ΕΥΓΛΥΚΑΙΜΙΚΗ ΔΙΑΒΗΤΙΚΗ ΚΕΤΟΞΕΩΣΗ: ΠΑΛΑΙΟΣ ΓΝΩΡΙΜΟΣ Η ΝΕΑ ΟΝΤΟΤΗΤΑ;

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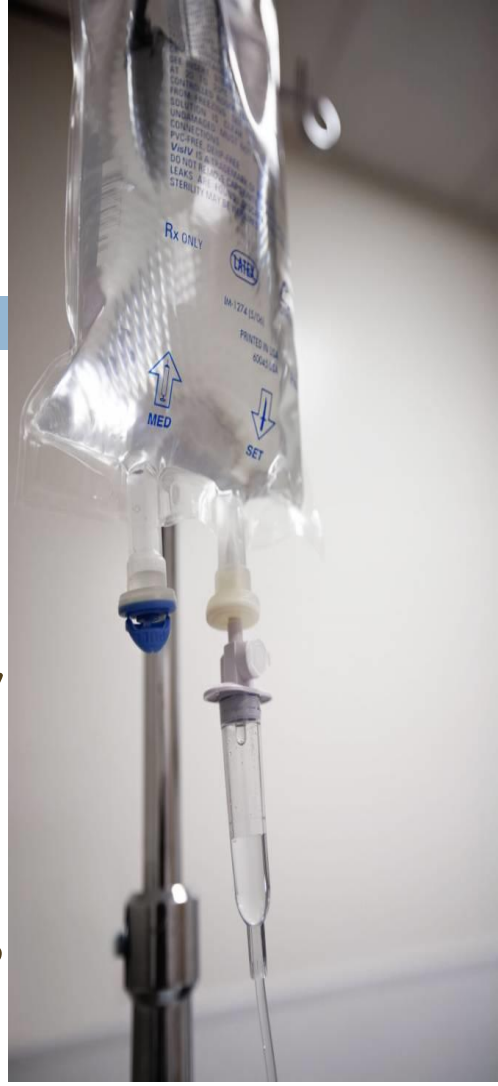
Πανεπιστημιακό Γ.Ν "ΑΤΤΙΚΟΝ"

Περιστατικό

- Ασθενής 52 ετών προσέρχεται στα καρδιολογικά ΤΕΠ λόγω έντονης αδυναμίας, καταβολής και ναυτίας με αίσθημα οπισθοστερνικής δυσφορίας. Εισαγωγή στην καρδιολογική.
- Α/α: σταθερή ΣΝ, με 2PTCA προ έτους, υπό ατορβαστατίνη 40 mg, Duoplavin, Dilatrend 6,25x2, Atacand 16mg.
- ΣΔ ΙΙ από 10ετίας, υπό glimepiride 4mg, metformin 2000mg. Λόγω πρόσφατης HbA1c 8% προσετέθη empagliflozin 10mg την οποία ξεκίνησε 2 μερες πριν την έναρξη των συμπτωμάτων
- Ο ασθενής περιγράφει από 24ωρου έντονη αδυναμία, υπνηλία και ναυτία με ανορεξία

