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ORIGINAL ARTICLE

Comparing Sterofundin to 0.9% Sodium Chloride Infusion in Managing Diabetic Ketoacidosis: A Pilot Study

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ABSTRAK

Penggantian cecair adalah rawatan utama untuk kencing manis ketoacidosis (DKA). Pada masa ini pilihan terbaik daripada cecair masih diperdebatkan. 0.9% Normal Saline (NS) yang menyebabkan ketidakseimbangan metabolik dan asidosis metabolik biasanya digunakan. Sterofundin® merupakan kristaloid alternatif yang dianggap mempercepatkan resolusi asidosis. Kelebihan dalam kandungan sterofundin adalah perbezaan kecil besar ion (SID) kepada plasma dan kandungan klorida yang lebih rendah. Objektif utama kajian ini adalah untuk membandingkan kadar resolusi asidosis dalam pesakit DKA antara rawatan dengan 0.9% saline normal dan Sterofundin® dalam 12 jam. Objektif lain adalah untuk membandingkan perbezaan yang signifikan ion (SID),12 jam pelepasan keton darah dan keseimbangan elektrolit antara kedua-dua kumpulan. Kajian ini adalah kajian terbuka dilabel percubaan trial kawalan rawak. Kajian ini dijalankan selama 6 bulan. Saiz sampel sebanyak 18 orang telah diperolehi dan (n = 9) untuk setiap lengan. Perbezaan utama antara kedua-dua kumpulan adalah awal median 2 jam peningkatan tahap pH (NS = +0.006 vs Sterofundin = +0.05, P = 0.063), bagaimanapun tidak ketara. Keton, pengurangan jurang anion, normalisasi bikarbonat, sodium, klorida, urea dan tahap kreatinin gagal menunjukkan sebarang perbezaan yang signifikan antara kedua-dua kumpulan. Dua belas jam paras klorida median kenaikan adalah lebih tinggi dalam kumpulan NS (+11) berbanding dengan kumpulan sterofundin yang (+6). Tidak ada perbezaan antara kematian dan morbiditi. Perbandingan kedua-dua kumpulan cecair, tidak terdapat perbezaan biokimia penting sepanjang rawatan DKA. Ini adalah kajian pilot yang memerlukan trial klinikal yang lebih besar di masa akan datang.

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Kata kunci: jurang anion, diabetic ketoacidoses, keton, ph , saline, sterofundin

ABSTRACT

Fluid replacement is the mainstay treatment for diabetic ketoacidosis (DKA). Currently, the best choice of fluids is still debatable. An amount of 0.9% sodium chloride is commonly used. Sterofundin® is an alternative crystalloid that is assumed to expedite resolution of acidosis. Advantages in sterofundin content being smaller significant ion difference (SID) to plasma and lower chloride content. The main objective of the study was to compare rate of acidosis resolution in DKA patients between treatment with 0.9% normal saline and Sterofundin over 12 hrs. Other objectives were to compare significant ion difference (SID), 12-hr blood ketone clearance and electrolyte balance between the two groups. The study was a prospective open labelled randomized control trial. This study was conducted over 6 months. Sample size of 18 was obtained with 9 for each arm. Main difference between two groups was initial median 2-hr pH level improvement (NS = +0.006 vs. Sterofundin = +0.05, P=0.063), however not being significant. Ketone, anion gap reduction, bicarbonate normalisation, sodium, chloride, urea and creatinine levels failed to show any significant differences between both groups. Twelve-hour median chloride levels increments were higher in the NS group (+11) compared to the sterofundin group (+6). There was no difference between mortality and morbidity. Comparing the two fluid groups, there was no significant biochemical differences during treatment of DKA. This was a pilot study that can initiate further clinical trials.

Keywords: anion gap, diabetic ketoacidosis, ketone, ph, saline, sterofundin

INTRODUCTION

Diabetic ketoacidosis (DKA) is among the most serious acute complications of diabetes. It is diagnosed these criteria are met; elevated capillary blood glucose (> 11 mmol/L), elevated capillary ketones (> 3 mmol/L) or > 2+ positive urine ketones and venous pH < 7.3 and/or bicarbonate < 15 mmol/L. Management principles include initial fluid and potassium replacement, intravenous insulin infusion, intensive monitoring and targeted investigation (Malaysian Clinical Practice Guidelines 2015).

The ideal fluid for managing diabetic ketoacidosis (DKA) is controversial. Following substantial fluid loss due to osmotic diuresis, fluid deficit can be estimated up to 100 ml/kg which is corrected within 24 hrs. Crystalloid 0.9% normal saline (NS) is currently the mainstay therapy for fluid replacement. Fluid replacement regiment for a systolic BP > 90 mmHg is 1000 mL of NS for the 1st hr, another 1000 mL of NS for next 2 hrs and 1000

mL for the remaining 4 hrs (Malaysian Clinical Practice Guidelines 2015).

