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Hydroxycarbamide: clinically, effective but parents still delay starting.

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INTRODUCTION

Sickle cell anaemia (SCA) is an autosomal recessive haemoglobinopathy, identified by dysmorphic red blood cells (RBC), that in low oxygen states 'sickle' causing blood vessel obstruction. Clinical manifestations include unpredictable vaso-occlusive pain crises, limiting patient quality of life.

Paediatric complications include acute chest syndrome (ACS), pain and stroke. SCA affects 15 000 UK patients. Management combines lifestyle measures, prophylactic medication and use of disease modifying therapies. The only cure for paediatric patients is bone marrow transplant.

Hydroxycarbamide (HU) has become gold standard for SCA treatment. Several studies; the baby HUG Trial (2011), INTO and Lobo (2013) demonstrate HU usage correlates with; reduced pain crises, hospital admissions, ACS and blood transfusions in child and adult patients. HU works by increasing percentage foetal haemoglobin (HbF), reducing percentage HbS. It also lowers white cell count; beneficial as inflammation can precipitate sickling.

Despite evidence highlighting its efficacy**, uptake of HU in children with SCA remains low.**

AIM & OBJECTIVES

Aims:

1. Firstly, to compare the **clinical benefits of hydroxycarbamid**e up to 24 months post starting the medication, compared to their sickle experience before.
2. Secondly to asses any **negative effects** experienced by patients using HU.
3. Finally we measured **blood parameters** to asses the haematological effect.

Objective: We hope to **demonstrate the efficacy** of this medication and **encourage its increased usage in paediatric patients** as well as raise awareness for the management of a condition that is not widely understood.

METHOD

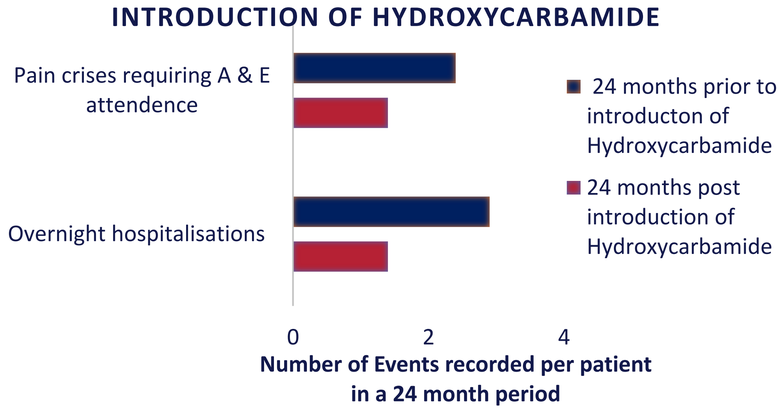
Data from **(n=172) patients** (0 to 18 years) with Hb SS or SC SCA were obtained from a **South London Hospital Trust**. Using electronic patients records (EPR) we obtained **data retrospectively, on outcomes 24 months prior to and during HU use.**

We measured; no. pre treatment discussions, no. of pain crises hospital attendance, bed days, no. of ACSs and emergency transfusions. EPR was used to note side effects. Haematological parameters, haemoglobin (Hb), HbF and MVC and reticulocyte count, were measured at baseline, 12 and 24 months post HU introduction.

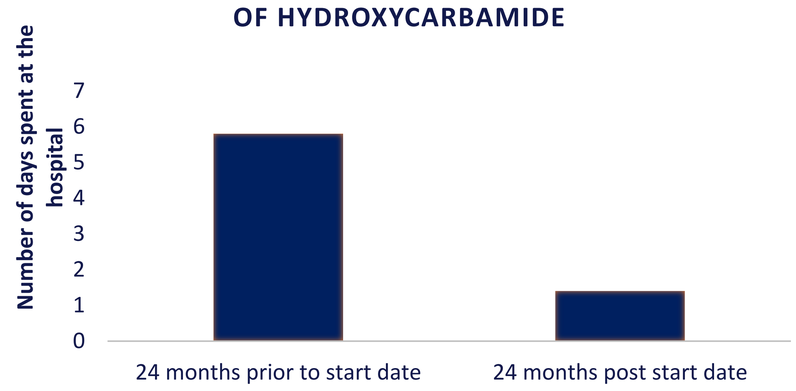
RESULTS

Among 59 patients started on HU, we found **reduced hospital attendance for pain, ACS and emergency blood transfusions** over 24 months. Hb and HbF percentage had upward trends over the 24 months. Only 10 patients discontinued HU treatment due to inefficacy or intolerance. Just 20% of children were started on HU on first discussion. The average discussion to treatment time was 5.2 months.

