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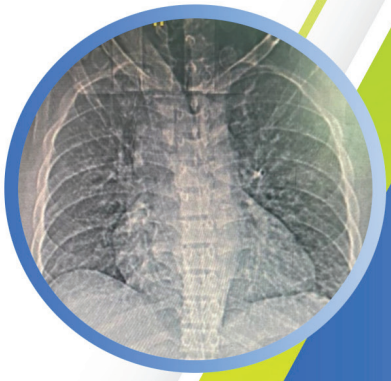
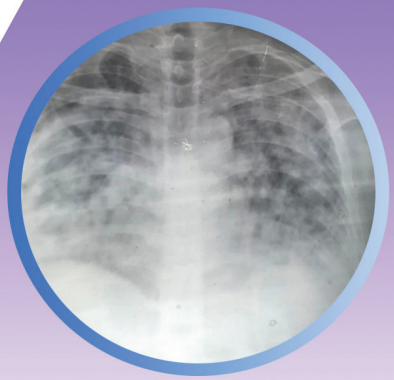
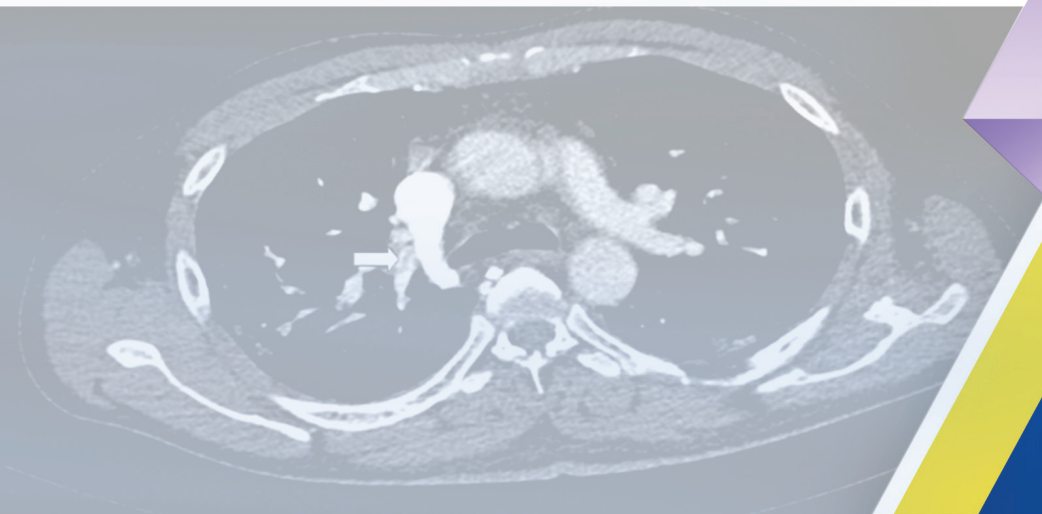
Original Articles

Original Research



Case Report





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Editorial

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PULMONARY EMBOLISM IN ESKD AND COVID-19 – A KNOWN COMMON PROBLEM YET TOO MUCH UNKNOWN

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ABSTRACT

Venous thromboembolism (VTE) is common in COVID-19 infection, particularly in those with severe disease. Here we report a case of pulmonary embolism (PE) in an end stage kidney disease (ESKD) patient on maintenance haemodialysis with COVID-19 infection. The clinical manifestations of PE in this case were non-specific, and were masked by the other concurrent illnesses. Patient was persistently hypoxic despite optimal management of the other concurrent illnesses, and PE was eventually diagnosed based on CT pulmonary angiogram. This case highlights a few important issues that, VTE incidence is unacceptably high despite pharmacological prophylaxis, and clinical manifestations of PE in CKD patients with COVID-19 are non-specific and are frequently thought to be due to other concurrent illnesses. Optimal treatment of PE in COVID-19 is unknown, and data is even more scarce in CKD population. Current treatment recommendations are largely extrapolated from data of non-COVID-19 population, though large prospective trials are underway.

Keywords: *Pulmonary Embolism, COVID-19, Chronic Kidney Disease, End Stage Kidney Disease*

INTRODUCTION

At the time of writing up this case report, the COVID-19 pandemic has already been around for more than a year. As we have seen more cases of COVID-19, and more data on this novel disease has been published to date, we slowly understand this disease better, though there are still lots of unknown.

Venous thromboembolism (VTE) is extremely common in COVID-19 infections, particularly those with severe disease, with incidence up to 46%, even with pharmacological prophylaxis (1). On the other hand, VTE is also very common in CKD populations, with an estimated two to three times higher incidence in those with CKD stage 3-4 compared to those with normal kidney function, and carries higher mortality (2). Pulmonary embolism (PE) is the commonest VTE in COVID-19 infection, and is associated with more severe disease and poorer mortality outcome (3). Although scientific data on covid-19 has been explosive in the last one year, data on incidence of PE in CKD population with COVID-19 is scarce. Much is also unknown on the optimal diagnostic, prophylactic and therapeutic approach of this condition in COVID-19 patients, and current guidelines are largely extrapolated from data of general population. Here we reported a case of PE in an end stage kidney disease (ESKD) patient receiving maintenance haemodialysis with COVID-19 infection. It is not an uncommon scenario in our present routine practice but it highlighted a few learning points, revealing there are in facts lots of unknown.

CASE REPORT

Our patient was a forty-four-year-old gentleman with ESKD on maintenance haemodialysis for 4 years. He presented to us with sudden onset of shortness of breath after the end-of-week gap of dialysis. He gave a history of dry cough for three days but denied fever. He was tachypneic on arrival, blood pressure was 210/123 mmHg, and his arterial blood gas showed marked hypoxemia requiring non-invasive ventilation. He was clinically overloaded, with bilateral crepitations on auscultation of the lungs and pedal oedema up to mid shin.

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Blood investigations noted leucocytosis with total white cell count of 17.5 x109/L and raised C-reactive protein (CRP) at 134 mg/dL. Plain chest radiograph was done showing bilateral heterogenous patchy opacities (figure 1).

