



**PEDIATRIC STAGGERED PARACETAMOL OVERDOSE WITH
FULMINANT HEPATORENAL SYNDROME AND BILATERAL
RENAL CALCULI- MANAGEMENT CHALLENGES**

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<p>Article Info <i>Received 25/05/2014</i> <i>Revised 19/06/2014</i> <i>Accepted 22/06/2014</i></p> <p>Key words: Adolescent, staggered overdose, Paracetamol, Hepatorenal syndrome, Urinary tract infection, Renal stones, ESWL, Peritoneal dialysis.</p>	<p>ABSTRACT We report a case of staggered paracetamol overdose secondary to calculation of estimated body weight from a formula rather than the actual body weight in a 12-year-old boy who developed potentially lethal severe fulminant form of hepatorenal shut down. This not only required several days of intensive care treatment but the course was complicated by bilateral renal stones and the liver function was quickly returning back to normal but his renal function was lingering way behind. The possibility of reflux anuria led to further investigations and interventional procedures during his multiple organ failure period. Bilateral staged double J stent insertion followed later by extracorporeal shock wave lithotripsy (ESWL) produced therapeutic effects and complete recovery. Adolescent iatrogenic staggered paracetamol overdose causing secondary potentially lethal hepatorenal syndrome and causing confusion with reflux urolithiasis related anuria is rare. We report the first such rare case presenting as unintentional iatrogenic pharmacotoxicity who responded well to treatment with complete recovery.</p>
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INTRODUCTION

Staggered paracetamol overdose in an unintentional iatrogenic form is uncommon in children and adolescents. The unintended staggered overdose pharmacotoxicity of short duration in most case is benign, short lasting and self-limiting [1-3]. We wish to report an unusual case of adolescent unintended iatrogenic staggered overdose that presented to us with fulminant hepatorenal failure requiring intensive care admissions and several other interventions before successful outcome.

Case report

A 12-year-old boy had complex medical history with special needs, severe arthrogyphosis, learning difficulties, kyphoscoliosis, difficult venous and endotracheal access, fed via gastrostomy and was wheelchair bound. He attended pediatric accident and emergency department with upper respiratory tract infection, tonsillitis and gastritis and was given oral co-amoxiclav and paracetamol calculated on expected weight by formula. He presented after 1 week with poor intake, oliguria,



constipation, overflow soiling and dysuria. He was tender in the suprapubic area and there was evidence of fecal loading in the rectosigmoid area. There was no renal angle tenderness, he was afebrile and vital signs were all stable.

The urine dipstick showed bilirubin 2+, ketone 4+, RBC 3+, protein 3+, pH 6.0, and nitrites were positive. Urine culture did not grow any organisms. All blood tests on the day of admission, and two days later, were within normal limits. Plain x-ray abdomen and chest were normal. Constipation responded to phosphate enema in the accident and emergency department and he opened bowels satisfactorily. As oral intake was poor he was admitted to monitor adequate input and output under medical team.

He had ongoing abdominal pain and as he had suspicion of a urinary tract infection he underwent an ultrasound scan (USS) of his abdomen. USS showed two large calculi within the calyces of the right kidney without any evidence of hydronephrosis. Largest of the calculi measured over 1 cm in length. No distal ureteral dilatation was seen and the bladder contained small amount of urine. CT KUB showed several calculi on the right side in the upper, mid and lower pole and a small calculus in the lower pole of left kidney measuring less than 1 cm. There was no hydronephrosis. On the following day, patient had sudden deterioration of his consciousness. He suddenly deteriorated with confusion, low Glasgow coma scale, respiratory infection, hepatic failure and hepatic encephalopathy secondary to paracetamol, hepato-renal syndrome, renal failure and had no urine output for several hours. He was transferred to pediatric intensive care unit, intubated and ventilated. The patient was found to have staggered overdose of paracetamol as his actual weight was half the calculated weight. He had fulminant hepatic encephalopathy with anuria.

