CASE REPORT

# Ibuprofen-related renal tubular acidosis in pregnancy

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**Summary:** Ibuprofen-related renal tubular acidosis (RTA) has not been previously described in pregnancy but its occurrence outside of pregnancy is being increasingly described. In this case, a 34-year-old woman presented in the third trimester of pregnancy with Type 1 or distal RTA related to ibuprofen and codeine abuse. It was complicated by acute on chronic renal dysfunction and hypokalemia. Delivery at 37 weeks gestation due to concerns of evolving preeclampsia resulted in the birth of a healthy neonate. RTA and hypokalemia were remediated and ibuprofen and codeine abuse ceased. Some renal dysfunction however continued. Thorough and repeated history taking as well as vigilance for this condition is suggested.

**Keywords:** nephrology, maternal-fetal medicine, drugs (medication), clinical pharmacology

## INTRODUCTION

Hypokalemic renal tubular acidosis (RTA) has been increasingly reported as a complication of ibuprofen abuse[1–3] with several significant case series being reported recently.[4,5] While greater awareness of this particular complication is increasing, its incidence and effects in pregnancy have not been reported. Here we present such a case, which has resulted in the birth of a healthy neonate and short-term correction of both RTA and ibuprofen abuse although renal dysfunction has persisted.

## CASE REPORT

SB is a 34-year-old woman who presented to a secondary centre with nausea, emesis, and diarrhoea at 36 weeks gestation (gravida 3, para 2). This was associated with acute renal dysfunction, hypokalemic hyperchloremic metabolic acidosis and normal serum anion gap (Table 1). Serum bicarbonate is known to physiologically decrease in pregnancy;[6–8] however, hyperchloraemic metabolic acidosis in this patient may have been present since at least 16 weeks gestation. A urinary protein:creatinine ratio was 79 mg/mmol (pregnancy reference range <30 mg/mmol), with no dysmorphic red blood cells, casts or eosinophils. Glycosuria, a potential marker of proximal tubular function, was absent throughout. Distal tubular function was impaired as shown by the consistent urinary pH of 5.5 (reference range pH 4.5–8, <5.3 with acidosis) and positive urinary anion gap (6 mmol/L). The interpretation of these findings was of Type 1 or distal RTA.

On examination, SB was normotensive (BP 120/70), tachycardic (HR 100) in sinus rhythm and clinically mildly hypovolemic. There were no clinical signs of preeclampsia (Table 2).

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Her history was of chronic hepatitis C virus infection, past hepatitis B virus infection, intravenous drug use and subsequent methadone therapy. The previous pregnancies had been 13 years and 7 years prior with a different partner, and had both resulted in term spontaneous vaginal deliveries with no antenatal or postnatal complications.

Initial management on presentation in this pregnancy was with intravenous electrolyte replacement and fluid rehydration. Oral sustained release potassium chloride 1200 mg twice daily was commenced and continued throughout admission. This successfully corrected her hypokalemia; however, the patient was dependent on ongoing oral potassium supplementation, her metabolic acidosis did not significantly improve, and renal function did not return to baseline. At the same time pitting oedema to the calves became apparent, systolic blood pressure rose to 140 mmHg and proteinuria increased (protein:creatinine ratio 124 mg/mmol).

Additional history uncovered previously undisclosed ibuprofen/codeine abuse. The patient had been consuming between 30 and 90 tablets of ibuprofen 200 mg/codeine phosphate 12.8 mg per day for the previous six years, since ceasing methadone therapy several months after the birth of her second child. This had continued throughout this pregnancy until 36 weeks and four days gestation. Consensual urinary drug screening detected benzodiazepines, cannabis metabolites, amphetamine-like substances, methadone and opiates. Similar findings of polysubstance ingestion have been previously reported in the context of salicylate-related acid-base abnormalities.[9] None of these substances, however, have a reported significant association with RTA.[10,11] Glue sniffing was denied, excluding toluene exposure. The patient was advised to cease all ibuprofen/codeine use at this time. Methadone therapy to prevent opioid withdrawal was re-instituted.

Over the subsequent week, SB's hyperchloremic metabolic acidosis significantly improved and potassium requirement decreased. The patient underwent induction at 37 weeks

Table 1 **Markers of renal function**

| | Baseline (10 years ago) | 3 weeks pre-conception | 8 weeks gestation | 11 weeks gestation | 16 weeks gestation | 36 weeks gestation (presentation) | 36 weeks +1 day gestation | 36 weeks +2 days gestation | 36 weeks +3 days gestation | 36 weeks +4 days gestation | 36 weeks +5 days gestation | 36 weeks +6 days gestation | 37 weeks gestation (delivery) | 1/7 post delivery | 2/7 post delivery | 3/7 post delivery | 4/7 post delivery | D/C (5/7 post delivery) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Creatinine (umol/L) | 70 | 92 | 90 | 112 | 99 | 144 | 125 | 118 | 116 | 119 | 113 | 120 | 121 | 119 | 121 | 134 | 121 | 110 |
| Urea (mmol/L) | 4.2 | 6.6 | 5.2 | 5.7 | 6.6 | 4.0 | 3.4 | 2.5 | 1.8 | 1.3 | 1.8 | 2.2 | 2.9 | 2.8 | 2.5 | 2.8 | 2.8 | 3.4 |
| eGFR (mL/minute) | >90 | 61 | 62 | 48 | 56 | 36 | 43 | 45 | 46 | 45 | 48 | 45 | 44 | 45 | 44 | 39 | 44 | 49 |
| $K^+$ (mmol/L) | 4.1 | 3.4 | 3.4 | 3.4 | 3.3 | 2.4 | 3.1 | 3.2 | 3.1 | 4.1 | 3.8 | 3.9 | 4.3 | 4.0 | 3.8 | 3.5 | 3.4 | 3.9 |
| $HCO_3$ (mmol/L) | 25 | 18 | 21 | 19 | 17 | 11 | 14 | 12 | 11 | 14 | 14 | 15 | 14 | 15 | 15 | 16 | 18 | 19 |
| Cl (mmol/L) | 101 | 109 | 106 | 109 | 114 | 111 | 119 | 119 | 120 | 116 | 117 | 114 | 113 | 112 | 111 | 112 | 111 | 111 |
| Urine protein: creatinine (mg/mmol) | | | | | | 79 | | 113 | 124 | | | | 144 | | | | | |

