Oral tranexamic acid as a novel treatment option for persistent haematuria in patients with sickle cell disease

Niall F. Davis, Barry B. Mcguire, Leo Lawlor, Peter O'Gorman, Kiaran J. O'Malley, John M. Fitzpatrick

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Corresponding Author: Mr Niall F Davis, MB BCh BAO

Corresponding Author's Institution: Mater Misericordiae Hospital

First Author: Niall F Davis, MB BCh BAO

Order of Authors: Niall F Davis, MB BCh BAO; Barry B McGuire; Kiaran J O'Malley; John M Fitzpatrick

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Authors Contact Details:

1. Niall F Davis
   Department of Urology, Mater Misericordiae Hospital, Eccles Street, Dublin 7, Ireland
   Email: nialldavis2001@yahoo.com
2. Barry B McGuire
   Department of Urology, Mater Misericordiae Hospital, Eccles Street, Dublin 7, Ireland
   Email: barrymcguire2@yahoo.co.uk
3. Kiaran J O'Malley
   Department of Urology, Mater Misericordiae Hospital, Eccles Street, Dublin 7, Ireland
   Email: kiaranomalley@hotmail.com
4. Prof. John M Fitzpatrick
   Department of Urology, Mater Misericordiae Hospital, Eccles Street, Dublin 7, Ireland
   Email: jfitzpatrick@mater.ie

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Corresponding Author:

John M Fitzpatrick

Corresponding Author's Institution:
Professor John M. Fitzpatrick,
Professor of Surgery,
Consultant Urological Surgeon,
The Mater Misericordiae Hospital,
47 Eccles St.,
Dublin7,
Ireland.
Ph: +353 1 8308530
Fax: +353 1 8300345

Email: jfitzpatrick@mater.ie

First Author:

Niall F Davis, MB BCh BAO

Order of Authors:

1. Niall F Davis,

2. Barry B McGuire;

3. Kiaran J O'Malley;

4. John M Fitzpatrick

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Oral Tranexamic Acid as a Novel Treatment Option for Persistent Heamaturia in Patients with Sickle Cell Disease

NF Davis, BB McGuire, KJ O'Malley, JM Fitzpatrick.

Department of Urology,

Mater Misericordiae University Hospital

Eccles Street

Dublin 7

Ireland

Corresponding Author's Institution:

Professor John M. Fitzpatrick,

Professor of Surgery,

Consultant Urological Surgeon,

The Mater Misericordiae Hospital,

47 Eccles St.,

Dublin7,

Ireland.

Ph: +353 1 8308530

Fax: +353 1 8300345

Email: jfitzpatrick@mater.ie

A 17 year old Nigerian female (para 1+0) with sickle cell disease (genotype HbSS) presented to the emergency department in sickle crisis with a four day history of gross haematuria with clots. The crisis settled quickly but her haematuria continued unabated. Urine was sterile and serum creatinine was 52mmol/L. This was her first episode of haematuria. She had no other relevant past medical or family history. For fourteen days the patient was treated with intravenous fluids, analgesia and repeated blood transfusion. She underwent a number of investigations during this time.

CT urography and angiography demonstrated bilateral papillary necrosis and thrombus within the bladder. Selective bilateral renal arteriogram showed four renal arteries but no vascular abnormality or active bleeding point. Cystoscopy was performed and thrombus was evacuated. Following administration of furosemide a jet of blood coming from the left ureteric orifice was seen. Both ureters were catheterised and samples taken for culture and sensitivity including tuberculosis and mycoplasma were negative. Non-contrast CT identified a small focus of petechial haemorrhage in the lateral calyx of the midpole of the left kidney. A gradient echo MRI showed no dephasing abnormality to suggest blood product in either kidney. The assumed diagnosis was haematuria secondary to papillary necrosis due to increased fibrinolysis in a patient with sickle cell disease.

Despite sophisticated imaging techniques and invasive investigations no bleeding focus was identified and severe haematuria continued until treatment with oral tranexamic acid (1g QDS) was commenced. The patient's haematuria ceased on the fourth of seven days of treatment and her haemoglobin remained stable. She was discharged 24 days after initial presentation and had no further episodes of gross haematuria at three months follow up.

Patients with sickle cell anaemia are well known to show evidence of microscopic haematuria but severe persistent haematuria is a rare complication with only several small retrospective reviews, case reports and analyses published on the subject. Severe haematuria is more common in sickle trait rather than disease [1]. This may be due to the higher prevalence of the trait than the disease, or to the higher haematocrit seen in people with sickle trait predisposing to a tendency towards sludging [1]. The haematuria reported is usually painless, however reports of flank pain are most likely due to colic from ureteral obstruction [2].

Bleeding can be continuous or intermittent and may last several months. Interestingly, massive haematuria (as in our case) is mostly from the left kidney [2,3] and can sometimes be identified on cystoscopy at the left ureteric orifice [2] or from the tip of a papilla on ureteroscopy. Explanations for bleeding from the left side include elevated venous pressure due to the many tributaries of the left renal vein. This leads to a relatively greater anoxia in the left renal medulla increasing the likelihood of sickling [4]. Bleeding in the contralateral kidney has been reported in 10-20% of patients [1] and as such nephrectomy as a treatment option [3] has fallen quickly out of vogue.

The focus of treatment in this condition is to inhibit the fibrinolytic system and prevent liquefaction of the clot at the bleeding site, thus promoting haemostasis and healing. Treatment with episilon-aminocaproic acid inhibits fibrinolytic activity and can stop bleeding within 3-7 days of starting therapy [5]. Aminocaproic acid is an analogue of lysine that competitively inhibits plasminogen activators (streptokinase, urokinase tissue activators). Side effects such as intra-glomerular thrombosis and urinary obstruction [6] as well as convulsions, cardiac and hepatic dysfunction have been described.

Tranexamic acid exerts its anti-fibrinolytic activity primarily by forming a reversible complex with plasminogen which results in inhibition of fibrinolysis. While prolonged treatment may increase the risk of a thrombosis, large scale studies reveal that the incidence of this in women taking tranexamic acid for the treatment of menorrhagia is no different from the spontaneous incidence of thrombosis in women

[7]. Tranexamic acid is at least seven times more potent than aminocaproic acid when inhibiting fibrinolysis on a molar basis [8].

We report the first use of tranexamic acid in the treatment of persistent haematuria in patients with sickle cell disease. This antifibrinolytic agent should be considered as a treatment option in similar cases with appropriate multidisciplinary involvement.

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