The blood and urine cultures were all negative. Full blood count, serum electrolytes and C - reactive protein were normal. The paracetamol levels were very high at 52 mg/L, ammonia 110 mg/L, urea 15 mmol/L and creatinine 147 mmol/L. Liver function showed bilirubin 27

mmol/L, ALP 195 IU/L, AST 2543 IU/L, ALT 7725 IU/L, GGT 374 IU/L, LDH 1956 IU/L, PT 33.2, APTT 41.6 and fibrinogen 1 gm/L.

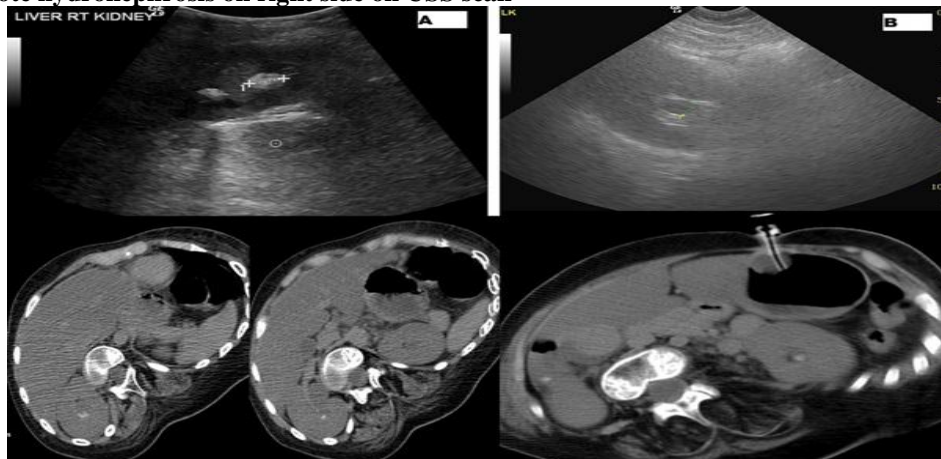
Abdominal ultrasound and CT scan showed bilateral renal stones with right sided hydronephrosis (Fig 1). He improved with liver failure on treatment but renal function did not pick up. So he underwent staged procedures of peritoneal dialysis catheter insertion, cystoscopy, retrograde studies and bilateral JJ stent insertions and he gradually improved to normal.

Initially it was thought that he had urinary tract infection or respiratory tract infection leading to septicemia and multiple organ failure. Actually he did not grow any organisms from the urine, blood, line or any surface skin swabs, had viral upper respiratory tract infection and in retrospect his deterioration was solely due to gradual staggered dose related hepatic and renal failure leading to coma and had no proven respiratory or urinary infection.

His paracetamol toxicity, encephalopathy, respiratory tract infection and hepatic failure started recovering fast but patient had no urine output. He therefore underwent cystourethroscopy and retrograde studies on the right side which did not reveal any stone or obstruction on either side and there was no hydronephrosis. He had an abdominal radiograph later on which revealed the contrast in the right ureter was seen throughout its full length, so urinary flow impairment at vesicoureteral junction was suspected. He, therefore, underwent cystourethroscopy and bilateral insertion of JJ stents uneventfully. He then started having polyuric phase of recovery of his renal failure. He was now transferred back to the main ward but has still high output polyuric phase and needed supplementary intravenous fluids to maintain the fluid balance.

Subsequently he underwent lithotripsy for bilateral renal stones uneventfully and JJ stents were removed. At 1 year follow up he was well, asymptomatic and had no stones.