Περιστατικό συνέχεια

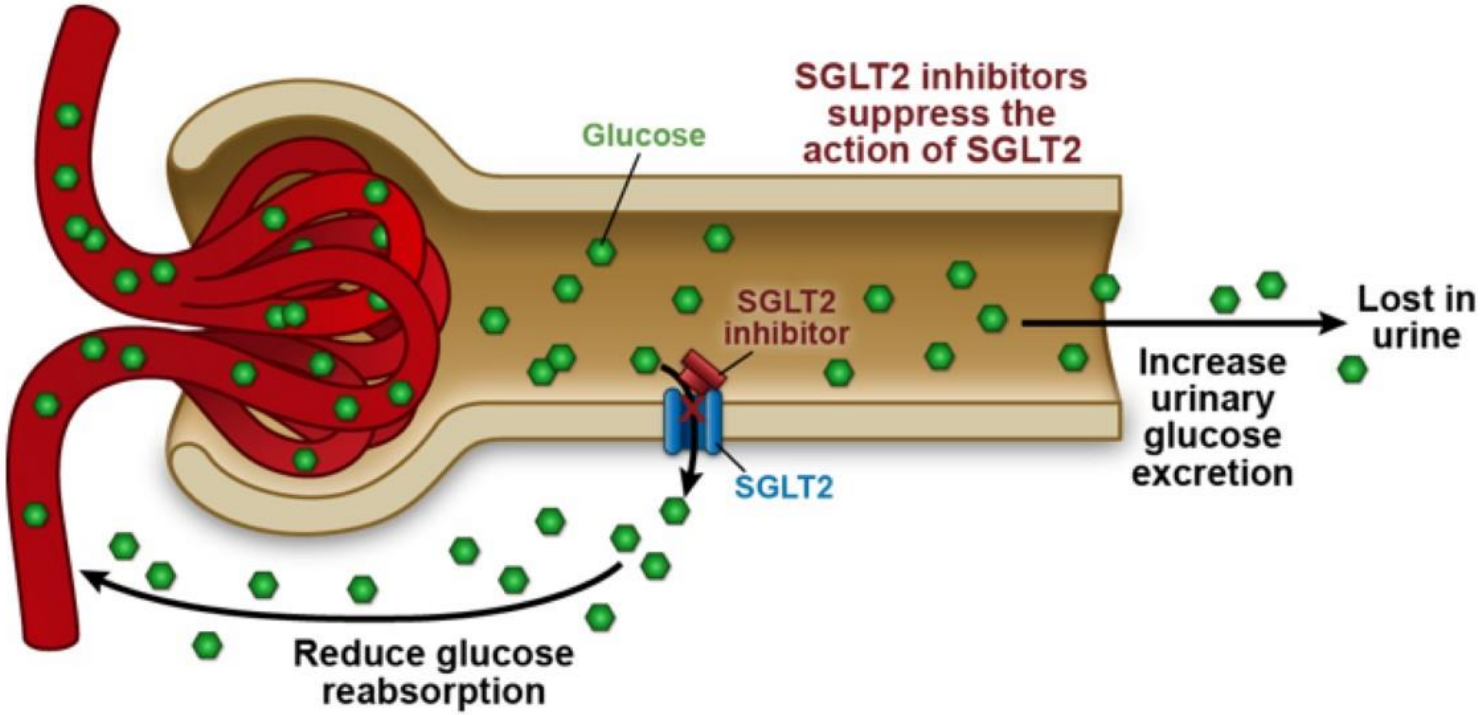


- Α/ε: μείωση επιπέδου συνείδησης. Απύρετος, ΑΠ 105/85mmHg, BMI 26mg/m2, waist 108
- Σχ 120 mg%, ουρία 60 mg/dl, Κρεατινινη 1,0 mg/dl, **Καλιο 5,9 meq/l**, Na 149meq/l, **WBC 14500/m3**, Ht 46%, CRP 2mg/dl
- Αέρια αίματος **PH 7.1, HCO3- 7 meq/l**, SO2 98% PO2 110, PCO2 25, anion gap ⬆
- Ετέθη N/S 0,9% για ενυδάτωση και εκλήθη το Διαβητολογικό Τμήμα

Διάγνωση: Ευγλυκαιμική κετοξέωση

SGLT2 Inhibitor Mechanism of Action

- SGLT2 inhibitors work in the proximal tubules of the kidney to block the reabsorption of glucose back into the blood system, thus reducing blood glucose levels



- DKA is a severe metabolic condition usually characterized by hyperglycemia resulting from a relative insulin deficient state

Jabbour SA. *Postgrad Med*. 2014;126:111-117.[1]

FDA-approved SGLT2 Inhibitors

- SGLT2 inhibitors are currently FDA-approved for use in patients with T2D
- Uncommon clinical presentation of DKA in patients with T2D
- DKA leads to an increase in acidic metabolites (ie, ketones, ketoacids)

Brand Name	Active Ingredient(s)
Invokana®	Canagliflozin
Invokamet®	Canagliflozin and metformin
Farxiga®	Dapagliflozin
Xigduo™ XR	Dapagliflozin and metformin extended-release
Jardiance®	Empagliflozin
Glyxambi®	Empagliflozin and linagliptin

FDA website.[4]

First Case Report of DKA by a SGLT2 Inhibitor

- 32-year-old Japanese woman with T2D and Prader-Willi syndrome
- On strict low carbohydrate diet
- Presented with serum bicarbonate of 3 mEq/L, arterial pH of 7.055 but non fasting serum glucose level of 191 mg/dL
- Laboratory evaluations showed severe ketoacidosis
- On a SGLT2 inhibitor (ipragliflozin*)

*This agent is not yet approved by the US FDA.

Hayami T, et al. *J Diabetes Invest*. 2015 Feb 20. [Epub ahead of print][3]

FDA Drug Safety Communication

- May 15, 2015
  - 20 cases of acidosis, reported as DKA, ketoacidosis, or ketosis in patients treated with SGLT2 inhibitors from March 2013 to June 6, 2014, identified via the FDA Adverse Event Reporting System (FAERS)
  - All patients seen in ED or hospital
    - Emergency physicians, PCPs, diabetologists/endocrinologists need to be aware of issue and correctly diagnose and treat
    - Anesthesiologists and surgeons also need to be aware
  - Since June 2014, additional cases of DKA and ketoacidosis in patients treated with SGLT2 inhibitors have been reported to the FAERS

FDA website.[4]

Acta Diabetol 30: 251–253, 1993

ACTA
DIABETOLOGICA

1993

Short communication

Euglycaemic diabetic ketoacidosis: does it exist?