He was treated as acute pulmonary oedema and community acquired pneumonia. He was started on intravenous ceftriaxone and urgent haemodialysis was commenced with an ultrafiltration volume of 3 litre. Nevertheless, his tachypnoea and hypoxia did not improve much after haemodialysis. His nasal and oropharyngeal COVID-19 PCR were positive. He was immediately

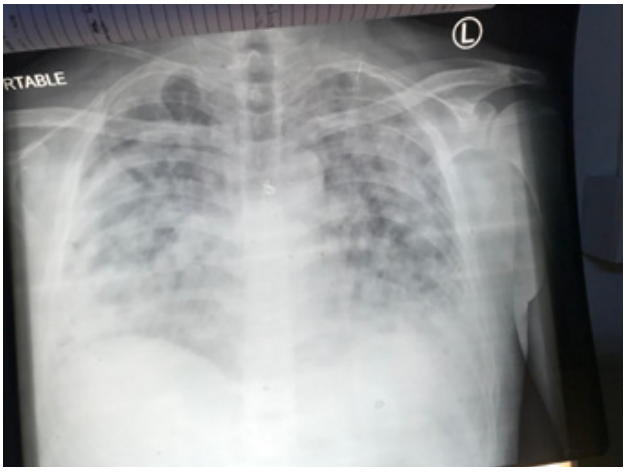

Figure 1: Plain chest radiograph showing bilateral heterogenous patchy opacities

started on intravenous dexamethasone, prophylactic doses of subcutaneous enoxaparin, and was transferred to the regional infectious disease centre for further management. After the transfer, favipiravir and intravenous methylprednisolone were started for his COVID-19 pneumonia. His low molecular weight heparin (LMWH) was continued for VTE prophylaxis. He had persistent fever and raised CRP levels and the antibiotic was escalated to intravenous piperacillin-tazobactem. Unfortunately, he suffered from non-ST elevation myocardial infarction (NSTEMI) as well, for which he was given double antiplatelets and statin. With regards to his acute pulmonary oedema and fluid retention, he was regularly dialysed every 48 hours with target ultrafiltration volume of 2.5-3.0 litre.

After one week of hospitalization, his fluid retention was much improved. Plain chest radiograph was repeated, showing improvement of pulmonary oedema, but presence of bilateral ground glass opacities likely attributable to COVID-19 pneumonia (figure 2). He became afebrile with his total white cell count and CRP levels reducing in trend. Blood culture did not show any growth. He also completed five days of therapeutic anticoagulant for his NSTEMI. Despite the above, he still remained hypoxic requiring face mask oxygen support. At this point of time, D-dimer was taken which was significantly raised at >3000 mcg/ml.

An urgent computed tomography pulmonary angiogram (CTPA) was performed, showing filling defects involving bilateral segmental branches of pulmonary arteries (figure

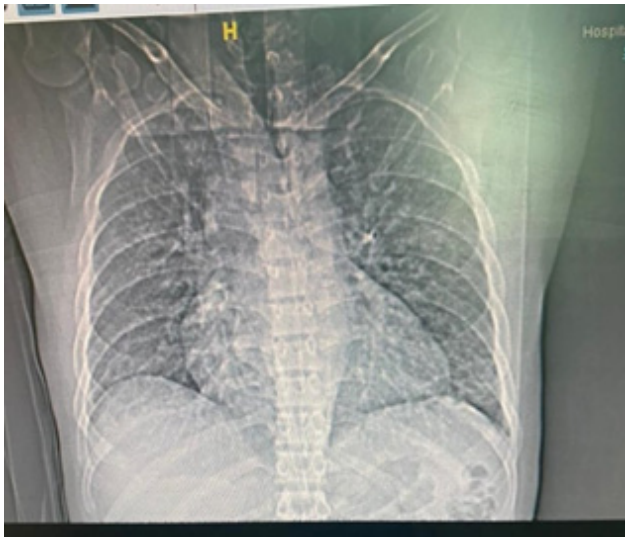

Figure 2: Repeated plain chest radiograph after one week of hospitalization showing improvement of pulmonary oedema, with presence of bilateral ground glass opacities likely attributable to COVID-19 pneumonia.

3). Bilateral pulmonary embolism was diagnosed and he was started on therapeutic anticoagulant, subcutaneous enoxaparin. After few days of therapeutic anticoagulation, his oxygen requirement was able to tapered down, and eventually, off from oxygen support. His general condition improved and he was discharged after twenty days of hospitalization. He was planned for therapeutic anticoagulation with low molecular weight heparin (LWMH) for three months.

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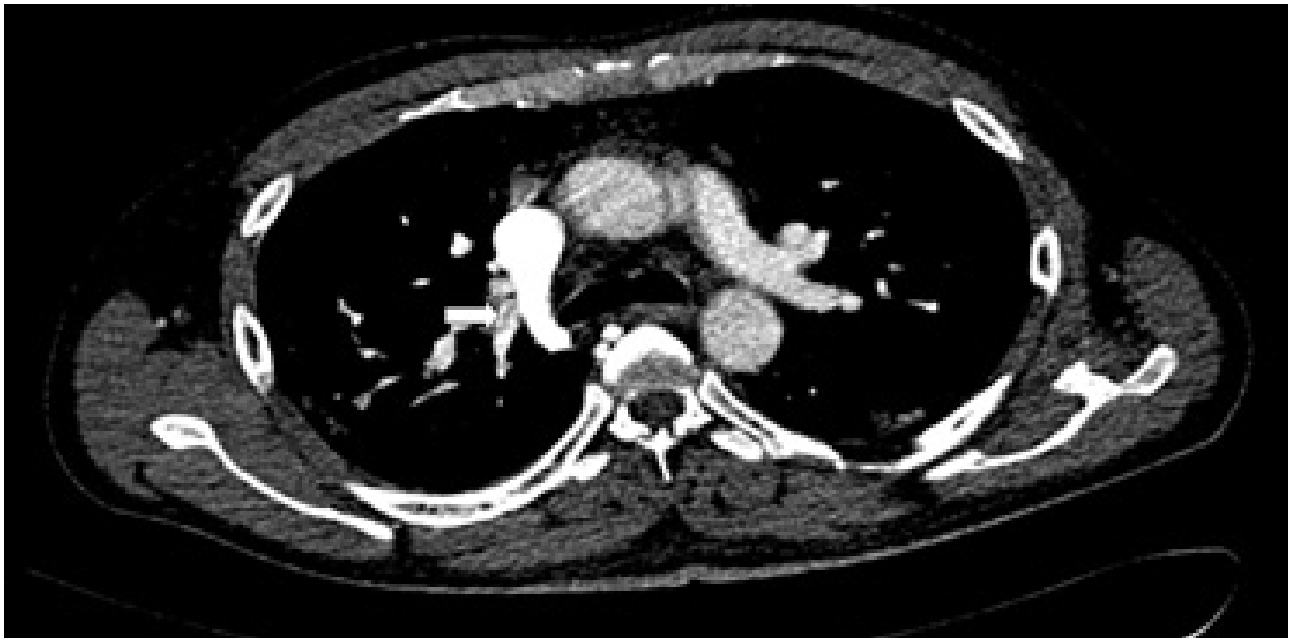

