited from randomised–control trials and EBM, for example stroke management and the Stoke Prevention Trial in Sickle Cell Anaemia (STOP) [31]. However, this is yet to be established for transition programmes.

In the UK, the National Institute for Health and Clinical Excellence (NICE) makes guidelines for clinical practice based on EBM. Developing an evidence-base for SCD for NICE guidelines will help standardised clinical practice and reduce the geographical variation identified in the management of SCD [4]. Developing EBM in SCD transitioning to drive NICE guidelines is also important to help secure funding for transitioning. Howard et al. [14] found no comprehensive transition services for UK adolescents with SCD; thus building an evidence-base for SCD transitioning may identify areas of unmet need and lead to the inclusion of the wide range of services required in SCD transition into NICE guidelines.

An evidence-base for transition programmes will also help identify practices associated with better patient outcomes. Incorporating the findings of good-quality research can identify practices with better clinical indicators and those that are inefficacious or potentially hazardous; these findings may then be formally adopted in clinical

practice. For example, the STOP trial [31], which evaluated the use of chronic transfusion in preventing initial stoke in children identified as high risk through TCD, resulted in the incorporation of long-term blood transfusion for the primary prevention of stroke in high-risk adolescents in clinical practice [4]. In terms of SCD transitioning, it has been previously stated that adolescents are at higher risk of death soon after transitioning; herein lies a potential area to establish an EBM to identify which features of transition programmes are associated with low or elevated risk of death following transition.

Limitations

One key limitation in this study surrounds the generalizability of the findings. A number of the studies had small sample sizes and there is the possibility of selection bias, given the use of non-random and convenience sampling in many of the primary studies [9,20,25]. Many studies were conducted at a single site; resource availability and organisational procedures may vary between hospitals and may exert an effect on study findings. Also, several studies included in this review originate from the US, where fundamental differences in the health-system, as exemplified by the multiple citing of concerns regarding the insurance coverage [9,32], contribute to difficulties in generalizing findings to the UK setting.

Conclusion

SCD is a common inherited haemoglobinopathy affecting a significant proportion of the UK adolescent population. Advances in the management of the condition in childhood has resulted in an increase in median life expectancy, such that those with SCD are now expected to survive until their fifth decade and need to transfer to ACC during adolesence. Effective transition programmes should adequately prepare adolescents and parents for the responsibilities associated with ACC, such as patient self-management; this promotes the continuity of care and results in improved patients outcomes. Current transitioning programmes have been developed based on the expert opinion of those renowned in the field of SCD and adolescent medicine, however there is a lack of systematic review of these existing programmes and hence, EBM in this field. In conclusion, there is a need for high-quality research to identify the best methods for delivering optimum transition care for young adults and it is hoped that further research will be undertaken to address this area of unmet need.

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