Fig. 1 Abdominal USS and CT scan showing A. Right sided multiple renal stones biggest being 10 mm and B. solitary left renal stone. Note hydronephrosis on right side on USS scan



DISCUSSION

Paracetamol is the commonest accidental self-ingested and iatrogenic single or staggered overdose drug in the UK¹. Adolescent paracetamol overdose is usually accidental or suicidal and iatrogenic form is very rare. Staggered unintentional iatrogenic overdose due to formulaic use in the outpatients or in the accident and emergency departments is usually a short term measure as in an inpatient as normally the patient will be actually weighed in the ward. However, in outpatients or accident and emergency departments were patients with simple infections or inflammations are discharged home, utmost care should be exercised in switching them to actual weight before they leave the department otherwise seemingly minor error or prescription and administration can prove fatal with associated medicolegal implications.

Calculation of patient weight using formulas in pediatric patients by medical or nursing staff is often inaccurate and leads to prescribing errors both in the calculation of the toxic dose of drugs ingested by patients and the dose of drugs administered in treatment and actual weight should be taken [2]. The estimated weight and not actual weight is being used in A & E, ITU and emergency setting quite often based on formula and should be converted to actual measured weight soon otherwise it leads to staggered overdose due to this error and not only it can cost money but at times the life of the patient. It is quite a common and accepted practice to use estimated formulaic body weight in accident and emergency department, intensive care unit or high dependency unit setting and even advanced pediatric life support manual allows it for the first dose but then the key message has to go across that it should be converted to actual weight for the next dose which has not happened and all of us has to pay a heavy price for this seemingly simple rule to be overlooked!

Staggered overdose is very dangerous and should start treatment immediately no matter what the blood levels of the paracetamol are as the toxicity is cumulative. However, our patient was later admitted to the ward and before he could be adjusted to his actual weight related dose; he went into hepatic encephalopathy followed by renal failure making the management decisions and treatment algorithms more difficult and challenging. Staggered overdose is a very serious condition as opposed to a single overdose and therefore we should start treating irrespective of the blood levels. Staggered overdose is altogether a different entity and potentially a life threatening event as opposed to single overdose in which repair mechanisms will help recover patient soon and is relatively straight forward to diagnose. Treatment is only required if the drug levels are high enough to require

treatment while in staggered doses the drug levels are immaterial and treatment is started straight as the repeated overdoses would have done multiple damages and treatment should be started even before the drug levels are available due to this reason. This is the key message given to all accident & emergency department junior doctors at all time but has not been widely known to others. Renal involvement in children with developmental disabilities is very common and should be suspected for early management [3]. Urinary tract stasis, sepsis and stone formation is common and they do require antibiotics and analgesic anti-inflammatory medications to salvage the renal function. When the hepatic function was quickly returning the anuria was thought to be due to obstruction on one side and reflux anuria without obstruction is possible [4]. Moreover, the problem of reflux anuria requires bilateral stenting in a setting of hepatorenal shut down and coagulation abnormalities. The risks involved were out of proportion but when liver function was recovering we have to give a benefit of doubt and he actually recovered.

To the best of our knowledge, this is the first case of acute severe adolescent staggered unintentional iatrogenic paracetamol overdose which led to hepatorenal shut down requiring staged management with peritoneal dialysis catheter insertion, cystoscopy and insertion of bilateral double J stent insertion followed later by ESWL for bilateral renal stones with successful recovery.

CONCLUSION

Adolescent iatrogenic unintentional staggered paracetamol overdose leading to potentially lethal and severe hepatorenal failure requiring intensive care treatment and several other interventions is rare. Calculated weight for single emergency dose should be changed over to actual weight dose whenever possible and it is easy to miss in a patient with learning difficulty and being wheelchair bound in an accident and emergency department setting with no safety netting at home to correct it. Staggered overdose is more dangerous than single overdose and should be immediately treated irrespective of serum drug levels as opposed to single overdose. It may lead to life threatening fulminant hepatic encephalopathy. If patient is predisposed to renal problems, hepatorenal syndrome may confuse the management decisions considering both possibilities and needs to address both issues together and separately. Physically / mentally challenged child is more susceptible to urinary tract infections and renal stone formation and if detected early can be treated with antibiotics and lithotripsy successfully without the need for percutaneous lithotripsy or an open operation.

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