Figure 3: CTPA image showing filling defect in segmental branch of right ascending pulmonary artery (white arrow).

DISCUSSION

As mentioned in the introduction, VTE is common in CKD population while VTE is also very common in COVID-19 infection. Our patient has both the conditions predisposing him to pulmonary embolism. His initial presentations were very commonly seen in our daily nephrology practice and were typical of acute pulmonary oedema and pneumonia. The alarming sign here was that his hypoxemia did not improve despite optimal management of his concurrent illnesses, namely, acute pulmonary oedema, COVID-19 pneumonia, and acute coronary syndrome. D-dimer test was done at this juncture followed by CTPA and finally the diagnosis of PE.

This case illustrated the non-specific manifestations of PE which can be confused and easily attributed to other concurrent illnesses. Given the fact the VTE is extremely common in COVID-19 infection and also CKD populations (1-2), clinicians must have high level of suspicion and low threshold for diagnostic imaging when encountering patients with COVID 19 and CKD. Clinical scoring systems such as Wells has been widely utilized but were unreliable in inpatient settings and even less so among critically ill patients. D-dimer is widely utilized as well and has been validated in CKD population showing excellent negative predictable value yet poor positive predictive value. However, D-dimer has additional value in terms of prognosis in COVID-19 infection. It was found that higher D-dimer values are associated with higher in-hospital mortality and more severe disease among COVID-19 patients (4). Therefore, the value of D-dimer in COVID-19 is two-fold - to exclude VTE when clinical suspicion is not high, to prognosticate and risk stratify. When clinical suspicion of PE is high, diagnostic imaging is warranted without delay, regardless of clinical scoring and D-dimer value.

This case also highlighted the fact that PE can still happen in ill COVID-19 patients despite receiving prophylactic anticoagulant. There has been data showing current pharmacological prophylactic strategies are inadequate to prevent VTE in severe COVID-19 cases (5). With regards to treatment of PE in COVID-19, current guideline recommendations from societies such as ACCP (American College of Chest Physicians) and ISTH (International Society of Thrombosis and Haemostasis) are largely extrapolated from data of non-COVID-19 population. Such data is even more scarce in CKD populations, and the above mentioned guidelines did not make any specific recommendations or suggestions pertaining to CKD patients. While large RCTs (ClinicalTrials.gov Identifier: NCT04372589, NCT04505774) are underway examining the optimal prophylactic and treatment strategies for VTE in COVID-19, we look forward to data on CKD populations as this group of patients are vulnerable when facing COVID-19 with higher mortality rate, their data are desperately needed.

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CONCLUSION

Pulmonary embolism is common in COVID-19, the risk may even be higher in CKD population due to their pro-thrombotic risk, though data is lacking. Making clinical diagnosis of PE in COVID-19 is challenging as clinical manifestations are very non-specific, and scoring systems are unreliable, thus clinical suspicion must be high. D-dimers has two-fold values in COVID-19 - good negative predictive value, and prognostication. Diagnostic imaging should be pursued when suspecting PE, regardless of clinical scoring and D-dimer.

Optimal strategies of VTE prophylaxis and treatment in COVID-19 are still unknown, these data are even more scarce in CKD population. Data on optimal strategy of VTE prophylaxis and management in COVID-19 are desperately needed, while large RCTs are underway. We look forward to these new data, particularly in CKD population.

ACKNOWLEDGEMENT

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USE OF PROPHYLACTIC ANTIBIOTIC IN MICTURATING CYSTOURETHROGRAPHY: INTRAMUSCULAR VERSUS ORAL AND IMPACT ON PATIENT'S STRESS

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ABSTRACT

Introduction:
Our centre has been practicing pre-procedural single dose of intramuscular(IM) gentamicin as Urinary Tract Infection(UTI) prophylaxis for Micturating Cystourethrography(MCUG).

Objectives:
Primary: Compare impact on stress among children undergoing IM gentamicin and oral TMP for MCUG
Secondary: Evaluate the effectiveness of IM gentamicin and oral TMP in preventing post procedure urinary traction infection (ppUTI), family preference of antibiotic administration and adherence to antibiotic prophylaxis.

Methods:
This study conduct in two phases, each lasted 9 months. First phase patients received single dose IM gentamicin prior to MCUG except patients with eGFR< 60ml/min/1.73m2 to receive oral trimethoprim. Second phase patients received 3 days of oral trimethoprim started day before the procedure. Preferences type of antibiotic prophylaxis and stress scores of having respective antibiotic were recorded after the procedure. They were followed up with phone interview at one week and later in clinic.

Results:
56 patients were recruited. (IM gentamicin, n=17, oral trimethoprim, n=39). The median age was 9 months (4 days–14 years).
Mean stress score of IM gentamicin group was 3.9, oral trimethoprim group recorded 0. (p =0.000)
Three oral trimethoprim users (7.89%) developed ppUTI, none from IM gentamicin group. (p =0.546). All 3 were younger than 3 months.
Ninety percent of the patients preferred oral trimethoprim. The oral trimethoprim group reported a full adherence. The positive pick-up rate of urinary tract anomaly from MCUG was 34%.

