

Early Onset Clean Intermittent Catheterization May Decrease Prevalence and Severity of Urinary Concentration Defects in Myelomeningocele Patients with Neurogenic Bladder: A Retrospective Cohort Study

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Purpose: Myelomeningocele is the most severe form of spina bifida. Management of urologic consequences of spina bifida is life long, demanding and costly for both the patient and the public health system. There is a paucity of data in the literature regarding concentration defects and their consequences on this disease. This paper aims to describe retrospectively the effect of early onset clean intermittent catheterization (CIC) in on the severity of urinary concentration defects in myelomeningocele patients with neurogenic bladder in a retrospective observational study.

Materials and Methods: In this 10-year retrospective cohort study, children with myelomeningocele were selected with the Convenience sampling method. Demographic characteristics, polyuria index ratio (PIR) defined as 24 hour urine output of each patient divided by the maximum normal urine output of the same patient in a healthy state, and nocturnal polyuria index (NPI) were compared between early starters (< 2 years old) or late starters (\geq 2 years old) groups.

Results: Seven patients who underwent cystoplasty were excluded and 130 patients (63.8% male, 5.4 ± 3.2 years old, 14.3 ± 2.83 Kg, 28.5% early onset CIC) were investigated. PIR > 1 in inset (1.7 ± 0.2 vs. 2.2 ± 0.5 , $P = 0.021$) and outset (1.5 ± 0.32 vs. 2.5 ± 0.7 , $P = 0.004$) were lower in early starters group than in late starters group. NPI in inset (0.2 ± 0.007 vs. 0.32 ± 0.10 , $P = 0.018$) and outset (0.25 ± 0.15 vs. 0.42 ± 0.095 , $P = 0.007$) were also lower in the early starters group. No further adverse events were reported during the follow-up period.

Conclusion: Early onset CIC is more effective than late-onset CIC in preserving the urinary ability of kidneys in myelomeningocele patients.

Keywords: myelomeningocele; neurogenic bladder; clean intermittent catheterization; urinary concentration

INTRODUCTION

Myelomeningocele is the most dangerous and severe form of spina bifida, characterized by nerve roots, spinal cord, and meninges protrusion through vertebrae defects^(1,2). This condition brings chemical and mechanical damage to the intrauterine environment before birth^(3,4). Deficiency in urine concentration in this disease is associated with a high prevalence and in the long run, it can lead to functional kidney damage⁽²⁻⁴⁾. The standard treatment for these patients is surgical closure. The patients may also need a shunt for hydrocephalus or require urinary catheterization^(5,6).

Myelomeningocele is associated with various sequelae such as lower limb paraplegia, muscle weakness, musculoskeletal deformities, and bowel and bladder dysfunction^(2,3).

Neurogenic bladder is a common urological disease caused by neurological pathologies^(9,10). About 98% of patients with myelomeningocele have a neurogenic bladder. Important goals of treatment in these patients are ensuring safe storage pressures, adequate bladder

emptying, and preventing kidney damage, to improve the quality of life⁽¹¹⁾.

Although the effect of partial urinary tract obstruction on the concentrating ability of kidneys is clarified there is a paucity of data in the literature regarding concentration defect and its consequences on specific situations of MMC patients with neurogenic bladder⁽¹²⁻¹⁴⁾.

There were remarkably few complications associated with clean intermittent catheterization (CIC) in myelomeningocele⁽¹⁵⁾. Role of concentration defect and increasing amount of dilute urine on an already neurologically un-healthy bladder has not been addressed. Effect of pre-emptive IC on this problem would give us a hint about role and mechanism of concentration defects as this has been shown to significantly reduce the rate of enterocystoplasty⁽¹³⁾. The authors performed a preliminary observational study to support the idea that CIC might affect urine concentration. Therefore, the present study was conducted to describe the prevalence and severity of urinary concentration defects in myelomeningocele patients pre-emptively treated by IC at an earlier age Vs late starters.

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Table 1. Demographic characteristics of myelomeningocele patients at early or late clean intermittent catheterization

Variables	CIS, mean (S.D)/ n (%) early starters (n = 37)	late starters (n = 93)	P-value
Age (year)	1.01 (0.21)	5.7 (1.12)	< 0.001 *
Sex			
male	24 (64.8)	59 (63.4)	0.624 **
female	13 (35.2)	34 (36.6)	
Weight (Kg)	7.42 (1.01)	15.06 (2.42)	< 0.001 *

Notes: CIC, clean intermittent catheterization; SD, standard deviation; *Student t test, **Chi-square test

MATERIALS AND METHODS

In this retrospective cohort study, patients with myelomeningocele referred to our center in 10 years (September 2011 to September 2020) were selected using the Convenience sampling method. Including criteria were: a) age ≤ 14 years, b) access to clinical records, and b) both male and female. Defects in the necessary information required for this study and using of nephrotoxic drugs (such as diuretics or aminoglycosides) in a period of two weeks leading to the measurements in archived documents, were the exclusion criteria.

