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Anocutaneous Reflex Revisited: How Valuable Is Its Determination in Children with Spina Bifida? A Descriptive Study in A Cohort of 217 Patients

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ABSTRACT

AIM: To determine the clinical value of anocutaneous reflex (AR) in children with neurogenic bladder due to spina bifida (SB).

MATERIAL and METHODS: Patients who were diagnosed with SB were prospectively evaluated; moreover, AR and bulbocavernous reflex were examined. Patients were divided into those with and without AR. Age, gender, diagnosis, ventriculoperitoneal shunt presence, symptomatic urinary tract infections, leg movements, clean intermittent catheterization and anticholinergic therapy, lesion level, urodynamic detrusor, and sphincter activity were evaluated. Chi-square test and univariate regression analysis were done. The AR value was evaluated by two by two contingency table.

RESULTS: This study evaluated 217 patients (109 boys and 108 girls). AR was present and absent in 53 and 164 patients, respectively. Anticholinergic therapy was necessary in 37.7% and 23.8% of patients with and without AR (p=0.015), respectively. Patients with AR had higher lesion level (p=0.005), more detrusor overactivity, and less detrusor underactivity (p=0.007). Less detrusor sphincter dyssynergia (DSD) was noted in patients with AR (p=0.029). AR specificity was 83%, and positive predictive value in predicting detrusor overactivity and DSD was 76% and 80, respectively.

CONCLUSION: AR determination is a valuable and simple tool in neurogenic bladder. This report delineates the clinical significance of this reflex and is the largest cohort describing this significance. This simple examination should not be skipped in the initial evaluation and follow-up of these patients.

KEYWORDS: Spina bifida, Neurogenic bladder, Anocutaneous reflex, Children

ABBREVIATIONS: AR: Anocutaneous reflex, **SB:** Spina bifida, **BCR:** Bulbocavernous reflex, **VP:** Ventriculoperitoneal, **UTIs:** Urinary tract infections, **CIC:** Clean intermittent catheterization, **DSD:** Detrusor sphincter dyssynergia, **EMG:** Electromyography, **SBA:** Spina bifida aperta, **SBO:** Spina bifida occulta, **ICCS:** International Children's Continence Society

INTRODUCTION

Neurogenic bladder dysfunction is an important clinical condition with potential life-threatening risks for the upper urinary tract. Mortality may occur in as much as 20% of neonates with this disease in their first year of life if this condition is not properly treated (2). Detailed clinical evaluation is mandatory to identify those patients with these potential risks. Spina bifida (SB) is the most common etiologic factor causing neurogenic bladder dysfunction in children. Spinal cord injury during spinal anomaly development is the

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main reason for this dysfunction and causes damage to the neural pathways controlling bladder function. Afferent and efferent neural circuits for the bladder are conducted by the hypogastric, pelvic, and pudendal nerves. Parasympathetic activity via pelvic plexus controls micturition, and these nerves originate from the S2 to S4 vertebral foramina. Total synergy is necessary between detrusor and urinary sphincter to facilitate complete urine evacuation from the bladder, which is simply sphincter relaxation during detrusor contraction (8).

The anocutaneous reflex (AR) is generated with a similar neural arc necessary for micturition. This reflex can be defined as the external anal sphincter muscle contraction when perianal skin is stimulated by pricking or pinching. Similarly, bulbocavernous reflex (BCR) needs the peripheric neural pathways originating from the S2 to S4 sacral nerve roots. This time stimulation of the glans penis in boys and clitoris in girls causes external anal sphincter contraction, which is detected by concentric needle electromyography (EMG), rectal examination with the finger, or simply inspection. Needle EMG or rectal examination may be disturbing for children; thus, contraction inspection may be more suitable even though its reliability may be limited compared to former methods (5,11).

Limited information was noted in the literature regarding the use of AR and BCR in neurogenic bladder dysfunction due to SB in children. This study aims to identify the clinical value of these reflexes, which has not been delineated yet in this patient group. Also, this study is believed to report the largest patient cohort in the literature on this subject.