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Abstract. The original criteria described for euglycaemic ketoacidosis (initial blood glucose less than 16.7 mmol/l and plasma bicarbonate equal to or less than 10 mmol/l) were identified in 23 of 722 consecutive episodes (3.2%) of diabetic ketoacidosis. True euglycaemic ketoacidosis (initial blood glucose 10 mmol/l or less) was rare, occurring in 0.8–1.1% of all episodes depending on the defining plasma bicarbonate concentration. Management of euglycaemic ketoacidosis with low-dose continuous intravenous infusion of insulin together with adequate fluid replacement was effective. The clinical and biochemical data did not support the concept of euglycaemic ketoacidosis as a separate entity. The importance of ketone testing rather than glucose testing in the diagnosis of ketoacidosis is, however, emphasized. The importance of adequate insulin and fluid therapy in those few episodes where blood glucose is normal or near normal at presentation is also highlighted.

Key words: Diabetic ketoacidosis – Euglycaemic ketoacidosis

Introduction

Blood glucose monitoring is useful in the daily management of insulin-treated diabetes mellitus. Monitoring for urinary ketones, however, is essential for the recognition of ketoacidosis. Reliance on blood glucose results alone may actually be misleading [1]. The term 'euglycaemic' but who had continued subcutaneous insulin injections. Treatment consisted of fluid replacement and large doses of insulin covered by carbohydrate infusion. The authors recommended that 0.9% saline should be avoided. We have reviewed our experience of ketoacidosis to ascertain whether other features support the syndrome as a separate entity and to consider the application of modern therapy with low-dose insulin regimens [4, 5].

Materials and methods

All patients with diabetic ketoacidosis admitted to the Accident and Emergency Department or wards of the hospital were recorded annually from 1975 to 1991 inclusive. Ketoacidosis was defined as uncontrolled diabetes mellitus requiring therapy with intravenous fluids and in which the initial plasma bicarbonate was 15 mmol/l or less with significant ketonuria (at least ++ on Ketostix testing). Treatment of all episodes included a low-dose insulin regimen using either intramuscular injections hourly or a continuous intravenous infusion (1–6 U/h). Intravenous 0.9% sodium chloride was given until the blood glucose level fell below 10 mmol/l. Intravenous dextrose (5%) was then substituted. Sodium bicarbonate was used in only a few cases when the admitting clinician felt that the acidosis was too severe to await correction by fluids and insulin. A venous blood glucose concentration of 10 mmol/l or less was defined as true euglycaemia. The frequencies of the precipitating causes of euglycaemic ketoacidosis were compared with those of the other cases by the χ^2 test. P values of more than 0.05 were considered non-significant.

Results

Table 1. Plasma bicarbonate concentrations in episodes of ketoacidosis presenting with blood glucose levels of less than 16.7 mmol/l and less than 10 mmol/l during the period of study

Glucose less than (mmol/l)	Bicarbonate less than or equal to (mmol/l)	Number of episodes (%)
16.7	10.0	23 (3.2)
16.7	15.0	43 (6)
10.0	10.0	6 (0.8)
10.0	15.0	8 (1.1)

Table 2. Precipitating causes of 722 cases of diabetic ketoacidosis admitted during the period of study, classified according to whether they satisfied the euglycaemic criteria of Munro et al. (initial blood glucose less than 16.7 mmol/l, bicarbonate less than or equal to 10 mmol/l) [2]

Precipitating cause	Cases satisfying criteria of Munro et al. ($n=23$)	All other cases of diabetic ketoacidosis ($n=699$)
Infection	6 (26.1)	211 (30.2)
Other illness	4 (17.4)	74 (10.6)
Insulin error	2 (8.7)	92 (13.2)
Nil identified	10 (43.5)	246 (35.1)
New diagnosis	1 (4.3)	76 (10.9)

Table 3. Response of blood glucose and plasma bicarbonate concentrations to low-dose insulin infusion in the patients who satisfied the criteria of Munro et al. Median values with ranges in parentheses are shown. Comparisons were made by the Mann-Whitney U test

	0 h	6 h	P value
Glucose (mmol/l)	13.5 (4–16.7)	9.25 (2.6–19.6)	0.001
Bicarbonate (mmol/l)	9 (5–10)	15.0 (8–23)	<0.001

presentation in six episodes (0.8%). No significant correlation was found between the initial blood glucose and the plasma bicarbonate concentrations in the total series ($r=0.03$).

Episodes satisfying the criteria of Munro et al.

