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Acute Respiratory Infection with CNS Excitation Symptoms—Consider Theophylline Over-Dosage

Theophylline is an effective broncho-dilator at therapeutic levels but administration of excessive amounts may produce serious toxicity including arrhythmias, seizures and death(1). We conducted a descriptive study during October-December 2002 on children presenting with acute respiratory infection (ARI) and CNS excitation symptoms to find out the cause for CNS excitation symptoms. The age, sex, clinical manifestations, concurrent medical illness and medications were recorded. Serum theophylline level samples were collected as soon as child arrived in emergency department in addition to serum electrolytes, serum calcium, CSF analysis and chest radiograph. Serum theophylline levels were determined by high-performance liquid chromatography (HPLC).

During the study period, a total of 10 children presented with acute respiratory infection and CNS excitation symptoms. 6 cases had evidence of acute theophylline over dosage. The clinical features of these children are given in *Table I*. The most common manifestations were irritability (100%), tremors (83.3%), seizures (66.6%), and vomiting (50%). Tachycardia and tachypnea were seen in all children. Hyperglycemia was seen in 2 (33%) children. All these 6 children had received theophylline preparations by local practitioners before admission. Out of the remaining 4 children, 2 had hypoxic seizures, one had acute CNS infection and one had probable inborn error of metabolism.

The average pediatric serum half-life of theophylline is slightly less than the average adult serum half-life of four hours(2). The usual pediatric range is wide (2 to 12 hours)(3) and varies inversely with age, being quite prolonged in premature neonate. Correlations between serum theophylline levels and drug toxicity in children are scanty. Therapeutic range of serum theophylline levels were between 5-10 µg/mL in neonates and 10-15 µg/mL in infants. In 1993 Powel EC(4) had observed that seizures developed with a theophylline concentration of >50 µg/mL. In our study children had CNS signs even at serum theophylline concentration between

TABLE I–*Clinical Profile and Investigations of Children with LRI and Theophylline Overdosage*

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	%
Age	45 days	50 days	75 days	65 days	90 days	70 days	
Sex	Male	Female	Male	Male	Male	Male	
Irritability	+	+	+	+	+	+	100
Tremors	+	+	-	+	+	+	83
Seizures	+	+	+	+	-	-	67
Vomiting	-	-	+	-	+	+	50
Hyperglycemia	+	-	-	-	-	+	33
S. theophylline level (µg/mL)	16.2	17.7	18.9	26.8	21.6	24	
S. Na, K, Ca	Normal	Normal	Normal	Normal	Normal	Normal	
CSF analysis	Normal	Normal	Normal	Normal	Normal	Normal	
Diagnosis	Bronchiolitis	Bronchiolitis	Pneumonia	Pneumonia	Pneumonia	Pneumonia	
Outcome	Well	Well	Well	Well	Well	Well	

15-30 µg/mL. This may be due to the variation in time interval between theophylline administration and serum sampling of theophylline levels. In our study we could not assess the actual time interval between theophylline administration and serum. sampling for theophylline as all children were treated for ARI with theophylline preparations elsewhere before admission.

Douglas Baker had documented increased predisposition for theophylline toxicity in children with viral respiratory infection(5). 23% of their cases of theophylline toxicity occurred in children with respiratory infection receiving appropriate amount of theophylline. Most of our cases also had probable viral respiratory infection predisposing to theophylline toxicity.

Our observation highlights the possibility of theophylline over dosage in young infants treated for acute respiratory infection presenting with CNS excitation symptoms. Care should be taken to ensure appropriate dosage and frequency when administering theophylline preparations to young infants with respiratory infection.

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Posterior Urethral Valves with Down's Syndrome presenting as Scrotal Urinary Sinuses

A one and a half year old male was brought to us with bilateral anterior scrotal sinuses of one month duration (*Fig. 1*). The sinuses were draining clear urine. The child had earlier presented to another hospital with fever and bilateral inflamed scrotal swellings. This was thought to be a scrotal abscess and was drained. Initially it drained pus but subsequently scrotal sinuses were formed which drained clear urine intermittently. The child was dysmorphic and had features of Downs' syndrome. He was well hydrated and the bladder was not palpable at the time of examination. The parents felt that the child had normal urinary stream. There was no history of antenatal oligohydramnios. Biochemical renal functions were normal. Ultrasound examination of the urinary tract did not reveal any abnormality. Micturating cysto-urethrogram showed a dilated posterior urethra suggestive of posterior urethral valves. Cystoscopy showed a hugely dilated posterior urethra. Large openings of the ejaculatory ducts were seen opening above the semilunar valves located below the Veru in the posterior urethra. Trans-urethral fulguration of valves was done at 5,7 and 12 O'clock position. The scrotal sinuses healed in a weeks' time and the child is well and having good urinary stream after four years. His biochemical renal functions are normal. However there is mental retardation due to Down's syndrome.

Posterior urethral valves (PUV) present with varying severity and grades of obstruction to the urinary tract. This unusual presentation of PUV as non healing scrotal sinuses after epididymo-orchitis has not been reported earlier. Association of PUV with Down's syndrome is also rare though reported(1). Epididymo-orchitis is caused by retrograde flow of infected urine through the ejaculatory ducts. The mechanism of retrograde flow of urinary stream into the testes may be explained as follows. The severe

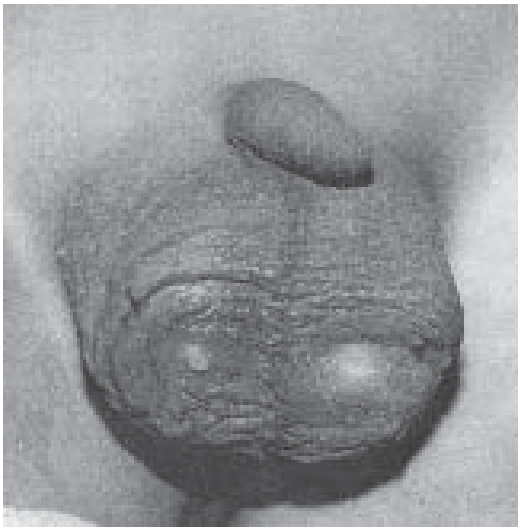

Fig. 1. Uninary leak from scrotal sinus.