MATERIAL and METHODS

This study included patients admitted to the spina bifida center diagnosed with neurogenic bladder dysfunction due to either spina bifida aperta (SBA) or spina bifida occulta (SBO). This prospective, descriptive, and cross-sectional clinical study was approved by the institutional review board. Clinical history was taken during the initial examination, and previous tests (e.g., urinary ultrasonography, scintigraphic examinations, and urodynamic results) were examined. Physical examination with abdominal palpation was routinely done to detect any stool impaction, lumbar inspection to observe the level of the defect, and AR and BCR to examine peripheral sacral neural reflexes from the S2 to S4 nerve roots.

Patients were divided into two groups: those with and without AR. Clinical parameters, age, gender, diagnosis, presence of ventriculoperitoneal (VP) shunt, symptomatic urinary tract infections (UTIs), leg movements, need for clean intermittent catheterization (CIC) and anticholinergic therapy, lesion level during the inspection, and detrusor and sphincter activity during the urodynamic assessment were evaluated. Leg movements were evaluated as partial, present, and absent. Lesion levels were anatomically defined as thoracolumbar, lumbar, and lumbosacral. Detrusor activity was classified as overactive, underactive, and normal, whereas sphincter activity was named as detrusor sphincter dyssynergia (DSD) and normal. DSD was diagnosed: a) when a sphincteric contraction coupled with detrusor contraction, b) in the presence of detrusor underactivity or normal activity when the urinary sphincter was unable to relax to facilitate complete bladder emptying as this observation showed the dyscoordination between detrusor and sphincter.

Urodynamic studies were conducted following the standard protocol recommended by the International Children's Continence Society (ICCS), and ICCS terminology was used to define the results (1,3).

Statistical Analysis

Statistical analyses were done using Statistical Package for Social Sciences, version 22.0 (SPSS Inc., Chicago, IL, USA). Numeric values were given as mean ± standard deviation. Numerical and categorical data were compared using the Pearson chi-square test and univariate regression analysis. The value of the anocutaneous reflex was also evaluated using the two by two contingency table. A p value <0.05 was considered statistically significant.

RESULTS

Between January 2018 and January 2021, 356 patients were evaluated with the diagnosis of SB. Consequently, 217 patients who had full information were included. The remaining patients had either no information on the reflex activity or these reflexes could not be obtained due to patient-related causes. Of the patients, 109 and 108 were boys and girls, respectively. Additionally, 192 and 25 were patients with SBA and SBO, respectively. AR was present and absent in 53 and 164 patients, respectively. The distribution on age, gender, diagnosis, need for VP shunting, CIC, UTIs, and leg movements were insignificant between patient groups (Table I); moreover, BCR was present in 90.5% of patients with AR ($p<0.0001$). However, BCR was present in 12.7% of patients without AR. Anticholinergic therapy was necessary for 37.7% and 23.8% of patients with and without AR, respectively ($p=0.015$). Patients with AR had higher-level lesions ($p=0.005$), more detrusor overactivity, and normal detrusor function with less detrusor underactivity ($p=0.007$). DSD was detected with urodynamics in 80.4% and 92.8% of AR-positive and AR-negative patients, respectively ($p=0.029$; Table I). Univariate logistic regression analysis confirmed the significance of anticholinergic therapy, lesion levels, detrusor activity, and sphincter activity when AR was present. AR specificity was 83%, and positive predictive value was 76% and 80% in predicting detrusor overactivity and DSD, respectively, in this patient group (Tables II and III).

DISCUSSION

SB is a developmental anomaly of neural tube closure and is the main etiological reason for neurogenic bladder dysfunction in children. Neural injury due to the primary closure defect, mechanical and chemical trauma during fetal life, or postnatal conditions (e.g., tethered cord syndrome, infections, or iatrogenic events) cause various voiding abnormalities in these patients. The background of these abnormalities lies in the neural control of the bladder. The detrusor muscle of the bladder is under the control of the autonomic nervous system.