Efficacy of NS in resolving metabolic acidosis compared to other crystalloids is questionable. High chloride content, low strong ion difference (SID) and high hydrogen ion levels are among factors that can delay metabolic acidosis resolution following normal saline infusion (Yunos et al. 2010; Waters et al. 1999; Waters et al. 2001; Reid et al. 2003; Scheingraber et al. 1999). The effect is compounded when a large amount of normal saline is used in the treatment of DKA. Strong ion difference (SID) is defined as the difference between strong cations (Na, K, Mg, and Ca) and strong anions (Cl- and lactate).

An alternative to normal saline is balanced solution such as sterofundin, ringers lactate, hartmann and plasmalyte. These solutions have electrolyte composition and SID near similar to plasma (Guidet et al. 2010). The likelihood of developing hyperchloraemia is less compared to normal saline. This study was designed to compare the rate of acidosis resolution between normal saline and a balanced solution. Sterofundin as a balanced solution was selected due to its affordability, availability and absence of lactate. It also had the lowest SID (29) and low CO_2 content (1.5/L) compared to other balanced solution (Langer et al. 2014).

MATERIALS AND METHODS

Ethical approval was obtained before conductance of the study (Project Code: FF-2015-128) and registered under the National Medical Research Register (NMRR), allowing the study to be done in the hospital. General objective of this study was to compare rate of acidosis resolution between infusing NS and Sterofundin in DKA patients within 12 hrs. Specific objectives were to measure patient's significant ion difference, blood ketone and electrolytes (sodium, potassium, chloride, magnesium and calcium) in both groups within 12 hrs of treatment.

The study was designed as a prospective open labelled randomized control trial. Sterofundin was used for fluid replacement therapy compared to the standard therapy of NS in DKA patients. The study was conducted over six months from 1st June 2015 to 30th December 2015. Recruitment of patients was made from the initial presentation to the emergency department, after criteria of DKA was met. Patients who were included fulfilled the criteria of DKA according Malaysian Clinical Practice Guidelines which were adapted from Gosmanov et al. (2014). The diagnostic criteria were: capillary blood glucose more than 11 mmol/L, capillary ketones more than 3 mmol/L or urine ketones 2+ and venous pH less than 7.3 and/ or bicarbonate less than 15 mmol/L. Patients who were administered more than 500 ml other intravenous fluids or 50 mL of sodium bicarbonate within 24 hrs, less than 18 yrs of age or complicated with congestive heart failure or end stage renal failure were excluded from this study. Statistical analysis was done using IBM SPSS version 22.0.0

STATISTICAL ANALYSIS

The sample size was calculated using a general purpose statistical software (STATA). The sample size was estimated using a two sample comparison population of n total= 70. Sixty percent of acidosis resolution rate within the 6-12-hr period was expected from the normal saline group in comparison to 80% from sterofundin group. Test Ho: p1 = p2, where p1 was the proportion in population 1 and p2 was the proportion in population 2. Assumptions area were as follows: alpha = 0.0500 (two-sided), power = 0.9000, p1 = 0.6000, p = 0.2000, n2/n = 1.00. Estimated required sample sizes: (n1= 35, n2 = 35). Unfortunately, we did not manage to reach the targeted sample size due to certain limitations. Hence, the study became a pilot study.

TREATMENT

Treatment protocols were adopted from the Joint British Diabetes Societies in Patient Care Group the Management of Ketoacidosis in Adults (Savage et al. 2011) and the Malaysian Clinical Practice Guidelines 2015 (Appendix 1). The study flow diagram was shown in Figure 1 and the DKA monitoring chart was shown in Appendix 2. The crystalloid used was randomizing between 0.9% normal saline and Sterofundin and the timing and blood investigations was modified for the purpose of the study. Randomization was based on the label sealed in a brown envelope attached to the treatment protocol. Adherence to DKA management protocol was monitored by emergency physician on duty. DKA monitoring chart was available to physicians as a guide in blood taking and monitoring.

OUTCOME MEASURES

Venous blood gas (VBG) for pH, Bicarbonate, Base Excess, Capillary and laboratory glucose, Renal profile (RP), Full Blood Count (FBC), Calcium, Albumin, Magnesium, Phosphate were taken during time of diagnosis. Serial blood investigation for VBG, blood ketone and RP was repeated at 2, 4, 8 and 12 hrs. The patient was studied until acidosis resolution was complete.

