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ORIGINAL ARTICLE

Time to fluid administration in paediatric diabetic ketoacidosis

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Background

Diabetic ketoacidosis is a medical emergency and merits prompt fluid therapy. Our aim is to evaluate whether fluids are started within one hour of presentation to hospital for children with diabetic ketoacidosis.

Methods

This is a retrospective study involving patients with diabetic ketoacidosis presenting to paediatric emergency department at Mater Dei Hospital between 2008 to 2017. Diabetic ketoacidosis was defined as per local protocol. Times at hospital presentation, medical visits in emergency department and wards and at start of fluid administration were recorded. Clinical and biochemical parameters for patients with start of fluids within one hour (Immediate Fluid Treatment) were compared to those with delayed fluid treatment; T-test was used for significance.

Results

Sixty episodes were included, with 34 males (60.7%) and mean age 7.42 years. Fluids were started at a median of 95.5 (IQR: 70.5 - 128.3) minutes following presentation and were mainly started in the admitting ward. Only 18% of patients received fluids within one hour of presentation (n = 11). Bicarbonate and pH levels were significantly lower in these patients, at 7.87 vs 11.48 mmol/l (p = 0.027) and 7.07 vs 7.21 (p = 0.002) respectively, when compared to those with delayed fluid treatment. Significantly more patients in the immediate fluid treatment group needed fluid boluses (73% vs 29%, p = 0.0006).

Conclusion

Fluids were delayed more than one hour from presentation in most paediatric diabetic ketoacidosis patients. Consideration should be given to commencing fluids in the paediatric emergency department or expediting their ward transfer, to decrease this delay in starting treatment.

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Diabetic ketoacidosis (DKA) is the leading cause of death in children under 15 years of age with type 1 diabetes mellitus[1] and is associated with a mortality rate of about 0.25%.[2] It is a medical emergency, with the initial treatment priority being the restoration of extracellular fluid volume through the intravenous administration of 0.9% sodium chloride solution, followed by intravenous insulin. However there may be considerable time lags between time of presentation and time to starting fluids, which may lead to worsening of the patients' condition prior to starting treatment.

AIM

Our aim is to evaluate whether fluids are started within a target time of one hour of presentation to hospital for children with DKA. Our proposed outcome is a more efficient pathway to starting fluid treatment for paediatric patients with diabetic ketoacidosis if indicated.

METHODOLOGY

This is a retrospective study targeting children presenting to the paediatric emergency department (PED) at Mater Dei Hospital in Malta and diagnosed with DKA over a ten year period, between 2008 to 2017. The patients were identified from the paediatric endocrinology service records. Written authorisation was obtained from the chairperson of the Department of Child and Adolescent Health and the Data Protection Office at Mater Dei Hospital to access the relevant data. Additional ethics approval was not deemed necessary since this is a retrospective observational study and did not involve any patient contact or interventions.

The biochemical criteria for diagnosis of DKA were defined as per local protocol[3] namely:

1. Blood glucose > 11 mmol/l (capillary or venous sample)
2. Metabolic acidosis - one or both of:
    - Venous pH < 7.3
    - Serum bicarbonate < 15 mmol/l
1. Ketosis - either of:
    - Ketonaemia (capillary blood ß-hydroxybutyrate > 3.0 mmol/l)
    - Ketonuria (≥ 2+ or ≥ moderate)

Blood ketone monitors were not available during the study period, so only urinary ketones were used as diagnostic criteria.

The paediatric DKA protocol was updated in 2016[3] based on recommendations from the 2015 paediatric DKA guidelines for the UK National Institute for Health and Care Excellence[4] and the British Society of Paediatric Endocrinology and Diabetes.[5] The main change was an overall decrease in the amount of total fluids, with restriction of fluid boluses, a change in the calculation of maintenance fluids and a change in calculating fluid deficit depending on venous pH levels rather than based on clinical examination findings. There were no changes in diagnostic criteria or initial choice of fluid (0.9% saline).

All paediatric patients who were admitted via the PED and diagnosed with DKA were included in the study. Of note, the maximum admitting age to paediatric wards was increased from 14 to 16 years of age in January 2012. Patients receiving fluids elsewhere prior to presentation, those admitted to other hospitals and those not fitting the above criteria for diagnosis of DKA were excluded.

The 'time to fluids' was defined as the time from presentation to hospital, i.e. registration at the emergency department, to the time intravenous fluids were first administered, namely the initial time documented on the DKA fluid chart or, alternatively, the time at which a fluid bolus was prescribed, in the case of those patients needing fluid boluses.

Patients in whom fluids were started within 60 minutes from presentation were described as the 'Immediate Fluid Treatment' group (IFT) while those in whom fluids were delayed longer than 60 minutes from presentation were designated as the 'Delayed Fluid Treatment' group (DFT). Potential factors affecting time to fluids between the two groups were assessed, with T-test being used for significance.