eGFR, estimated glomerular filtration rate per 1.73 $m^2$ (MDRD Equation)

Table 2 **Diagnostic matrix for preeclampsia versus renal tubular acidosis**

| | For diagnosis on presentation | Against diagnosis on presentation |
|---|---|---|
| Preeclampsia | Urine protein:creatinine >30<br>Acute kidney injury | Normal blood pressure<br>Normal platelet count<br>Normal liver function tests<br>Normal neurological examination |
| Renal tubular acidosis | Acidosis (lower than expected serum bicarbonate)<br>Hyperchloraemia<br>Normal serum anion gap<br>Hypokalemia<br>Acute kidney injury<br>*– proteinuria can be associated with this* | Diarrhoea<br>Emesis |

gestation due to concerns of preeclampsia developing (Figure 1), followed by vaginal delivery of a healthy neonate. There were no further complications for either mother or child and both were discharged five days postpartum. On delivery, the neonate weighted 2500 g and was reviewed by a paediatrician. Antenatal concerns of premature neonatal ductus arteriosus closure,[12,13] haemorrhage,[14] renal dysfunction[15,16] and opioid withdrawal did not eventuate. SB's renal function stabilized but did not fully return to baseline.

## DISCUSSION

This is the first reported case of ibuprofen abuse-related hypokalemic RTA and renal dysfunction occurring in pregnancy and highlights the importance of a thorough and repeated history-taking when clinical progress and diagnoses appear incongruent. Whether ibuprofen abuse and hypokalemia RTA results in other significant neonatal or antenatal complications is not known.

### DECLARATIONS

None to declare. The patient has provided informed consent for publication.

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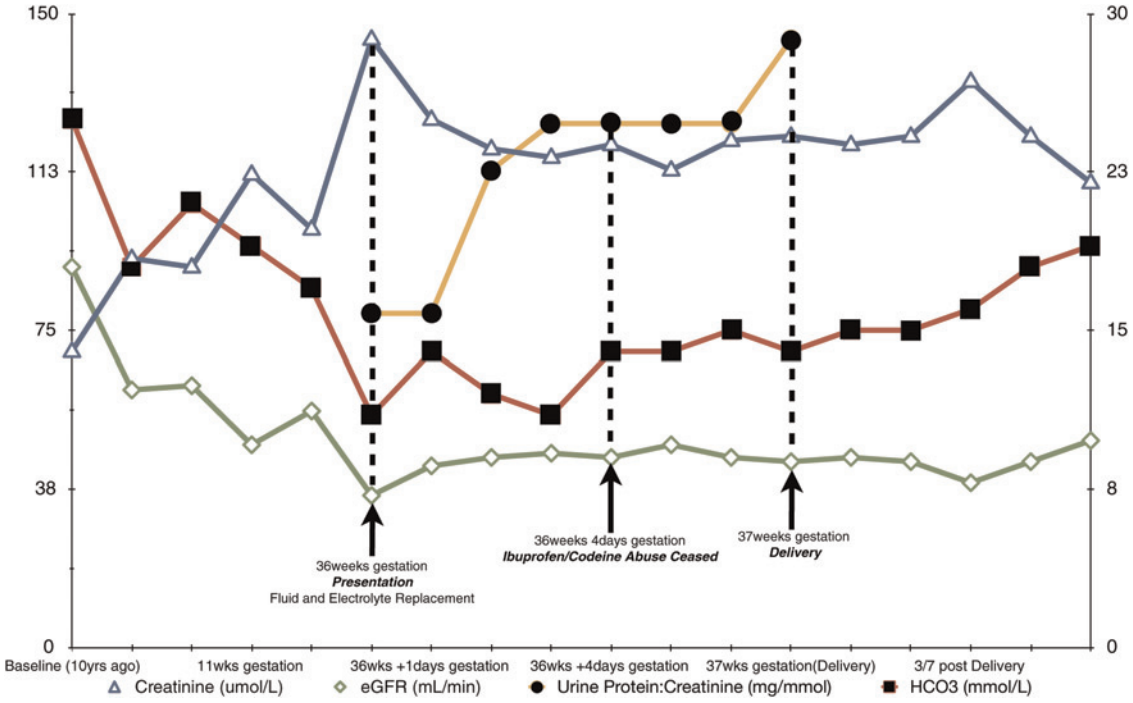


Figure 1 **Creatinine, estimated glomerular filtration rate, urine protein:creatinine and $HCO_3$ relationships**


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