The mean changes of pH, bicarbonate, blood ketone, SIDs, Anion Gap, Chloride and Sodium was measured over time and compared between the two group using student t-test to measure statistical difference. The protocol and the monitoring chart were identified by research ID. No personal details were available on the forms to protect the privacy and confidentiality. The subject was not given access to personal information and study data. The study data was kept for 5 yrs in online storage solution which was protected by industry standard security. The medical record was kept by the hospital as per hospital protocol.

RESULTS

The study was conducted for six months from 1st June 2015 and 30th December 2015. Data was collected from Hospital Kuala Lumpur and

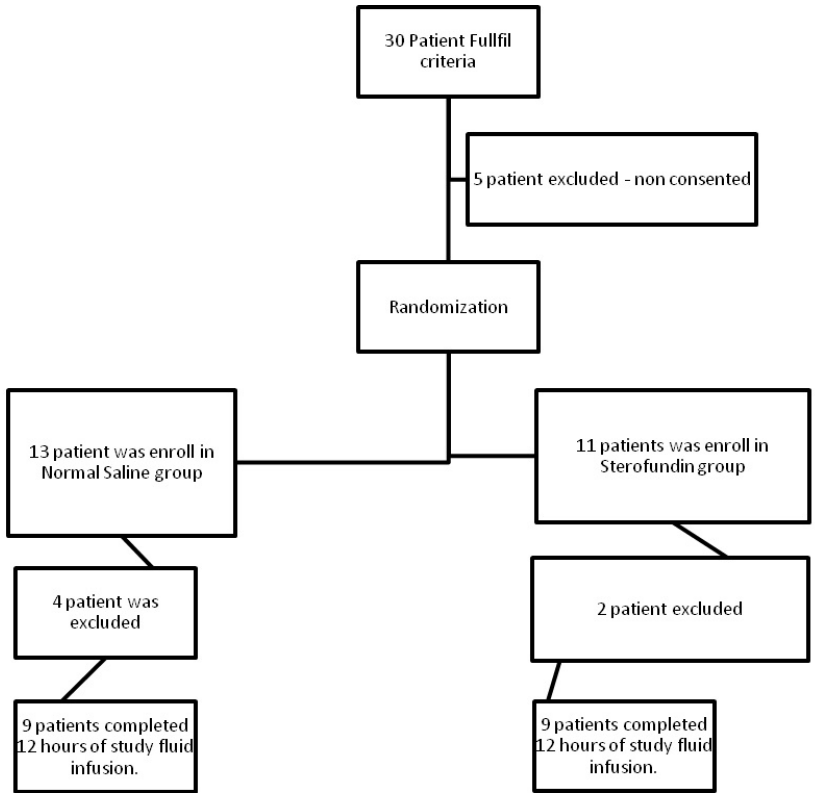

Figure 1: Study flow diagram

Universiti Kebangsaan Malaysia Medical Centre. Thirty patients were eligible for this study. Five patients were excluded because refusal of consent. Seven patients were excluded from the study because of non adherence to the protocol. Only 9 patients were obtained for each group.

DEMOGRAPHICS

The demographic of the patient is shown in Table 1. The samples were homogeneous between the two groups. There was no significant difference between the 2 groups in terms of baseline characteristics and initial blood parameter values. The mean total insulin, fluid and urine output for the 12 hrs were similar between the 2 groups.

THE ACID BASE STATUS AND ELECTROLYTES

The median changes of all blood parameters monitored over 12 hrs were shown in Table 2. The most significant difference between the two groups was pH increment within the first two hrs. Sterofundin showed an impressive median improvement of 0.05, whereas the NS group showed slight fall of 0.01 in median pH. There was no significant difference in SIDs, ketone clearance, anion gap reduction