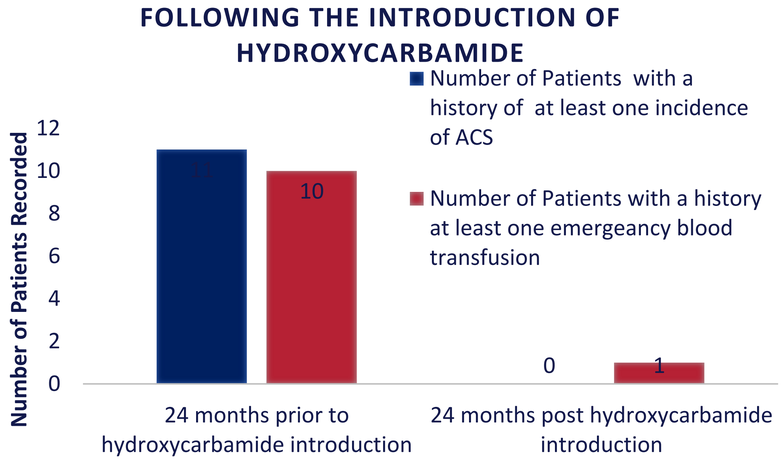
HOSPITAL ATTENDANCE PRIOR AND FOLLOWING THE INTRODUCTION OF HYDROXYCARBAMIDE



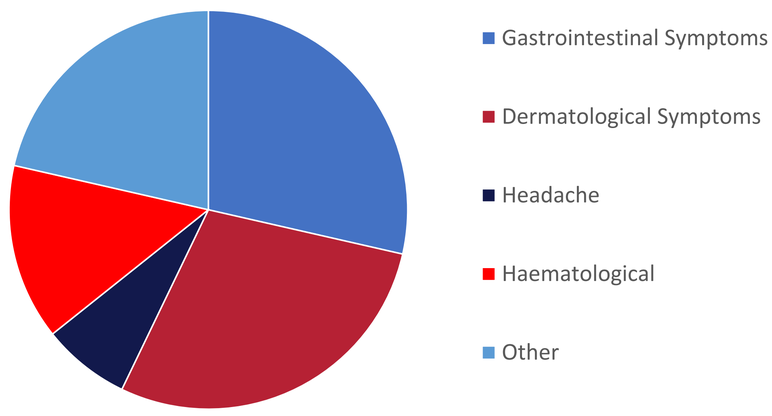
LENGTH OF HOSPITAL ADMISSIONS IN SICKLE PATIENTS BEFORE AND AFTER INTRODUCTION OF HYDROXYCARBAMIDE



SICKLE CELL COMPLICATIONS PRIOR TO AND FOLLOWING THE INTRODUCTION OF HYDROXYCARBAMIDE



PATIENT REPORTED SIDE EFFECTS OF HYDROXYCARBAMIDE



Key findings: 13 patients reported side effects.
GI symptoms, manifested as vomiting, diarrhea and abdominal pain, dermatological symptoms included rashes and itching and haematological signs were low Hb (anaemia) and myelosuppression.

HAEMATOLOGICAL PARAMETERS

Key findings: Haemoglobin levels increased from 85.2 g/L (baseline) to 98.8 g/L (12 months) and 93.1 g/L (24 months) **Fetal haemoglobin count also increased** from 11.5% to 20.7% (baseline and 24 months respectively) Reticulocyte and white cell and neutrophil counts decreased

	Hb (g/L)	WCC (10^9/L)	Neutrophils (10^9/L)	Platelets (10^9/L)	Reticulocytes (10^9/L)	MCV (fL)	HbF (%)	Creatinine (µmol/L)	Bilirubin (µmol/L)	ALT (IU/L)	ALP (IU/L)	n
Baseline O months	85.2	11.2	4.6	328.6	255.7	81.6	11.5	36.3	35.2	29.5	186.6	35
12 months	98.8	8.1	3.5	316.4	157.1	92.8	21.5	34.9	24.5	27.4	164.8	16
24 months	93.1	8.4	3.9	279.8	149.2	88.9	20.7	34.1	24	34.6	178.4	14

CONCLUSIONS

The effect of HU in our patient population is overwhelmingly positive, consistent with previous studies. However as of May 2019 just 46 out of a potential 172 patients were using HU and 20% of patients required 3 or more discussions before being put on HU. Most indications were due to worsening symptoms rather than prophylaxis and parental uncertainty was a common factor in this hesitancy to medication use.

Hydroxycarbamide has a significant clinical impact in paediatric patients who suffer from SCA complications during childhood. Furthermore, we can suggest that ,based on our results, it is an efficacious tool for managing SCA in children with clear long term benefits , however in spite of its positive clinical profile, more work needs to be done to ensure its increased use for manging patients with sickle cell anaemia .

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