Conclusion:
Oral trimethoprim significantly alleviates the stress of the procedure with excellent family adherence and family preference. Oral trimethoprim should be choice of antibiotic prophylaxis for children > 3 months old.

Keywords: stress, post-procedural UTI, antibiotic prophylaxis, MCUG/ VCUG

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INTRODUCTION

Micturating cystourethrography (MCUG) is also known as voiding cystourethrogram. It is a fluoroscopic imaging test for lower urinary tract pathologies; commonly to look for vesicoureteral reflux, abnormalities of the bladder and urethra such as posterior urethral valve. The commonest indications for this procedure are atypical urinary tract infections and postnatal hydronephrosis. Postnatal hydronephrosis are picked up more often now due to advancing antenatal ultrasonography services and subsequently lead to an increased number of MCUG requests.

This test requires urinary catheterization for injection of contrast which may lead to significant distress and also post-procedural urinary tract infection (1-7). Stashinko and Goldenberg reported 2 case reports which described significant stress suffered by the cases after the procedure and Phillips et al in 2007 has reported 46% of the patients have anxiety-linked behavior changes post MCUG (1-2). This rarely-discussed mental side-effect of the MCUG procedure is important to be explored for the patients as part of a holistic treatment approach.

As for physical outcomes after an MCUG, urinary tract infections (UTI) in very young children potentially pose significant morbidities such as urosepsis and renal scarring especially when it occurs in patients who had pre-existing renal anomalies. Historically, Mc Alister et al had observed a 16% risk of ppUTI in those without antibiotic prophylaxis (6) while Glynn & Gordon conversely demonstrated that the giving of antibiotic prophylaxis for MCUG procedure reduced the incidence of UTI from 17% to 1.4% (7). Craig et al much later observed none among those who were on antibiotic prophylaxis contracted a UTI (8).

Our division in the Tunku Azizah Hospital, Kuala Lumpur MCUG is performed as daycare procedure. There is an established practice of injecting one dose of intramuscular (IM) gentamicin as the antibiotic prophylaxis of choice just before MCUG. It was originally meant for the benefit of ensuring patient's compliance to the prophylaxis. However, gentamicin is known for its nephrotoxic potential and the intramuscular route of injection could furthermore add to the pain and stress from the mandatory urinary catheterization procedure to both patients and their caregivers. (9) For those patient who has renal impairment the prophylaxis antibiotic of choice will be oral trimethoprim (TMP).

Hence, a quality assurance initiative was carried out to reduce the MCUG-related stress by changing our practice of administering IM gentamicin to oral trimethoprim.

OBJECTIVE

Primary objective:

1. Compare impact on stress among children undergoing IM gentamicin and oral TMP for MCUG

Secondary objectives:

1. Evaluate the effectiveness of IM gentamicin and oral TMP in preventing ppUTI
2. Assess family preference of antibiotic administration
3. Assess adherence to antibiotic prophylaxis

METHODOLOGY

This is a cohort observational study using database from a quality assurance project that was conducted on children undergoing MCUG procedures in the Paediatric Institute, Hospital Kuala Lumpur and Hospital Tunku Azizah from 1stJuly 2018 until 31st December 2019.

Sample size

Sample size requirement was based on Krejcie and Morgan. Using the numerical local data of total MCUGs performed in the previous year, which was 60 individual cases, as well as allowing for a 20% drop-out, we calculated a sample size of 59. Due to the scarcity of cases, convenient universal sampling was used over two 9 month periods.

This study involved 2 phases:

Phase 1

Duration: 1st July 2018 until 31st March 2019 (9 months)
Prophylactic antibiotic administration:
Patients were kept on single dose of IM gentamicin 2.5mg/kg, unless estimated glomerular filtration rate (eGFR) is less than 60ml/1.73m^2/min, oral TMP is given. The eGFR is calculated using the "Bedside Schwartz" equation (2009) (10-11)

The IM antibiotic and the bladder catheterization were performed at day care centre prior to MCUG.

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Phase 2

Durations: 1st April 2019 until 31st December 2019 (9 months)

Prophylactic antibiotic administration:

Patients were prescribed 3 days oral TMP 4mg/kg BD and instructed to start one day before MCUG appointment date.

At day of procedure - The oral antibiotic adherence review and bladder catheterization were performed at day care centre prior to MCUG.

Inclusion Criteria: All patients who underwent MCUG during the study period.

Exclusion Criteria: Patients who were receiving ongoing treatment for UTI during MCUG

The perceived stress score and preferred route for antibiotic administration were recorded on data collection form by parents. Wong-Baker face scale was used as a surrogate assessment of the child's stress score as observed by the parents/caregivers with guidance from the day care staffs. This is in concordance with Volkl-Kernstock and Gazal' studies that also employed the face scale to correspond to the actual stress level suffered by the sampled children. (3,12)

The researcher would then get in touch with the parents at one week post-procedure via a phone interview. During this interview, symptoms of UTI were asked to the parents and documented. A subsequent follow up for counselling of the MCUG findings and recheck on incidence of ppUTI was then arranged within a month after the procedure.