Table 1: Baseline characteristics and blood parameters

Characteristics	Normal Saline (n=9)	Sterofundin (n=9)	p Value
Age	46.22 (28 – 73)	44.67 (22 -58)	1.000
Sex			
Male	4(44.4)	6 (66.7)	0.317
Female	5(55.6)	3 (33.3)	0.480
Pulse rate	126.3 (98 – 145)	103.89 (70 -144)	0.077
Blood pressure			
SBP	125.9 (96 -158)	123.3 (94 – 150)	0.605
DBP	77.0 (56 – 90)	74.1 (53 – 96)	0.297
Respiratory rate	22.2 (18 -28)	19.9 (16 -24)	0.136
SPO2 (%)	99.00 (98 -100)	99 (95-100)	0.370
GCS	13.7 (3 – 15)	15 (15 -15)	0.730
Random Blood Glucose	29.2 (18.3 -43.0)	28.2 (11.7 – 52.0)	0.796
pH	7.162 (7.000 – 7.243)	7.191 (7.070 – 7.318)	0.340
HCO3	10.6 (6.8 – 16.0)	12.1 (7.9 -17.3)	0.489
Blood Ketone	5.18 (3-7)	6.96 (5-8)	0.019
Na	132.4 (121-142)	131.67 (118 – 144)	1.000
Cl	94.4 (76.0 – 114.0)	96.2 (72.0 -112.0)	0.546
Potassium	4.98 (3.5 – 6.9)	4.58 (3.0 – 6.1)	0.436
Urea	10.2 (6.4 – 20.0)	10.2 (1.2 – 33.9)	0.113
Creatinine	108.3 (28.0 -226.5)	160.7 (54.0 – 385.0)	0.387
Lactate	3.78 (1.40 -8.78)	3.12 (1.00 -7.30)	0.297
WCC	16.9 (7.5 – 33.8)	13.8 (6.4 -28.4)	0.436
Hb	14.5 (11.3 – 18.0)	14.4 (10.0 -16.8)	0.931
Plt	293.1 (160 – 418.0)	277.9 (192.0 – 487.0)	0.666
Ca	2.29 (1.92 – 3.14)	2.23 (1.95 - 3.14)	0.796
Alb	32.89 (22.0 – 48.0)	33.54 (3.9 – 47.0)	0.546
Mg	1.04 (0.70 – 2.54)	0.95 (0.70 – 1.90)	0.863
Phos	1.34 (0.50 – 2.54)	1.09 (0.60 – 1.74)	0.387
Total Insulin (ml)	56.5 (40.0-87.0)	56.00 (18-81.5)	0.370
Total Fluid (ml)	4639.50 (2286 – 7853)	4898.3 (3000 – 6120)	0.888
Total Urine output (ml)	1540.00 (660 -12000)	1150.00 (800 -1750)	0.139
Infection (%)	9/9 (100)	6/9 (66.7)	
Non compliance	0/9 (0)	3/9 (11.1)	

and bicarbonate increment between the two groups over 12 hrs. There was no significant difference in potassium, sodium, urea and creatinine levels for both groups. However, as expected, chloride level in the NS group had an increase in trend compared to the Sterofundin group.

Table 2: Blood parameter changes in 12 hours

Variables	Time points	Normal saline Median (IQR)	Sterofundin Median (IQR)	P value
D in pH	0	0.00 (0-0)	0.00 (0-0)	1.000
	2	-0.006 (-0.343-0.104)	0.050 (-0.343 – 0.104)	0.063
	4	0.063 (-0.127 – 0.166)	0.050 (0.009 – 0.248)	0.436
	8	0.143 (-0.007 – 0.259)	0.143 (0.091 – 0.276)	0.796
	12	0.157 (0.115 – 0.279)	0.192 (0.065 – 0.289)	0.863
D in anion gap	0	0.00 (0-0)	0.00 (0-0)	1.000
	2	-1.50 (-10 – 11)	-4.8 (-17 – 16)	0.258
	4	-12.4 (-20 – 3)	-6.6 (-18 – 13)	0.666
	8	-14.1 (-24 – 7)	-10.2 (-33 – 4)	0.730
	12	- 16.0 (-24 – 3)	-11.7 (-27 – 3)	0.863
D in blood ketone	0	0.00 (0-0)	0.00 (0-0)	1.000
	2	-0.80 (-2 – 3)	-0.60 (-4 - 1)	0.931
	4	-1.80 (-4 – 3)	- 2.50 (-6 - 0)	0.258
	8	-2.30 (-6 - 2)	- 4.00 (-7 - -1)	0.077
	12	-3.70 (- 7 - 0)	-4.70 (-8 - -4)	0.113
D in bicarbonate	0	0.00 (0-0)	0.00 (0-0)	1.000
	2	0.40 (-2 – 4)	1.10 (-3 -4)	0.340
	4	3.30 (1 -12)	2.30 (-4 - 9)	0.730
	8	5.50 (2- 15)	5.70 (2- 10)	0.931
	12	5.10 (3 -15)	8.20 (2- 13)	0.297
Strong ion gap	0	0.00 (0-0)	0.00 (0-0)	1.000
	2	-1.50 (-10 11)	- 4.8 (-17 – 16)	0.258
	4	-12.4 (-20 -3)	-6.60 (-18 -13)	0.666
	8	-14.1 (-24 -7)	-10.2 (-33 -4)	0.730
	12	-16.0 (-24 -3)	-11.7 (-27 -3)	0.863
D in potassium (mmol)	0	0.00 (0-0)	0.00 (0-0)	1.000
	2	-0.3 (12 – 0)	-0.6 (-2 -1)	0.730
	4	-0.6 (-3 -1)	-0.3 (-5 -3)	0.546
	8	-1.0 (-3 -0)	-0.8 (-2 -1)	0.796
	12	-1.2 (-3 -0)	-1.1 (-3 -0)	0.863
D in chloride	0	0.00 (0-0)	0.00 (0-0)	1.000
	2	3.0 (-5 - 15)	6.0 (-5 – 30)	0.546
	4	9.0 (-11 - 23)	3.0 (-7 -31)	0.666
	8	12.0 (-22 - 33)	2.0 (-8 -36)	0.436
	12	11.0 (-10 -26)	6.0 (-7 -43)	0.931
D Sodium	0	0.00 (0-0)	0.00 (0-0)	1.000
	2	1.0 (-1 - 15)	2.0 (0 – 18)	0.436
	4	2.0 (-6 - 14)	1.0 (-1 - 18)	0.931
	8	2.0 (-10 - 22)	1.0 (-4 - 12)	0.489
	12	0.0 (-10 - 21)	3.0 (-3 - 27)	0.222