The time to fluids was also broken down by time of presentation, time at triage, time at PED medical visit and time at ward medical visit, in order to enable analysis of factors contributing to the delay.

RESULTS

A total of 65 episodes of DKA were identified in 60 patients. 5 episodes were excluded because of admission to another hospital (n = 3), direct ward admission and bypassing PED (n = 1) or intravenous fluid administration elsewhere prior to presentation (n = 1). Therefore 60 episodes of DKA in 56 patients

were included in the analysis, with 3 patients having more than 1 episode of DKA.

Median age at presentation was 7.96 (Interquartile Range (IQR): 3.45 - 10.82) years and 60.7% (n = 34) were males. The change in maximum admitting age to paediatric wards from 14 to 16 years, in January 2012, led to a significant increase in the mean age of patients with DKA, from 6.56 years to 9.13 years (p = 0.02). DKA presentations peaked during the month of July. Peak presentation time occurred during late afternoon, with 33.3% of patients (n = 20) presenting between 16:01 to 20:00 hours. Only 12% of episodes (n = 7) occurred in known diabetics and none of these patients were on pump treatment.

78% of patients (n = 47) had a duration of symptoms lasting more than 48 hours before presentation, with 6 patients presenting within the first 12 hours, 5 patients with symptom duration between 13 to 24 hours, and 2 patients with symptom onset 25 to 48 hours prior to presentation.

Less than half of the patients referred to hospital were documented as having DKA on the referral ticket (18/38). Overall the majority of patients were diagnosed as having DKA during the PED medical visit (56.6%; n = 34). For the remaining patients, DKA diagnosis was first documented at reception (n = 7); at triage (n = 4) and during the ward medical visit (n = 15).

Mean values (± SD) for capillary blood glucose, venous pH and bicarbonate at diagnosis were 28.48 (± 6.75) mmol/l, 7.17 (± 0.12) and 10.59 (± 4.21) mmol/l respectively. Urine ketone levels were between 3+ to 4+.

Fluids were started at the PED for 11 patients (18%), with the remaining 49 patients receiving their initial fluids in the admitting ward. In keeping with this, venous access, and the time when the first venous blood gas was taken, was established in the ward for 72% of patients (n = 43). This is in contrast to capillary blood glucose which was checked in PED for 88% of patients (n = 53).

A significantly higher proportion of patients for whom fluids were started in the PED needed fluid boluses (8/11) when compared to those for whom fluids were started on the wards (14/49), with p = 0.006.

Fluids were started at a median of 95.5 (IQR: 70.5 - 128.3) minutes following initial presentation to the PED Fluid administration occurred within the one hour target time only in 12 DKA episodes (20%). There were no significant differences in time to fluids when comparing known diabetics (7/60) to the other patients (mean time 99.4 vs 105 minutes; p = 0.72) and for patients referred with DKA to those not referred with DKA (mean time 97.23 vs 107.32 minutes; p = 0.53).

There was no significant difference for clinical parameters between the IFT and the DFT groups, as shown in Table 1. These included age, heart rate, respiratory rate, GCS, capillary refill time (CRT), systolic blood pressure (BP) and diastolic BP There was variable documentation of parameters, with heart rate being documented in practically all patients (59/60) and Glasgow Coma Scale being the least documented (29/60). The only difference noted was the respiratory rate, which was higher in the IFT group, but the difference did not reach statistical significance.

When looking at DKA diagnostic criteria for the two groups, there was no significant change in capillary blood glucose, but pH and bicarbonate levels were significantly lower in the IFT group, as documented in Table 1. This is reflected in the significantly higher number of patients in the IFT group who needed fluid

Table 1 *Clinical and biochemical parameters for IFT and DFT groups*

Parameter or Result	IFT Group (mean values)	DFT Group (mean values)	*p*-value
Age (years)	6.58	8.26	0.22
Heart Rate (beats/min)	128	120	0.27
CRT (seconds)	2.7	2.4	0.50
Respiratory Rate (breaths/min)	45	27	0.14
GCS	13	14	0.26
Systolic BP (mmHg)	119	115	0.73
Diastolic BP (mmHg)	69	72	0.55
Capillary blood glucose (mmol/l)	30.5	27.7	0.16
pH	7.07	7.21	*0.002*
Bicarbonate (mmol/l)	7.87	11.48	*0.027*