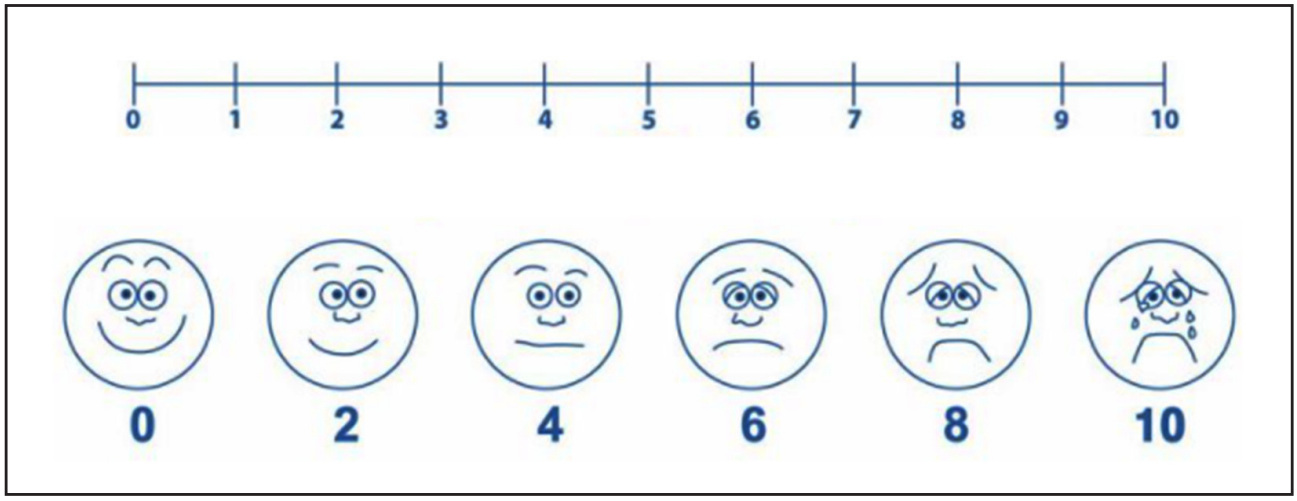

Figure 1. Modified Wong-Baker Face Scale for assessing stress in children

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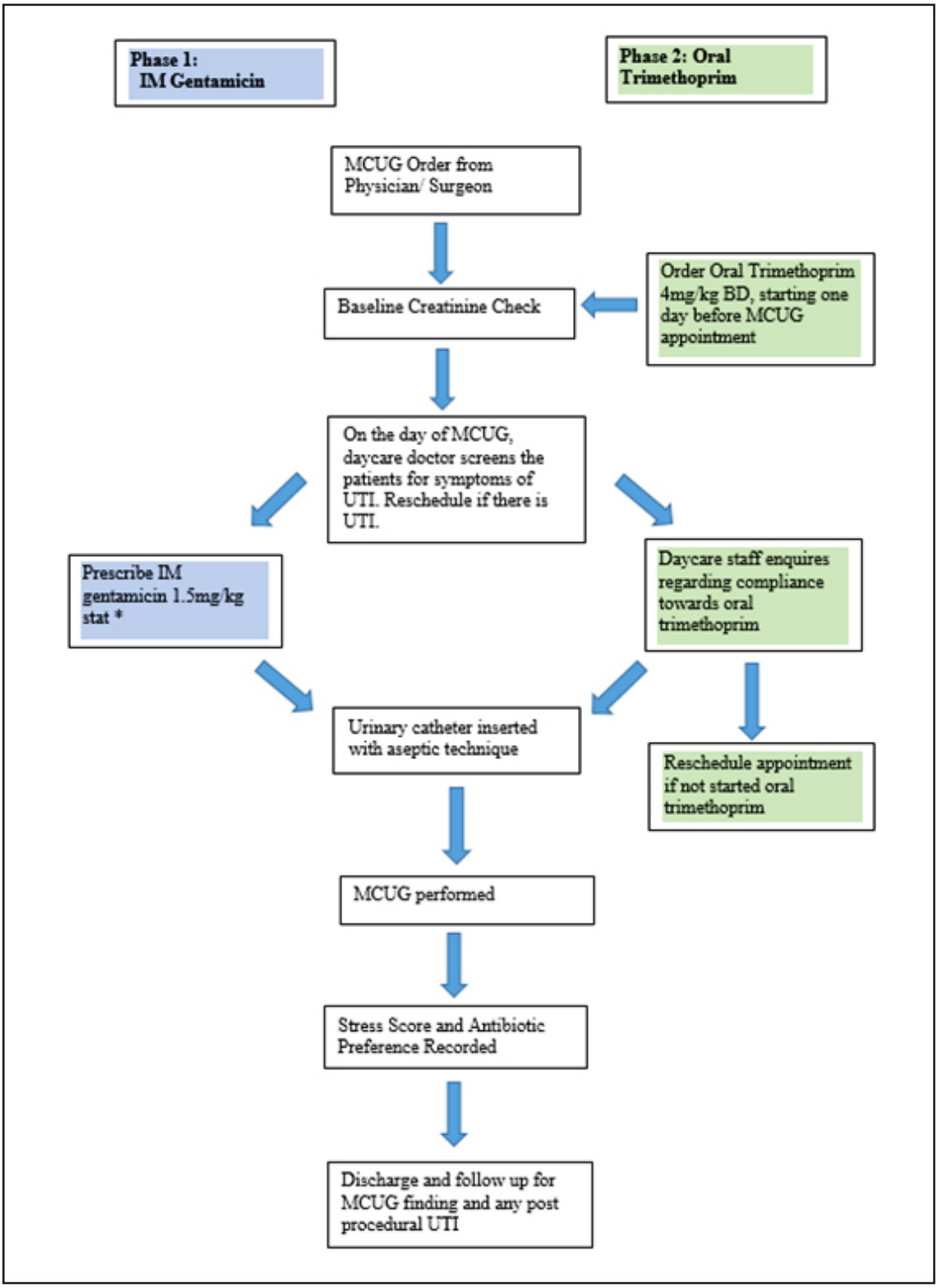
Diagram 1. Work Process



**During phase 1, patients with eGFR < 60ml/min/1.73m2 were given oral TMP instead.*

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DATA ANALYSIS:

The Statistical Package for the Social Sciences (SPSS) version 25 was used for analysis. Mann- Whitney U test was used to compare the mean stress scores between IM Gentamicin and oral trimethoprim group. Fisher exact chi square test was used to evaluate the differences in the incidence of ppUTI between the IM gentamicin and oral trimethoprim group and also incidence of ppUTI between the groups who are younger and older than 3 months.