Table 3: Mortality and morbidity

	Normal Saline	Sterofundin
Mortality (%)	0/9 (0)	1/9 (11.1)
None (%)	9 (100)	8/9 (88.9)
Renal replacement (%)	0/9 (0)	1/9 (11.1)
Pulmonary edema (%)	0/9 (0)	0/9 (0)
Hyperkalemia (%)	0/9 (0)	0/9 (0)
Others (%)	0/9 (0)	0/9 (0)

MORTALITY AND MORBIDITY

Morbidity and mortality of the study is shown in the Table 3. There was one death at discharge in the Sterofundin group. Patient deteriorated three days after admission and was intubated and required inotropic support. Cause of death was sepsis secondary to urinary tract infection. There was no significant difference in mortality and morbidity in between the two groups.

DISCUSSION

There was a notable difference in the initial biochemical parameters between both groups. The pH in Sterofundin group showed a steady increase compared to normal saline (Table 2). There was a difference in the change of median pH (-0.006 vs 0.05) within the first two hrs. Development of hyperchloremic acidosis from substantial infusion of normal saline explained these results. Nevertheless, range of results in both groups remains the same (-0.343 – 0.104). Physiological compensatory mechanism normalized the chloride and pH levels over time. Reduction in anion gap was also higher in the sterofundin group.

Ketone clearance occured more rapidly in the sterofundin group. Sterofundin does not cause increase in chloride content in the blood. Both group increased the bicarbonate and reduces of anion gap and significant ion difference over time. This was similar to the study on plasmalyte by Chua et al. (2012) in which the balanced solution resulted in rapid acidosis resolution and lower chloride levels.

Although, there was added potassium in Sterofundin, the potassium level in the Sterofundin group remained the same compared to the other group. In addition to this, continuous infusion of insulin reduced intracellular potassium level. This study showed that it is safe to use Sterofundin in DKA patient who has no renal failure. Sterofundin in DKA does not increase the potassium level in serum. On the other hand, it will pose benefits in preventing hypokalemia. It will be cost effective as the need of repleting potassium is not needed.

These findings are similar to the study done by Chua et al. (2012) and Mahler et al. (2011). Plasmalyte was used as the balanced fluid which caused less hyperchloremic acidosis compared to normal saline. Sterofundin has lower SID than Plasmalyte which can explain a higher significant effect on the biochemical

outcome. Plasmalyte has a SID of 54 in comparison to Sterofundin which has a SID of 29 and is closer to plasma. However, similar to their study, SID of patients was same in both groups. There was no difference for patients who underwent renal replacement therapy and these findings was similar to SPLIT trial (Young et al. 2015).

There is inadequate evidence at the moment to change the current recommendation in treating DKA. This study was introduced to the Emergency Department as an alternative protocol in managing DKA patients. The variable scale insulin infusion was more widely use before the implementation of the study although the fix scale insulin infusion was recommended by the British guideline since 2013. With use of integrated monitoring chart, the monitoring of the patient and serial timing of blood taking was more standardized. The record of blood ketone clearance could be emphasized by charting the reduction on a single page along with other important parameters such as potassium level, fluid rate and urine output. This helps the clinician to visualize the progress of the patient's serial biochemical parameters.

Small sample size was the main limitation of this study. One of the causes was poor adherence towards the implemented DKA sterofundin protocol. Once participant was admitted to medical ward, the fluid infused was changed to normal saline. This was mainly due to unfamiliar and unwilling practitioner in adhering to the protocol. Further education and thorough briefing should be done to all specialities involved in this study. This small sample size resulted in inadequate power to show any statistical difference and variability in the data between the 2 groups. An extension of the study is needed in order to recruit more patients.

Time length of each individual study was only 12 hrs due to logistic consideration and financial constraint. The time was not enough to look at full resolution of acidosis and ketone clearance. This should be extended to 24 hrs in order to see the full effect.