Table I: Study Parameters and Their Comparison According to the Presence of Anocutaneous Reflex

Parameters	AR(+)	AR(-)	p
Age (months)	47.9 ± 36.1	45.6 ± 41.5	0.713
Gender (n)			0.252
Girl	30	78	
Boy	23	86	
Diagnosis (n)			0.152
SBA	44	148	
SBO	9	16	
VP shunt (%)	62.3	57.7	0.714
sUTI (%)	30.2	34.4	0.727
Leg movements (%)			0.537
Partial	31.3	29.6	
Present	54.9	47.7	
Absent	13.7	22.5	
CIC (%)	32.1	42.1	0.196
ATC (%)	37.7	23.8	**0.047**
Level of lesion (%)			**0.005**
Thoracolumbar	34.7	29.5	
Lumbar	57.1	37.2	
Lumbosacral	8.2	33.3	
Detrusor activity (%)			**0.007**
Overactive	76.5	61	
Underactive	5.9	28.5	
Normal	17.6	10.3	
Sphincter activity (%)			**0.029**
DSD	80.4	92.8	
Normal	19.6	7.2	

AR: *Anocutaneous reflex,* ***SBA:*** *Spina bifida aperta,* ***SBO:*** *Spina bifida occulta,* ***VP:*** *Ventriculoperitoneal,* ***sUTI:*** *Symptomatic urinary tract infection,* ***CIC:*** *Clean intermittent catheterization,* ***ATC:*** *Anticholinergic,* ***DSD:*** *Detrusor sphincter dyssynergia.*

Table II: Two by Two Contingency Table of Anocutaneous Reflex in Predicting Detrusor Overactivity in Urodynamics

n	OAD(+)	OAD(-)
AR(+)	39	12
AR(-)	94	60

AR: *Anocutaneous reflex,* ***OAD:*** *Overactive detrusor.*
Sensitivity: 29%. Specificity: 83%. Positive predictive value: 76%. Negative predictive value: 39%.

Table III: Two by Two Contingency Table of Anocutaneous Reflex in Predicting Detrusor Sphincter Dyssynergia in Urodynamics

n	DSD(+)	DSD(-)
AR(+)	41	10
AR(-)	142	11

AR: *Anocutaneous reflex,* ***DSD:*** *Detrusor sphincter dyssynergia.*
Sensitivity: 22%. Specificity: 52%. Positive predictive value: 80%. Negative predictive value: 7%.

During the filling phase, the sympathetic iliohypogastric nerve relaxes detrusor via noradrenaline on beta-3 adrenergic receptors and contracts internal urinary sphincter with alpha-1A adrenergic receptors. Detrusor contraction with parasympathetic acetylcholine happens via the stimulation of muscarinic type 2 and 3 receptors when the bladder is full. This action is mediated by the pelvic nerve originating from the S2 to S4 nuclei of the spinal cord. External urinary sphincteric relaxation is also mandatory during detrusor contraction for total bladder emptying. This action is controlled by Onuf's nucleus located at the S2–S3 sacral level which is under the control of the pontine and suprapontine centers in the brain; thus, the sacral neural arc originating from the S2 to S4 is important in normal micturition in humans (15).

AR (an external anal sphincter contraction during the perianal pricking or pinching) and BCR (also an external anal sphincter contraction during glandular or clitoral stimulation by gentle squeezing) are conveyed by the same S2–S4 sacral spinal roots (7,11). This neural arc should be intact to obtain a proper response from this basic neurological examination. Little information exists in the literature regarding the clinical value of this examination in children with neurogenic bladder dysfunction.

Marshall et al. investigated the significance of AR in predicting the properties of safe bladder characteristics in a group of children with SB. They have observed no change in maximal detrusor pressures and leak point pressures between AR-positive and AR-negative patients. Their conclusion was that the absence of AR was a poor predictor for safe bladder pressures in SB (11). Williams et al. have studied 62 patients with myelomeningocele according to their AR response. No urodynamic difference was observed between higher and lower vertebral levels, and no urodynamic finding can be predicted from the peripheral neurological examination with AR (18). Wyndaele and De Sy similarly evaluated 47 children with myelomeningocele aiming to demonstrate any correlation between AR, BCR, and urodynamic findings. No correlation between clinical examination and urodynamics has been found and detrusor sphincter interaction was concluded to not be evaluated with the determination of AR and BCR, which was similar to the former study (19). These results are in contradiction with the findings of this study. Moreover, Sanders et al. have evaluated the prognostic value of AR for urinary incontinence in 111 children with SB. They observed that AR-positive children were more likely continent with CIC than AR-negative patients, and AR represented a good

prognostic factor for urinary incontinence (13). BCR has been regarded as a valuable tool in investigating neurogenic bladder dysfunction, and the absence of this reflex has been accepted to be a sign of neurologic lesion affecting conus medullaris (4,7,17); however, the presence of this reflex has been advised not to be accepted as a sole indicator for normal function as partial denervation may be present. Concentric needle EMG determination has been proposed for more accurate evaluation and the results can be evaluated as abnormal if the absence has been demonstrated with this method (17).