RESULTS:

A Total 61 MCUGs were conducted during the 18 months' study period. Seventeen of them had the single dose IM gentamicin prior to the procedure while 39 received 3 days oral TMP. The remaining 4 received intravenous (IV) antibiotics as part of their existing treatment for UTI when they were enrolled for the procedure and hence were excluded from the study. These are summarized in Diagram 2.

The numbers were skewed towards the oral trimethoprim group due to an unavoidable non-clinical factor which was the reduction of MCUG appointments in the first 9 months (IM Gentamicin group) when we were shifting to an entirely new premise which led to limited MCUGs being arranged during that period.

Mean age of the patients was 2.5 ±4 years, and the median age was 9 months old (range from 4 days to 14 years old).

The baseline characteristics of the subjects were demonstrated in table 1.

Diagram 2. Number of MCUGs performed and number of subjects in each group

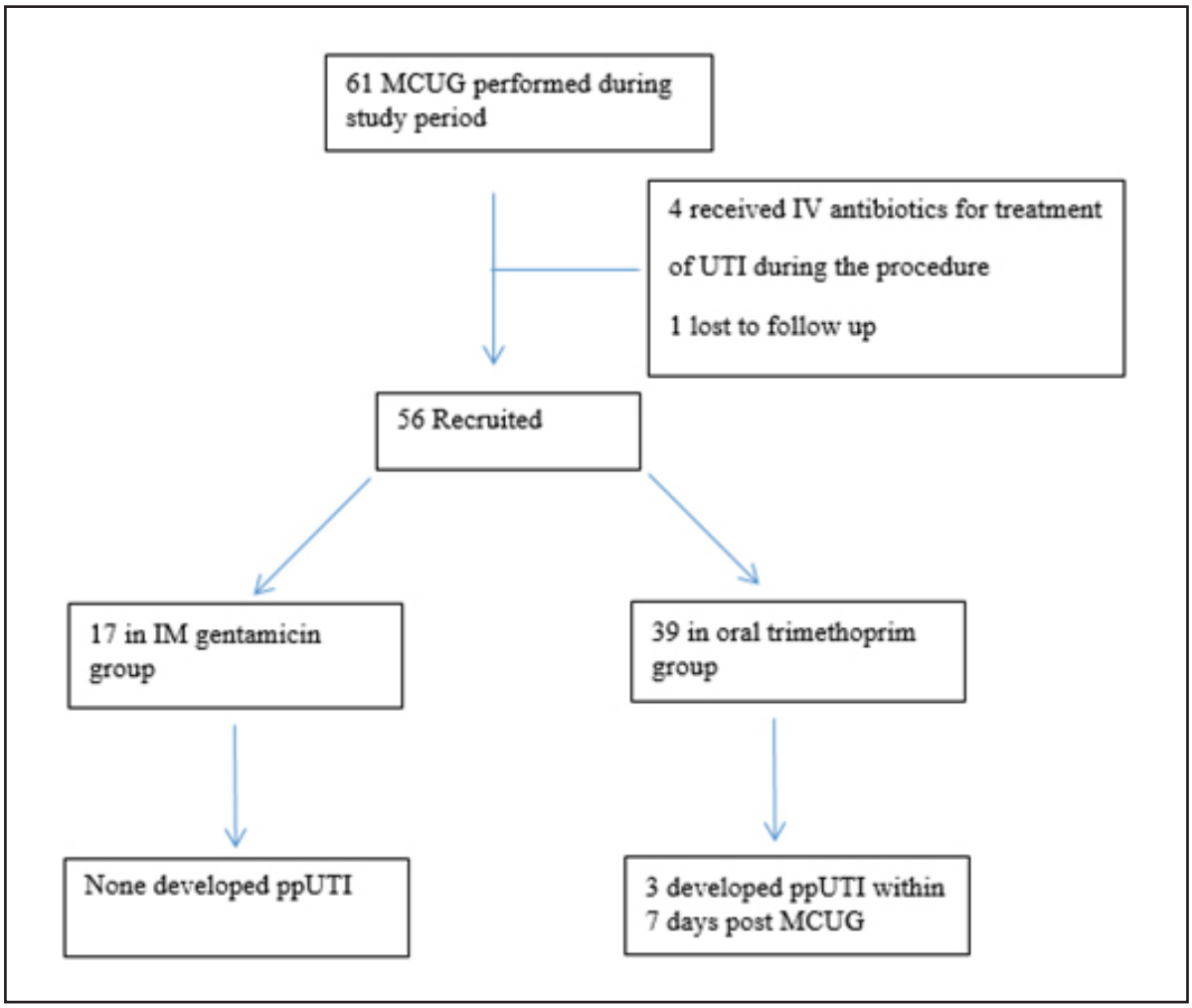

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Table 1. Baseline characteristics.

Characteristic	IM Gentamicin group	Oral TMP group	*p* value
Mean age **Median age (Interquartile range)** **Age** **< 1 year** **> 1 year**	1.7 0.5 (0.2) 10 7	2.9 1 (0.08) 19 20	0.727
Gender Male Female	13 4	24 15	0.364
Renal Function eGFR $\geq$ 60ml/min/1.73m^2 eGFR < 60 ml/min/1.73m^2	17 0	31 8	0.09
Indication for MCUG Hydronephrosis alone Hydronephrosis + UTI Hydronephrosis + RI UTI Reassessment after surgical procedure Assessment of bladder for surgical associations Renal Impairment **Duplex Kidney**	 8 5 2 2	 12 2 1 5 5 1 8 5	

Legend: *IM* - *Intramuscular*
IV - *Intravenous*
TMP - *Trimethoprim*
eGFR - *Estimated Glomerular filtration rate (Bedside Schwartz formula)*
UTI - *Urinary Tract Infection*
RI - *Renal Impairment*

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Stress Score

The IM gentamicin group had a mean score of 3.2 with median score of 2.5, while the oral trimethoprim group had a mean score of 0. The stress score categories are shown in Table 2 below.