The 23 episodes of euglycaemic ketoacidosis as defined by Munro et al. occurred in 22 patients (16 female, 6 male). The mean age in the 21 patients with insulin-dependent (type 1) diabetes was 25.3 years (SD 9.2, range 14–46 years) with a mean duration of diabetes of 9 years

In 14 of the 16 episodes normal or increased amounts of insulin had been taken in the 12 h before admission. Two patients stated they had stopped insulin, one 36 h and one 6 days before admission. The mean serum sodium concentration on admission in the 23 episodes was 135 (SD 4.9) mmol/l, serum potassium 4.5 (SD 0.8) mmol/l and serum urea 6.2 (SD 2.3) mmol/l.

Twelve (57%) of the 21 patients with type 1 diabetes had experienced at least one (range 1–11) other episode of ketoacidosis during the period of the study. One patient experienced two episodes of euglycaemic ketoacidosis. In the remaining 11 patients the initial blood glucose concentrations during their other admissions were very variable, ranging from 17 to 54 mmol/l. None of the 21 patients with type 1 diabetes died from ketoacidosis during the period of the study.

Blood glucose and plasma bicarbonate levels are shown for the patients satisfying the criteria of Munro et al. in Table 3. The low-dose insulin infusion resulted in a fall in glucose and a rise in bicarbonate after 6 h of treatment. Heavy ketonuria (+++ or ++) persisted in all patients except one after 6 h.

Discussion

The diagnosis of diabetic ketoacidosis rests on arbitrary clinical and biochemical criteria. The biochemical disturbance ranges from mild to severe. In this unit we use a plasma bicarbonate of 15 mmol/l with significant ketones as the main diagnostic criterion. There is no particular merit in the use of a plasma bicarbonate of 10 mmol/l or less, especially as mortality is not related to the degree of acidosis [6]. A blood glucose of less than 16.7 mmol/l in the original definition of euglycaemic ketoacidosis does have the practical merit of being approximately the upper limit of the second blood glucose range on the commonly used blood glucose monitoring stick (BM 1–44). These data show that blood glucose did not correlate with the degree of acidosis. Patients should be advised, therefore, that ketoacidosis can occur at any level of blood glucose. Ketones should be monitored when clinical features suggest ketoacidosis.

The clinical features of euglycaemic ketoacidosis suggest the reasons for the relatively low blood glucose include vomiting which reduces dietary carbohydrate and the maintenance of insulin therapy. This is supported by a study in insulin-dependent diabetic subjects in whom the observed rise in ketone bodies was greater in the fasted than in the fed state [7]. These euglycaemic patients may also be less dehydrated as suggested by normal

Τα κλινικά χαρακτηριστικά της ευγλυκαιμικής κετοξέωσης περιλαμβάνουν έμετο, αφυδάτωση, μειωμένη πρόσληψη υδατανθράκων και χαμηλές δόσεις ινσουλίνης, ενώ η συγκέντρωση κετονικών σωμάτων είναι μεγαλύτερη στη νηστεία παρά μεταγευματικά.

Jenkins et al, Diabetologia 1993

Euglycemic Diabetic Ketoacidosis In Pregnancy

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[1]St. Mary Medical Center, Long Beach, CA

Introduction:
Diabetic ketoacidosis (DKA) is characterized by hyperglycemia, acidosis, decreased serum bicarbonate, an elevated anion gap, and the presence of serum ketones. In pregnant patients, the prevalence of DKA among diabetics has been estimated to be approximately 10%. While DKA generally occurs when blood glucose is > 250, euglycemic DKA is a relatively rare condition characterized by serum glucose being normal or near normal, and particularly affects patients with poor oral intake or during pregnancy. Given the atypical presentation and potential for poor outcomes, it poses a formidable diagnostic challenge. We present a case of a Type II diabetic female patient with euglycemic DKA.