A significant detrusor overactivity and underactivity was observed in this study when AR was present and absent, respectively. This finding clearly shows that detrusor underactivity should be regarded as a condition with the denervation type of neural injury. More anticholinergic was needed in AR-positive patients which can be explained by increased detrusor overactivity in this patient group. DSD was significantly high in AR-negative patients. This result follows the results of Takahashi et al. which have shown that not only suprasacral lesions but also sacral or peripheral lesions can cause DSD (14). In light of these observations, peripheral neurological examination of sacral neural arc correlated with the urodynamic results in children's neurogenic bladder dysfunction despite some contradictory results in the literature (18,19). AR specificity was 83%, and positive predictive value was 76% and 80% in predicting detrusor overactivity and DSD in this study, respectively. AR was present more frequently in the thoracolumbar and lumbar myelomeningocele patients in this study and its absence was more in lumbosacral lesions. This observation is logical because peripheral nerves may be more preserved in higher spinal cord lesions and these nerves may be more prone for injury when lower lesions exist. BCR was present in 90.5% of AR-positive cases. These two reflexes denote the same neural arc; however, AR was absent in 12.7% of patients with BCR positivity. This may be due to the decreased perineal sensation of some patients although the neural arc was intact. Thus, AR should always be coupled with BCR, and the S2–S4 arc can be evaluated as normal in case of the presence of any reflex of the two. Abdominal contraction may form perianal contraction during this examination, and this issue should not be mixed with reflex activity.

BCR examination has been proposed in various clinical conditions. Cha et al. have used intraoperative monitorization of BCR to avoid neural injury in tethered cord surgery of patients with spinal dysraphism (6,9). They have stated that bladder function may be accepted to be preserved 6 months after untethering surgery if intraoperative BCR is intact (6). Overgoor et al. have proposed a selection protocol for patients undergoing dorsal penile and ilioinguinal nerve anastomosis to restore genital sensation in patients with SB and spinal cord injury. BCR determination has been used to select those patients suitable for this procedure. Their determination may have clinical applications in peripheral neurosurgical interventions because the absence of these reflexes may suggest injury to the sacral reflex arc (10,12,16).

Certain limitations exist in this study. Any study composing urodynamic evaluations may have limitations due to interpreter differences. AR determination was done by finger perianal pricking in this study; thus, concentric needle EMG has been proposed as a more accurate technique for the determination of perianal reflexes in the literature (12). However, needle EMG may not be appropriate in children because it may provoke pain and anxiety, it may be more time-consuming, and the proper setup may not be suitable for routine office practice. The concept of partial innervation exists, which makes neurological evaluation of neurogenic bladder dysfunction in SB difficult. These difficulties can be understood from the data of contingency tables in this study. Many signs and symptoms may overlap; thus, large patient groups may be mandatory to obtain statistical significance for these comparisons.

CONCLUSION

AR determination is a valuable and simple tool in the evaluation of the neurologic status of patients with neurogenic bladder. Urodynamic findings have a significant correlation with this neurological examination. Its presence and absence may be a sign of viability of sacral neural arc and denervation, respectively; however, the concept of partial innervation should be kept in mind while interpreting the results of this examination. AR determination should always be coupled with BCR determination as loss of perianal sensation may give false-negative results. This report delineates the clinical significance of this reflex and is believed to be the largest patient cohort describing its significance. This simple examination should not be skipped in the initial evaluation and follow-up of children with neurogenic bladder dysfunction.

AUTHORSHIP CONTRIBUTION

Study conception and design: KO, AC

Data collection: KO, AC, IA

Analysis and interpretation of results: KO, AC, NG, CC

Draft manuscript preparation: KO, AC, OA

Critical revision of the article: KO, AC, OA

All authors (KO, AC, NG, CC, OA, IA) reviewed the results and approved the final version of the manuscript.

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