CONCLUSION

Generally, with a limited sample size there was a noticeable difference between patients treated with sterofundin and normal saline for DKA. As this can be considered as a pilot study, it can pave way to more clinical trials in the future. There was earlier acidosis reversal, rapid reduction of anion gap and prevention of potassium depletion after with sterofundin infusion. This study can act as a platform for further studies in order to obtain significant outcome and change our current management of DKA patients.

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APPENDIX

1st Hour: Immediate Management

Step 1. Commence 0.9% saline drip using large bore cannula. (See box below for rate of fluid replacement)

Step 2. Commence a fixed rate intravenous insulin infusion (IVII) (0.1 unit/kg/hr based on estimate of weight).

50 units short-acting human insulin made up to 50 mL with 0.9% saline solution.

Step 3. Assess patient

- BP
- Pulse
- Temperature
- Respiratory rate
- Oxygen saturation
- Glasgow Coma Scale
- Hydration status
- Full clinical examination

Step 4. Investigations

- Capillary and venous blood glucose
- Arterial blood gases
- Blood or urinary ketones
- BUSE
- FBC
- Blood cultures
- MSU
- ECG (if indicated)
- CXR (if indicated)

Step 5. Outline monitoring regimen

- Hourly capillary blood glucose
- Vital signs and input-output charting hourly
- Venous bicarbonate and potassium at 60 minutes, 4 hours and 6-hourly thereafter
- 6-hourly BUSE and urine ketone
- Continuous pulse oximetry (if indicated)
- Continuous cardiac monitoring (if indicated)

Step 6. Look for precipitating causes and treat accordingly
Start broad-spectrum antibiotics if infection suspected

2nd - 6th Hour

Aims of treatment:

- Rate of fall of ketones of at least 0.5 mmol/L/hr, or
- Bicarbonate rise 3 mmol/L/hr, and
- Blood glucose fall 3 mmol/L/hr
- Maintain serum potassium in normal range
- Avoid hypoglycaemia

Step 7. Reassess patient, monitor vital signs

- Hourly blood glucose (lab blood glucose if meter reading "HI")
- 4-6 hourly blood or urine ketones
- Venous blood gas for pH, bicarbonate and potassium at 60 minutes, followed by 4-6 hourly (depending on the severity of acidosis)
- If potassium is outside normal range, reassess potassium replacement and check 1-2-hourly depending on the severity

Step 8 Continue fluid replacement via infusion pump as follows:

- 1000 mL of 0.9% saline with potassium chloride over next 2 hours
- 1000 mL of 0.9% saline with potassium chloride over next 4 hours
- Once blood glucose falls below 14 mmol/L:
  - Switch to 5% dextrose at 125 mL/hr and reduce insulin infusion rate to 0.05 units/kg/hour; or
  - Switch to 10% dextrose at 125 mL/hr with no change in insulin infusion rate.

More cautious fluid replacement in young people aged under 18 years, elderly, pregnant, have heart or renal failure. (Consider HDU and central line)

Step 9. Assess response to treatment

Insulin infusion rate may need review if:

- Blood ketones not falling by at least 0.5 mmol/L/hr
- Venous bicarbonate not rising by at least 3 mmol/L/hr
- Plasma glucose not falling by at least 3 mmol/L/hr
- Continue fixed rate IVII until ketones less than 0.3 mmol/L, venous pH over 7.3 and/or venous bicarbonate over 18 mmol/L

If ketones and glucose are not falling as expected always check the insulin infusion pump is working and connected and that the correct insulin residual volume is present.

If equipment is working but response to treatment inadequate, increase insulin infusion rate by 1 unit/hr increments hourly until targets achieved.

Additional measures

- Accurate fluid balance chart, minimum urine output 0.5 ml/kg/hr
- Consider urinary catheterisation if incontinent or anuric (does not pass urine by 60 minutes)
- Nasogastric tube with airway protection if patient obtunded or persistently vomiting
- Measure arterial blood gases and repeat CXR if oxygen saturation less than 92%
- DVT prophylaxis with low molecular weight heparin
- Consider ECG monitoring if potassium abnormal or concerns about cardiac status.

Initial Fluid & Potassium Replacement

Restoration of circulating volume is a priority

Systolic BP (SBP) <90 mm Hg
Likely to be due to low circulating volume, but consider other causes such as heart failure, sepsis, etc.

- Give 500 mL of 0.9% saline solution over 10–15 minutes. If SBP remains <90 mm Hg, repeat.
- Most patients require between 500-1000 mL given rapidly. Consider colloids e.g. Gelafundin if BP fails to pick up.
- Once SBP >90 mm Hg give 1000 mL of 0.9% saline over the next 60 minutes.