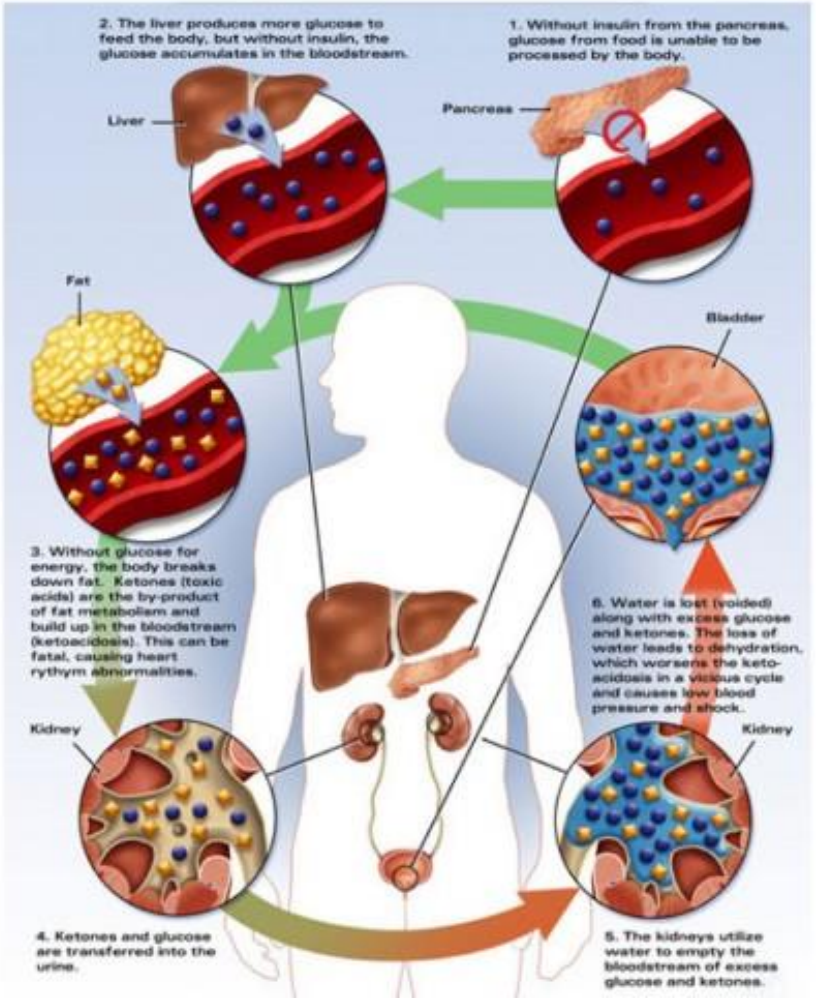
Description:
A 25 year-old G2P1 female at 35 weeks of gestation with history of insulin-dependent Type 2 diabetes presented to the emergency department with nausea and vomiting. The patient noted she had been off of insulin for the prior month as blood glucose levels had been well-controlled. Her previous regimen included NPH 38 units sub-cutaneous q PM and Humalog 24 units sub-cutaneous TID with meals. On admission, she was noted to have blood glucose of 121 mg/dL, bicarbonate level of 21, and anion gap of 13. On day four of admission, blood glucose levels ranged between 96-133, bicarbonate level noted to be 9, and anion gap was 14. ABG was done, which showed pH 7.30 and pCO2 23. Beta-hydroxybutyrate was 4.45. Urinalysis with large ketones and 2+ glucose. Endocrinology was consulted and it was felt that the patient was truly insulin deficient, and was euglycemic due to increased fetal glucose demand masking hyperglycemia. The patient was symptomatically improving and was tolerating a diet, and was then started on a regular insulin regimen. Her symptoms were completely resolved by day 7 of admission. Bicarbonate level was now noted to be 18 and anion gap was resolved.

Discussion:
This case illustrates the potential for DKA despite euglycemia, particularly during pregnancy. The presentation of DKA is similar in pregnant and nonpregnant women, with symptoms of nausea, vomiting, polyuria, and polydipsia. Patients typically present with acidemia, an elevated anion gap, and hyperglycemia. However, as many as 36%of pregnant women may have blood glucose levels less than 200 mg/dL. This case emphasizes that normal plasma glucose levels are not enough to preclude diabetic ketoacidosis. Nausea, emesis, and low caloric intake in an otherwise normal pregnant, diabetic woman requires further investigation to exclude DKA.

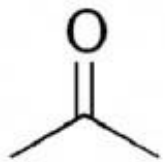
This abstract is funded by: None

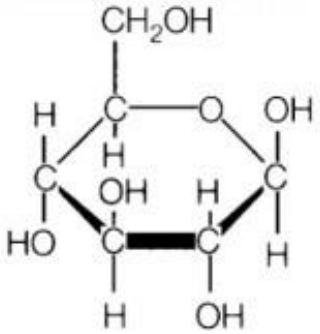
Don't confuse *Diabetic Ketoacidosis* with *Nutritional Ketosis*!

β-OHB: 15-25 mM



β-OHB: 0.5-3.0 mM





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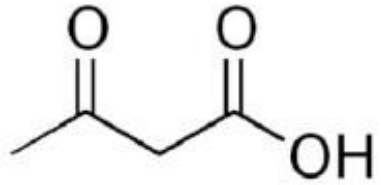
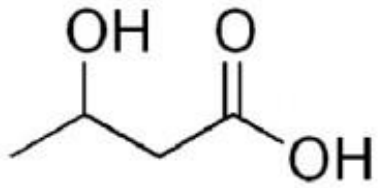