MCUG FINDINGS

A total of 56 MCUGs were recruited during the study period, 38 out of 56 (67.8%) had no abnormal findings from the MCUG. The MCUG findings were elaborated below. (Table 3)

Table 2. Stress Score

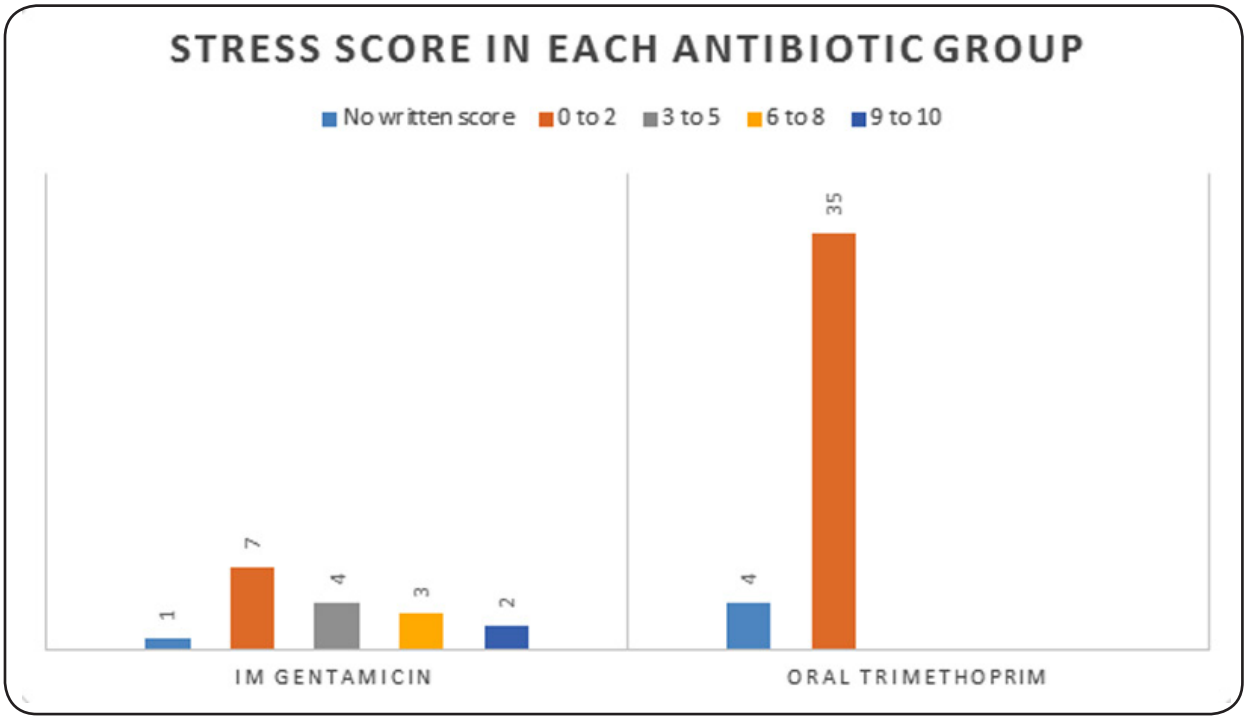

Table 3. Mann-Whitney U Test for Stress Score

Group	Mean +/- SD	Statistic Value
IM gentamicin	3.2 +/- 3.07	$p = 0.00$
Oral TMP	0 +/- 0	

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Table 3. MCUG Findings

MCUG Findings	N (%)
No detected	38 (67.8)
VUR	10 (17.8)
VUR + Ureterocoele	1 (1.8)
PUV	3 (5.4)
Ureterocoele Alone	1 (1.8)
Bladder Diverticuli	1 (1.8)
Ectopic Ureter (Reflux)	1 (1.8)
Urethral Stricture	1 (1.8)
Total	**56 (100%)**

Legend: *VUR - Vesicoureteric reflux*
PUV - Posterior Urethral Valve

A total of 49 MCUGs were done to look for a first-time diagnosis while 7 other cases were for reassessment purposes. (Table 4)

Hydronephrosis makes up almost half of the indications for a new case MCUG. When it is combined with a second indication (UTI or renal impairment), the percentage of a positive pick-up soars from 9% to 50-67%.

A high positive pick-up percentage is also seen in sole indications of UTI, duplex kidney or surgical associations ranging from 40-67%. On the other hand, when renal impairment is the sole indication for an MCUG, the likelihood of a positive finding is 12.5%. The pick-up rate is low because they are all crash landed ESRD patients as workup for transplant, they all have normal USG or just small kidneys.

Hydronephrosis when presented with renal impairment would be a strong indication for MCUG with a good pick-up rate for PUV. In this study however they had not fitted the antibiotic administration criteria as they received IV antibiotic as treatment of UTI.

Table 4. Positive MCUG Finding Outcomes when analyzed against each indication for MCUG

Indication for MCUG	No. of cases with positive findings	Total MCUGs per indication	Positive Pick-up Percentage (%)
Hydronephrosis - Hydronephrosis alone - Hydronephrosis with UTI - Hydronephrosis with Renal Impairment	 2 1 0	 20 2 1	 10 50 0
UTI alone	6	10	60
Duplex kidney	2	5	40
Assessment of bladder for surgical associations - Anorectal Malformation - Bladder Exstrophy	 1 1	 2 1	67
Renal Impairment without hydronephrosis	1	8	125
Reassessment after surgical intervention	5	7	71.4
Total	**19**	**56**	-

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INCIDENCE OF POST-PROCEDURAL UTI

We diagnosed post MCUG UTI with its definition being fever along with bacteria/ nitrite present in urine microscopy with or without a positive culture of more than 100,000 colony forming units/ml of a clean catched or catheterized urine sample.

None of the IM Gentamicin group developed a UTI after MCUG. In contrast to this, three of the patients from the oral Trimethoprim prophylaxis group developed fever within the first week of their MCUG (Table 5). One of the three children developed fever with seizures on the same day of MCUG but the urine culture returned back as no growth.

Fisher exact chi-square test was used to compare the incidence of ppUTI in both antibiotic groups, the outcome p value was 0.546 which was not significant. The risk of ppUTI was associated with younger age group (<3 months), with a p value of 0.035.