The information required for this study was extracted in the form of a checklist containing questions related to demographic information as well as information related to the disease, voiding diaries and laboratory findings already obtained in the center database. More precisely, this information included: demographic characteristics (age, sex, and weight), polyuria index ratio (PIR), and nocturnal polyuria index (NPI). Nocturnal polyuria index (NPI) was defined as the fraction of 24-hour urine output produced during the intended sleep period (nocturnal urine volume/24-hour urine volume)

Polyuria index ratio was calculated by dividing the patient's urine output by the maximal 24 hour urine output of the same healthy index patient regarding the definition of polyuria i.e. more than 4 ml/kg.hr in infants and children excluding neonatal period⁽¹⁶⁾ These indices were improvised as quantitative indices which can consider weight, age and body surface area regarding the adopted definition. In our case, the definition by weight was picked up due to ease of use.

Patients were divided into two groups based on whether

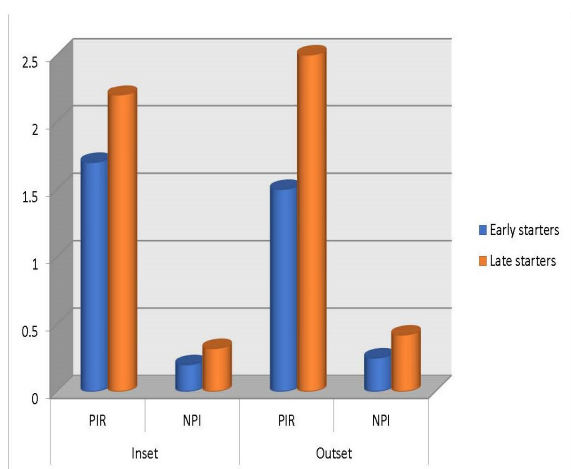


Figure 1: Distribution of PIR and NPI in early starters and late starters of CIC

Table 2. Mean (SD) for PIR above one in early starters and late starters of CIC

Variables	CIS, mean (S.D) early starters (n = 37)	late starters (n = 93)	P-value*	
PIR > 1	inset	1.7 (0.2)	2.2 (0.5)	0.021
	outset	1.5 (0.32)	2.5 (0.7)	0.004

Notes: CIC, clean intermittent catheterization, PIR, polyuria index ratio; SD, standard deviation; * Mann-Whitney test

they began clean intermittent catheterization (CIC) at early age (before two years old) as early starters or late starters (after two years old), and the information (PIR and NPI) was compared between these two groups. Patients were cared for according to routine standards. Finally, the data were analyzed with the Kolmogorov Smirnov, independent t test, Mann-Whitney, and chi-square tests, using Statistical Package for the Social Sciences 25.0 software (SPSS 25.0) and Stata software version 2.9 (Stata Corp., College Station, TX, USA). The primary assumption underlying the chi-square test, were no expected cell count less than 1 and at most 20% of the expected cell counts less than 5. The normality of the data was checked with the Shapiro-Wilk test. In all tests, the confidence level was 95% and the significance level was less than 0.05.

RESULTS

Seven who underwent cystoplasty during the course of study were excluded, and 130 patients (63.8% male) aged 5.4 ± 3.2 years and weighing 14.3 ± 2.83 Kg were investigated (Table 1). The age of early starters tended to be lower than late starters though not achieving statistical significance (19.1 ± 1.2 vs. 54.2 ± 2.3 and $P = 0.453$, respectively). The reason for the limitation of the volume of statistical samples is the small number of available patients. In this study, 130 performed CIC (37 patients (28.5%) had presented before two years old and 93 patients (71.5%) after two years of age).

According to the Table and Figure 1, the mean and standard deviation of PIR > 1 in inset ($P = 0.021$) and outset ($P = 0.004$) were lower in the early starters group

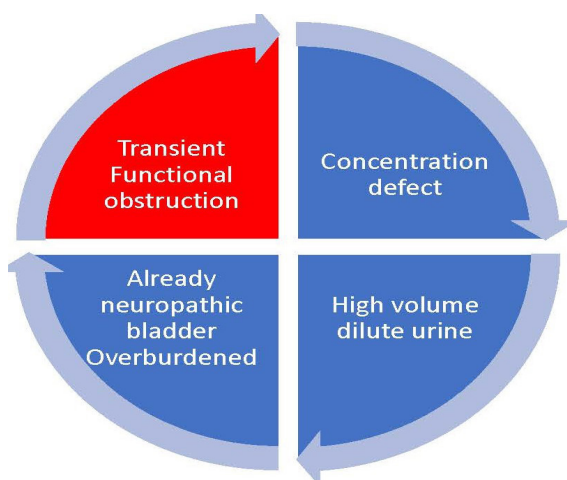


Figure 2: Urinary concentration defects in myelomeningocele patients with neurogenic bladder may lead to a vicious cycle of functional urinary tract obstruction and further concentration defect.