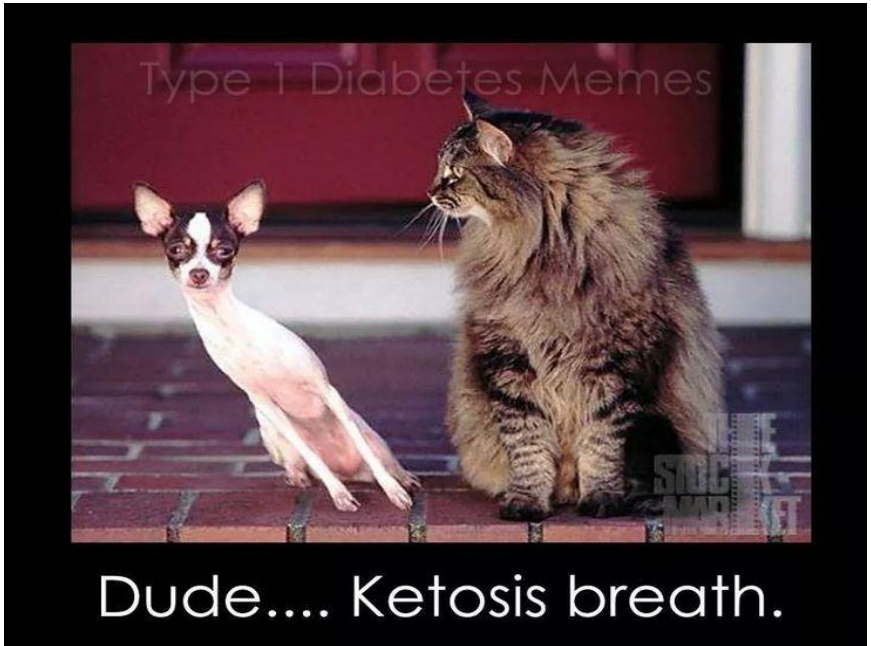


Table 4. Management Pearls In Alcoholic Ketoacidosis.

- A negative nitroprusside reaction does not rule out ketoacidosis.
- An increasingly positive nitroprusside reaction is consistent with an improvement rather than a worsening of the ketoacidosis.
- Patients in AKA *do not* need insulin.
- Fluid resuscitation in AKA should include dextrose *and* saline.

Presentation and Diagnosis of DKA

- Atypical presentation of DKA: high anion gap metabolic acidosis with elevated blood or urine ketones and normal, or slightly high blood glucose[a]
- Signs and symptoms: difficulty breathing, nausea, vomiting, abdominal pain, confusion, and unusual fatigue and sleepiness[a]
- If acidosis confirmed, the SGLT2 inhibitor should be discontinued; appropriate steps then taken to correct the acidosis; and blood glucose levels monitored[b]

Encourage patients to read the Medication Guide or Patient Package Insert that accompanies their SGLT2 inhibitor prescription.

a. FDA website.[4]

b. Westerberg DP. *Am Fam Physician*. 2013;87:337-346.[6]