ADHERENCE TO ANTIBIOTIC PROPHYLAXIS

There were no doubts with regards to the adherence to the single dosing of IM Gentamicin as it was given on the same timeframe of the bladder catheterization prior to the MCUG procedure. Parents from oral TMP group reported back to a complete compliance of their children to all 3 days of the prescribed antibiotics (A total of 6 doses per oral trimethoprim course).

PREFERENCE

Six out of the 17 sets of parents in the IM Gentamicin group (35.2%) preferred IM antibiotics over oral antibiotics. Their feedback was that IM antibiotics were perceived by them to be more effective than oral antibiotics. As for the 39 sets of parents in the oral TMP cohort, none expressed a preference to IM antibiotics.

DISCUSSION

Previous studies have reported between 27-46% of their studied population who had experienced severe distress from their MCUG procedure largely due to the need for urinary catheterization (2,13-14). On average, our centre conducts 50-60 MCUGs per year. We thus opted to replace the IM gentamicin with oral trimethoprim as peri-procedural prophylaxis to negate additional distress from the intramuscular injection. We also took into consideration the need for an assessment of oral trimethoprim compliance due to the potential hassle of rescheduling the MCUG if the patient was non adherent to the oral prophylaxis (15). A course of 3 days oral peri-

Table 5. Cases with post-MCUG infection in the Oral Trimethoprim Group

No.	Age	MCUG Indication	MCUG Result	Group	Presentation
1	3 months	Hydronephrosis	Normal	Oral	Escherichia coli UTI on day 6
2	5 days	Duplex Kidney	Ureterocoele	Oral	Enterococcus UTI
3	1 month	Duplex Kidney	Reflux to ectopic ureter	Oral	Fever with seizure on same day, with presence of urine leukocyte, no positive culture

Table 6. Comparison of Incidence of ppUTI among the children groups

Group	Number, *n*	*p* Value (95% CI)
IM gentamicin Oral TMP	0/17 3/39	0.546
<3-month old >3-month old	3/19 0/37	0.035

procedural prophylaxis has been widely practised in many other paediatric nephrology centres and supported by the NICE guidelines on this particular practice (15-16).

There is no simple assessment tool, as is impossible to separate pain from fear or stress by just perceiving their response. We adapted from Volkl-Kernstock and Gazal' studies that employed the face scale to correspond to the actual stress level suffered by the sampled children.

We see a significant difference in the reported stress scores between the IM Gentamicin and oral Trimethoprim groups. The latter reported zero stress onto the child from this route of antibiotic administration. This was slightly surprising as we anticipated a degree of stress for the parents from the oral group due to a possible difficulty in getting the child to swallow the oral medication.

There is yet to be a clear international consensus on the usage of prophylactic antibiotics for this MCUG procedure (17). Post-procedural UTI's (ppUTI) incidence was shown to be between 6-30% in earlier studies by Glynn et al, Maskell et al and Moorani et al (5,7,18). Antibiotic prophylaxis usage was subsequently suggested to reduce the incidence of UTI. (5,7-8,19) In recent studies however, studies by Johnson and Malhotra et al in 2017 found that the incidence of ppUTI to be very low in their cohort and did not support the usage of peri-procedural antibiotic prophylaxis. (20-21). However, both studies were retrospective in nature; more than half of their patients were already on existing antibiotics when they underwent the voiding cystourethrogram and retrograde urethrogram. Therefore, the potential benefit of the giving prophylaxis antibiotic during MCUG procedures cannot be completely brushed off.

On a further note, there are also several papers which focused on detection of complications associated with MCUG with UTI a particular outcome looked at. They showed a very low incidence of UTI for those who were put on antibiotic prophylaxis (8,22-24). Our study findings are consistent with that of Fried et al which was done in the year 1996 in that both oral and IM antibiotic demonstrated similar efficacy (15). In addition to this, the incidence of UTI in our oral trimethoprim group was not statistically significant while no UTI were seen in the IM Gentamicin group.

Overall, majority of the patients going for MCUG preferred oral over IM antibiotic because of the additional pain and discomfort associated with the injection. In view of this, our centre has decided to continue the practice of oral trimethoprim as the prophylactic antibiotic of choice for our planned MCUG procedures.

Another point of discussion from our study is whether we clinicians are over-investigating postnatal hydronephrosis using the MCUG tool. The incidence of VUR in patients with antenatally detected hydronephrosis was low i.e. 12-13% from two studies (25-26). Our study itself had shown a similar finding of 10% when hydronephrosis alone was the indication for the MCUG. However, when used together with a second indication e.g. UTI or renal impairment, the likelihood increases to 50-67% (Table 3).

Several limitations were identified by the researchers when conducting the study. First, we obtained an unequal sample size with the number in oral trimethoprim group nearly doubled that of the IM gentamicin group. This was due to the reduced appointments in the first half of the study when recruiting patients for the IM Gentamicin group due to a non-clinical situation i.e. a prolonged time spent in shifting to a new premise elsewhere. Secondly, pre-procedural urine was not screened for pre-existing asymptomatic UTI within a week of the MCUG appointment to ensure that any ppUTI would be solely associated with MCUG itself. Thirdly, adherence to oral Trimethoprim was reliant on the parent's history which is a potential source of reporting bias in the 3 cases of ppUTI in the oral group. We do not have electronic drug bottle cap tagging technology in our centre which could have helped offset this bias.

Lastly, our data comes from a single tertiary centre with a small sample size due to the scarcity of diseases screened for with MCUG. This is an area of research which can be further explored using a multi-centre study approach.

CONCLUSIONS

None from the oral Trimethoprim group recorded any stress from this route of administration and also had a recorded full adherence to this antibiotic prophylaxis. This meant no untoward postponements of MCUG appointments. Despite of 3 cases of ppUTI occuring in the oral trimethoprim group, there was no statistical difference compared to the IM gentamicin when used as an antibiotic prophylaxis. However, all the cases of ppUTI happened in the < 3 month old group. In short, we would recommend the use of oral trimethoprim as the prophylactic antibiotic of choice to minimize additional stress to the patient for the MCUG procedure in the older children who are > 3 months.

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