Addition of potassium is likely to be required in the second litre of fluid, especially if baseline potassium <5 mmol/L and to maintain potassium between 4-5 mmol/L.

Systolic BP on admission ≥90 mmHg

- Give 1000 mL of 0.9% saline for first 60 minutes

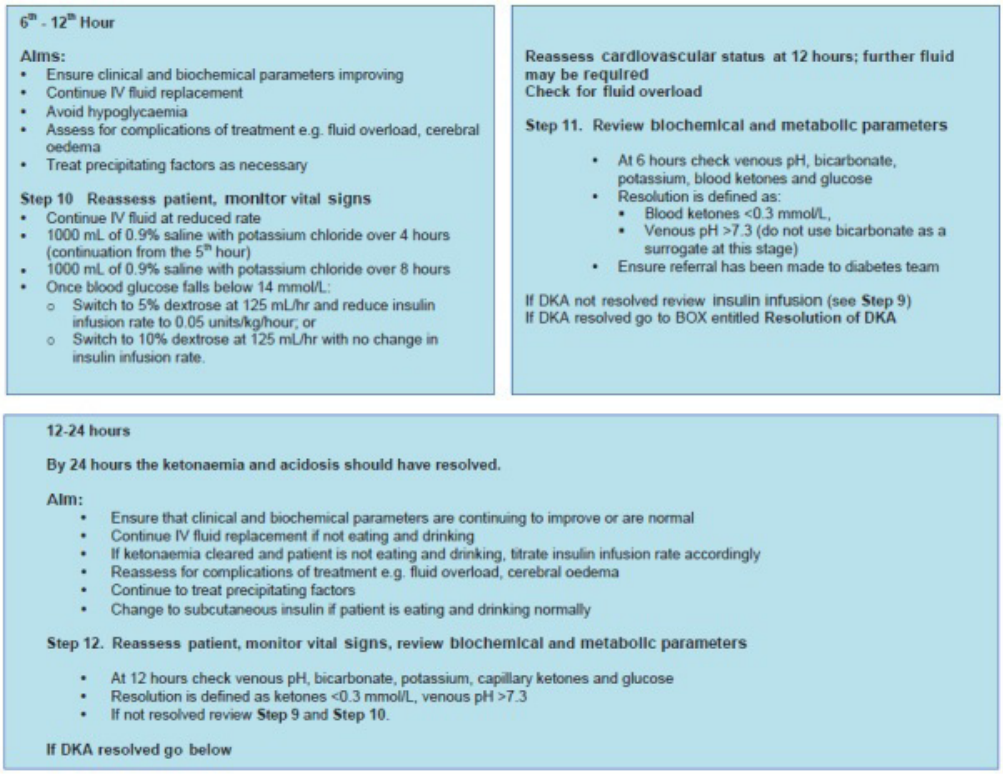
Potassium replacement:

Potassium level (mmol/L)	Potassium replacement mmol/L of infusion solution
>5.5	Nil
3.5–5.5	40 mmol/L (3 g KCL)
<3.5	Additional potassium required

Caution:
Withold potassium replacement if no urine output.

Intravenous bicarbonate:
The use of intravenous bicarbonate is not indicated to correct acidosis in DKA due to:

- Rise in pCO_2 in CSF which may lead to a paradoxical increase in CSF acidosis.
- Delay in the fall of blood lactate and ketone level.
- Risk of cerebral oedema especially in younger age groups.



Appendix 1: DKA Protocol Guidelines (Malaysian CPG 2015)

HKL ADULT DKA MANAGEMENT CHART

Date:	
Name:	
IC/Passport No:	
RN	
Wad:	

	ACTION	Criteria	Parameters	Value
☐	Confirm Diagnosis	☐ 1. Capillary blood glucose >11 mmol/L or known Diabetic	**DXT:**	mmol/L
	ALL 3 criteria MUST BE MET	☐ 2. Capillary blood ketones > 3 mmol/L or significant ketonuria ≥ 3+	**Ketones :**	mmol/L
		☐ 3. Venous pH <7.3 and/or venous bicarbonate <15mmol/L	**pH:**	
			HCO3:	mmol/L
☐	Time	☐ Time of diagnosis (T 0)	**HH:MM:**	
☐	Consent	☐ Consent Taken		
☐	Randomization	☐ Randomisation done	☐ Group A	☐ Group B

	ACTION		Value	Formula	Normal Range
☐	Calculations	☐ Serum Osmolality =	mOsmol/kg	$2(Na^+$	285-295mOs mol/kg
		☐ Anion Gap =	mmol/L	$(Na^+$	8-16mmol/L
		☐ Weight (Wt) =	kg		
		☐ Total Fluid Deficit (x) =	ml		100ml X IBW
		☐ Bolus Fluid (y) =	ml	10 ml X IBW	
		☐ Maintenance fluid (z) =	ml	$z = (x - y) / 6$	
		☐ Insulin rate =	unit/hr	0.1 unit X IBW	