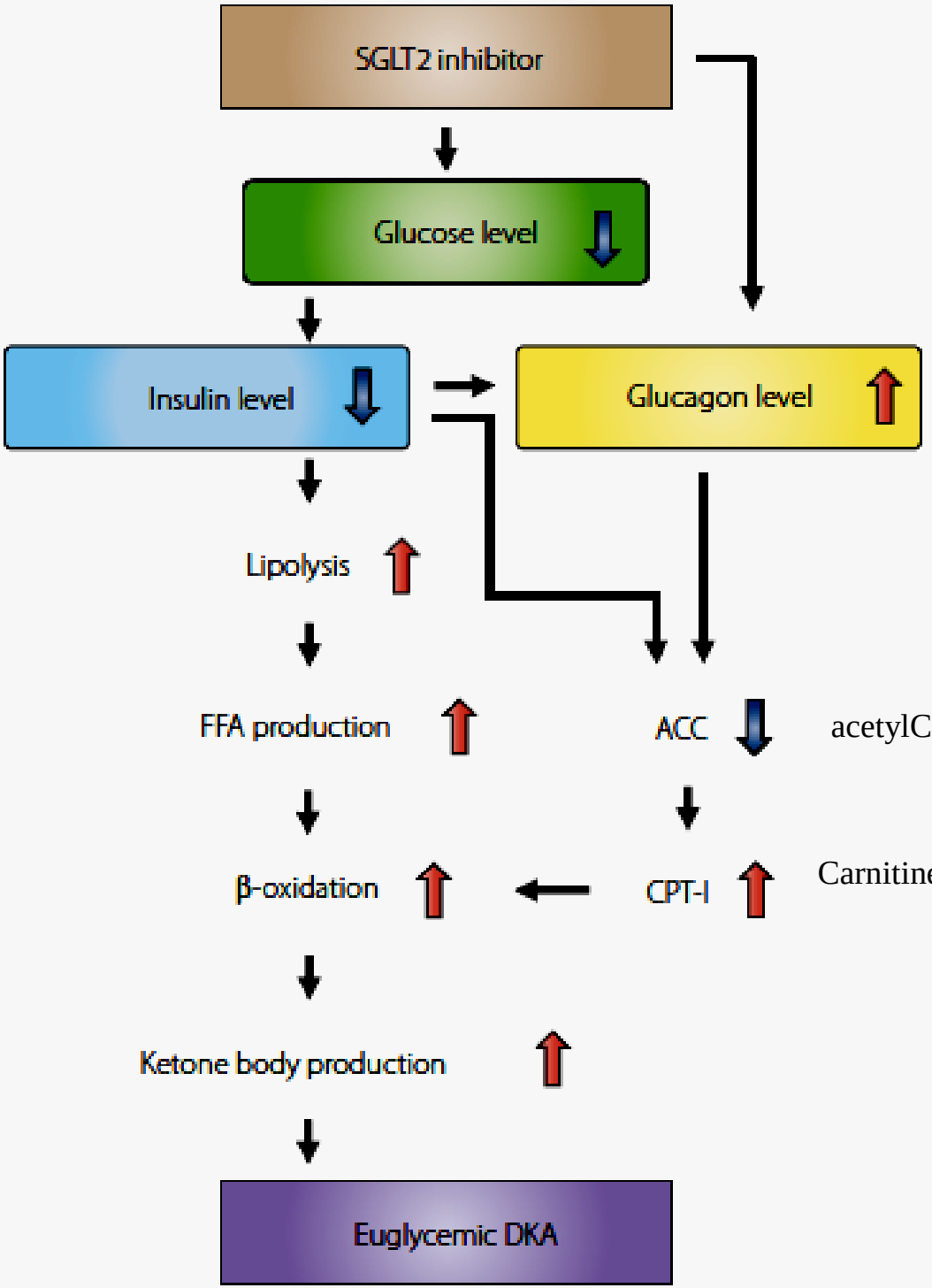
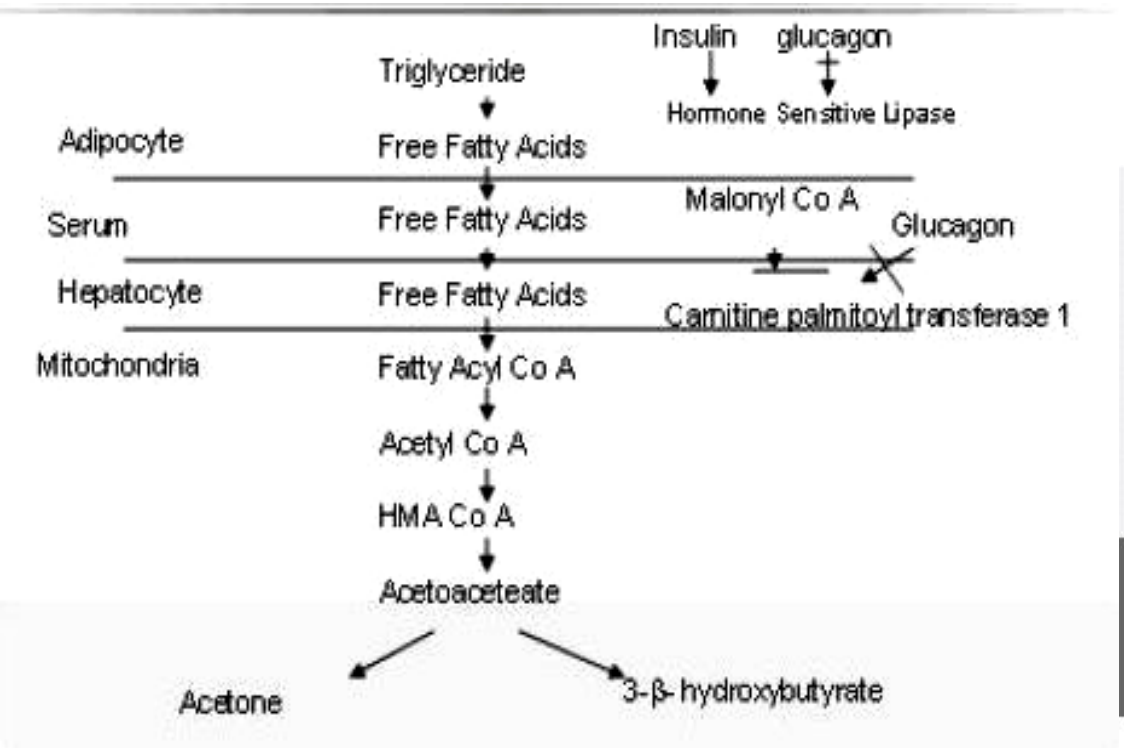


Figure 1 | Possible mechanism of euglycemic DKA induced by SGLT2 inhibitors SGLT2, sodium-glucose cotransporter 2; FFA, free fatty acid;

Mechanism of ketosis :

1. **Lack of insulin** stimulates lipolysis that deliver FFA used for ketogenesis.
2. **Excess glucagon** : Citric acid (the product of krebs cycle i.e. glucose metabolism that Is inhibited by glucagon as decribed before) is responsible for regulation of activity of acetyl coA carboxylase. The later synthesize malony coA in the liver which turn off carnitine acyl transferase 1 that is the rate limitting enzyme in ketogenesis. (so turn off the supply of substrate into krebs cycle and ketogenesis is automatically turned on).