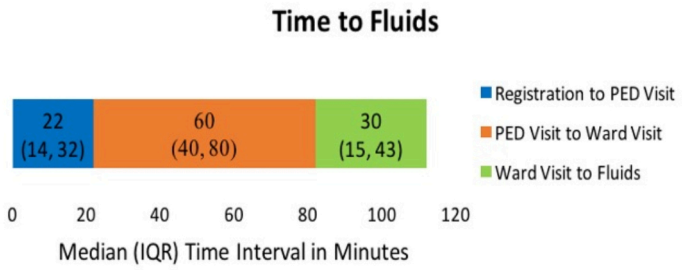

Figure 1 *Breakdown of time lag from presentation to start of fluids*

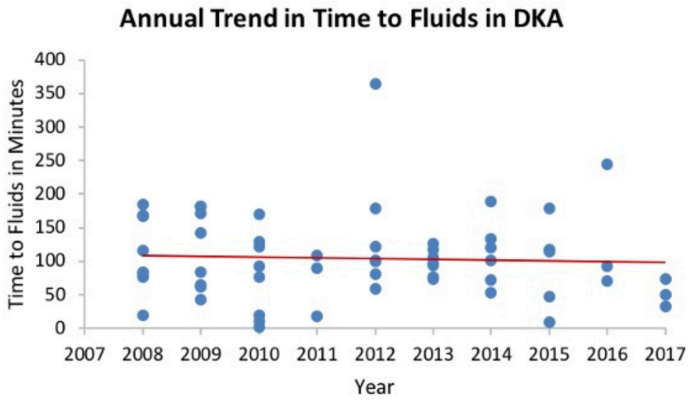

Figure 2 *Annual trend in time to fluids*

boluses when compared to the remaining patients (75% vs 23.9%, $p = 0.0009$).

Figure 1 shows the time delay which is broken down to three different timeframes. The median times from registration to PED visit was 22 (IQR: 14 - 32) minutes, from PED visit to ward visit 60 (IQR: 35 - 75) minutes and from ward visit to start of fluids 30 (IQR: 15 - 43) minutes. The longest delay occurred between PED and ward medical visits, with a median duration of 60 (IQR: 35 - 75) minutes.

The time to fluids remained constant over the ten year study period, as shown in Figure 2.

DISCUSSION

Intravenous fluid replacement should be started as soon as DKA diagnosis is confirmed.[6] There is no standard cut-off time advised for start of fluids in current DKA protocols in children or adults, but historically, a time to fluids of less than 30 minutes[7] or 60 minutes[8-9] in the Emergency Department was one of the standards recommended in the care of DKA.

Our study found a median time to fluids of 95 minutes. Studies involving adult DKA patients, mainly retrospective observational studies, have shown great variation in time to fluids, with one study by Singh et al showing a similar median time to fluids of 80 minutes (range 0 - 330 minutes).[7] However other studies have found that up to 80% of adult DKA patients receive appropriate fluid resuscitation in the initial hour following presentation.[8,10] The most recent study, by Edge et al[11], 2016, which compared treatment of adolescent patients with DKA in adult and paediatric units, found a similar time to fluids for both patient cohorts, with a median time to fluids of 34 (IQR:18 - 78) minutes for paediatric units and a time of 36 (IQR: 15 - 80) minutes for adult units. No other studies looking at time to fluids in paediatric DKA patients were identified.

Our time to fluids remained constant over the ten-year study period and was not impacted by changes in DKA protocol or admission age. The longest delays consistently occurred between the PED and ward medical visit, a time which also incorporates transfer time to the paediatric wards. In fact, most patients in the IFT group had their fluids started in the PED, thus avoiding this major delay to start of fluids. These patients had a higher respiratory rate, in keeping with worse acidosis (as evidenced by significantly lower pH and bicarbonate levels), which might have prompted the earlier venous access, investigations and initiation of fluids.

Venous access was established in the admitting ward for the majority of patients in our study, leading to a delay in the diagnosis of DKA. If venous access is performed at the PED, this would enable earlier diagnosis of DKA. This then raises the question of whether to start fluids at the PED or else expedite patient transfer to inpatient wards, to enable their initial management by the same medical personnel who are involved in their subsequent fluid management. Other potential barriers in our setting may have been the lack of blood ketone testing at the time of this audit and staff factors, with PED being manned by more junior staff than the inpatient wards.

Time to fluid administration has been shown to improve following regular educational sessions. One study by Freudenthal et al[9] showed an overall improvement in the rate of adult DKA patients receiving fluids within 60 minutes of arrival to ED from 58.6% to 74.1% over a four year period, following introduction of annual education sessions for acute medical staff. It is important to include emergency staff in training sessions since they will perform the initial management of these patients.

STRENGTHS AND LIMITATIONS

This is a retrospective observational study, but to our knowledge, we have included all paediatric DKA patients (rather than a representative sample). We also utilised a long time period of 10 years, in order to increase patient numbers.

CONCLUSION

Fluids were delayed more than one hour from presentation in the majority of paediatric patients with DKA. Consideration should be given either to commencing fluids in PED, to decrease this time lag in starting treatment, or else to more efficient transfer of these patients to the inpatient wards.

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