Fluid Regime

	ACTION		Amount	
☐	Is Patient in Shock?	☐ 10ml x Wt =	ml	consider other causes of shock
	A. SBP <90mmHg Give of study fluid 10-20ml/kg over 10 - 15mins , repeat if necessary	☐ 10ml x Wt =	ml	
		☐ 10ml x Wt =	ml	
		☐ 10ml x Wt =	ml	
		☐	ml	
	If SBP>90 mmHg go to B	Total Bolus Given (y) =	ml	

	ACTION	z =		Amount (a)		Rate		Time (HH:MM) Start	End
☐	Fluid Replacement	☐	For the 1st hour	z ml x Wt =	ml	a/1 =	ml/hr		
	B. If SBP>90 mmHg give maintenance fluid $z = (x - y) / 6$ over 24 hours period.	☐	Next 2 hours	z ml x Wt =	ml	a/2 =	ml/hr		
		☐	Next 2 hours	z ml x Wt =	ml	a/2 =	ml/hr		
		☐	Next 4 hours	z ml x Wt =	ml	a/4 =	ml/hr		
	Calculate the fluid regime for the next 24 hours	☐	Next 6 hours	z ml x Wt =	ml	a/6 =	ml/hr		
		☐	Next 8 hours	z ml x Wt=	ml	a/8 =	ml/hr		
☐	IV Fluid Adjustment	Continue study fluid (+KCl) as required to restore circulating volume Reassess patient's volume status frequently – HR, BP, urine output, JVP, oedema, chest auscultation – adjust rate of fluid infusions as necessary to ensure adequate BP/urine output and prevent volume overload							
		When DXT < 15mmol/L commence IV glucose 10% at 100mL/h to run ALONGSIDE 0.9% NaCl with KCl							

	ACTION					
☐	Baseline Investigations	☐	Venous blood gas (VBG - pH, HCO3 , SBE, lactate)			
		☐	Capillary Glucose (DXT			
		☐	Renal Profile (RP)			
		☐	Full blood count (FBC)			
		☐	Calcium, Albumin, magnesium, Phosphate			
☐	Consider other Investigations	☐ CXR ☐ UFEME ☐ ECG ☐ CT scan				
				Time To Take (HH:MM)		
☐	Repeat Blood Investigation	☐	@ 2 hour of treatment (T2)		☐ VBG	☐ RP
		☐	@ 4 hour of treatment (T4)		☐ VBG	☐ RP
		☐	@ 8 hour of treatment (T8)		☐ VBG	☐ RP
		☐	@ 12 hour of treatment (T12)		☐ VBG	☐ RP
		☐	@ 24 hour of treatment (T24)		☐ VBG	☐ RP

	ACTION			
☐	Potassium Replacement	Venous potassium level	Potassium (KCl) replacement	
☐		>5.5mmol/L	none	Life-threatening hypokalaemia may occur with insulin infusion
		4.5-5.5mmol/L	20 mmol/L	Cardiac
		3.5-4.4 mmol/L	40 mmol/L	replacement exceeds 20mmol/h; ensure baseline ECG has been performed
		<3.5mmol/L	senior advice*	*60-80mmol/L of KCl may be required

	ACTION		
☐	Insulin Regime	☐	Prescribe 50 units Actrapid in 49.5ml 0.9% NaCl (1unit/mL) solution
		☐	Commence a Fixed Rate Intravenous Insulin Infusion (FRIVII) at 0.1 unit/kg/hr , Maximum 15 mL/h (starting dose) Dose =
		☐	If patient normally takes a **long acting insulin analogue** (e.g. Lantus®, Levemir®) prescribe this at usual dose/time SC and ensure it is given IN ADDITION TO IV insulin
☐	**Reassesment response to treatment**		
	An adequate response to treatment is defined by: **fall in blood ketones of ≥0.5mmol/L/h** AND **rise in venous HCO3 of** ≥3mmol/L/h AND fall in capillary blood glucose (CBG) of ≥3mmol/L/h		Continue Fixed Rate Intravenous Insulin Infusion (FRIVII) until **venous pH >7.3 AND/OR**
			If patient is failing to respond as expected and/or DKA has not resolved by 24h, SEEK SENIOR/SPECIALIST ADVICE

	ACTION		
☐	Precipitating factors	☐	Infection / Sepsis
		☐	Non Compliance
		☐	Stress (e.g MI/CVA)
		☐	Idiopathic
		☐	Other please specify:

Appendix 2: HKL Adult DKA Management Chart