Table 3. Mean (SD) for NPI in early starters and late starters of CIC

Variables		CIS, mean (S.D) early starters (n = 37)	late starters (n = 93)	P-value*
NPI	inset	0.2 (0.007)	0.32 (0.10)	0.018
	outset	0.25 (0.15)	0.42 (0.095)	0.007

Notes: CIC, clean intermittent catheterization, NPI, nocturnal polyuria index; SD, standard deviation; * Mann-Whitney test

than in the late starters group, and this difference was significant.

The mean and standard deviation of NPI in inset ($P = 0.018$) and outset ($P = 0.007$) were lower in the early starters group than in the late starters group, and this difference was significant (**Table 2, Figure 1**).

DISCUSSION

Clean intermittent catheterization (CIC) is an effective, reliable long-term, and safe bladder management option for patients with myelomeningocele⁽¹⁶⁾. This 10-year cohort is the first study assessing the effect of early onset CIC on renal concentration defects of children with neurogenic bladder. The concept rose when we noticed in the literature that concentration defects induced by transient episodes of obstruction tend to persist beyond relief of obstruction⁽¹²⁾. The scenario may go on with a vicious cycle of obstruction leading to voluminous dilute urine overburdening of the bladder and leading to further functional obstruction (**Figure 2**). Early institution of IC which has been shown to be beneficial in several studies⁽¹³⁾ may actually decrease these episodes of transient obstruction. This leads us to the core concept of this study.

Analysis of data showed early onset CIC therapy played a major role in decreasing of polyuria index ratio (PIR) and nocturnal polyuria index (NPI) in children with myelomeningocele. According to the searches, few studies were found in this regard. Elzeneini et al (2019) instituted early CIC for all infants with spina bifida. Based on renal functional data, they recommend indwelling and then early CIC from birth in all patients with spina bifida⁽¹⁷⁾. In the other study, Li et al (2018) demonstrated that early CIC plays an important role in preserving bladder function in infants with neurogenic bladder, especially in the first year of life⁽¹⁸⁾. Proponents of early onset of CIC suggest that the benefits of improved conservation of renal function, bladder compliance, and bladder emptying outweigh the risk and potential discomfort and parental anxiety of early CIC⁽¹⁹⁾. None of these studies specifically highlighted the role of concentration defects. Contrary to these findings, Freeman et al (2022) could not demonstrate that younger age at CIC initiation increased the likelihood of achieving urinary continence in children with myelomeningocele. Limitations include a lack of urodynamic data, data on the reason for starting CIC and type of incontinence, and the observational nature of data collection⁽²⁰⁾.

We also found that no other adverse events were reported during the observation period in early onset CIC. This method is believed to decrease the need for future bladder augmentation and is well tolerated by families⁽²¹⁾. Currently, many providers initiate early onset CIC for MMC patients with the potential for neurogenic bladder, assuring the bladder can adequately empty and

the urinary tract and kidneys do not appear to be exposed to high pressure^(20,21).

Altogether, this study suggests that early onset CIC therapy decreases the number of PIR > 1 cases and abnormal NPI in children with myelomeningocele.

Presumably, this may have a role in decreasing the number of aggravating cases requiring complex bladder augmentation procedures, reducing the severity of upper tract deterioration, and protecting upper tract function among myelomeningocele patients with neurogenic bladder and imminent urinary concentration defects. This study has several limitations that may have influenced the results. First, we did not obtain data in a healthy control group. The small sample size decreases statistical power, and the relatively short observation duration of this study may have been insufficient to assess differences between the groups. Obviously, a large clinical trial is required to confirm our findings.

CONCLUSIONS

In conclusion, early onset CIC is more effective than late-onset CIC in preserving or impeding deterioration of the urinary concentrating ability of kidneys in myelomeningocele patients. Further studies are absolutely necessary to evaluate the long-term safety and clinical effect of early onset CIC on urinary concentration defects and presumably the final outcome of a neurogenic bladder of MMC patients.

CONFLICT ON INTEREST

The authors declare that they have no conflict of interest.

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