Μηχανισμος

1. This euglycemic DKA (euDKA) is more often associated in patients with type 1 diabetes in conjunction with starvation and acute illness

2. The best estimation based on an analysis of case reports suggests an incidence anywhere from 0.8% to 7.5%

3. The proposed mechanism suggests that SGLT2 inhs while lowering serum glucose, also reduces insulin secretion from pancreatic beta cells in a negative feedback fashion.

The lower serum insulin coupled with lower serum glucose consequently shifts energy metabolism to lipolytic activity and thus free fatty acid oxidation and ketosis.

In addition, ***this SGLT2inh induced insulin deficiency may promote fatty acid oxidation due to decreased production of malonyl-CoA which would normally inhibit the transport of FFA into mitochondira via carnitine palmitoyltransferase-I. Increased glucagon secretion is the cherry on top.***

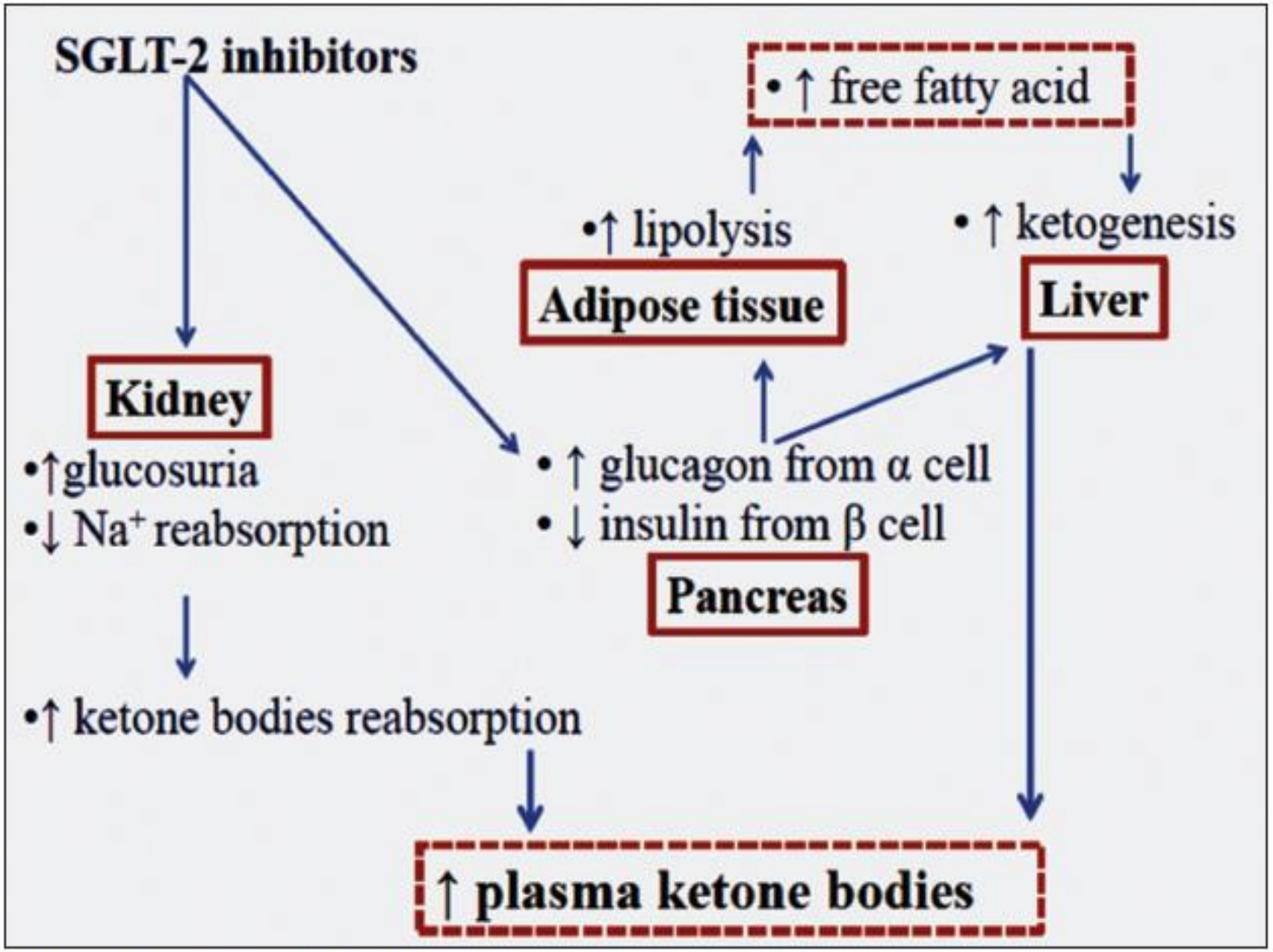


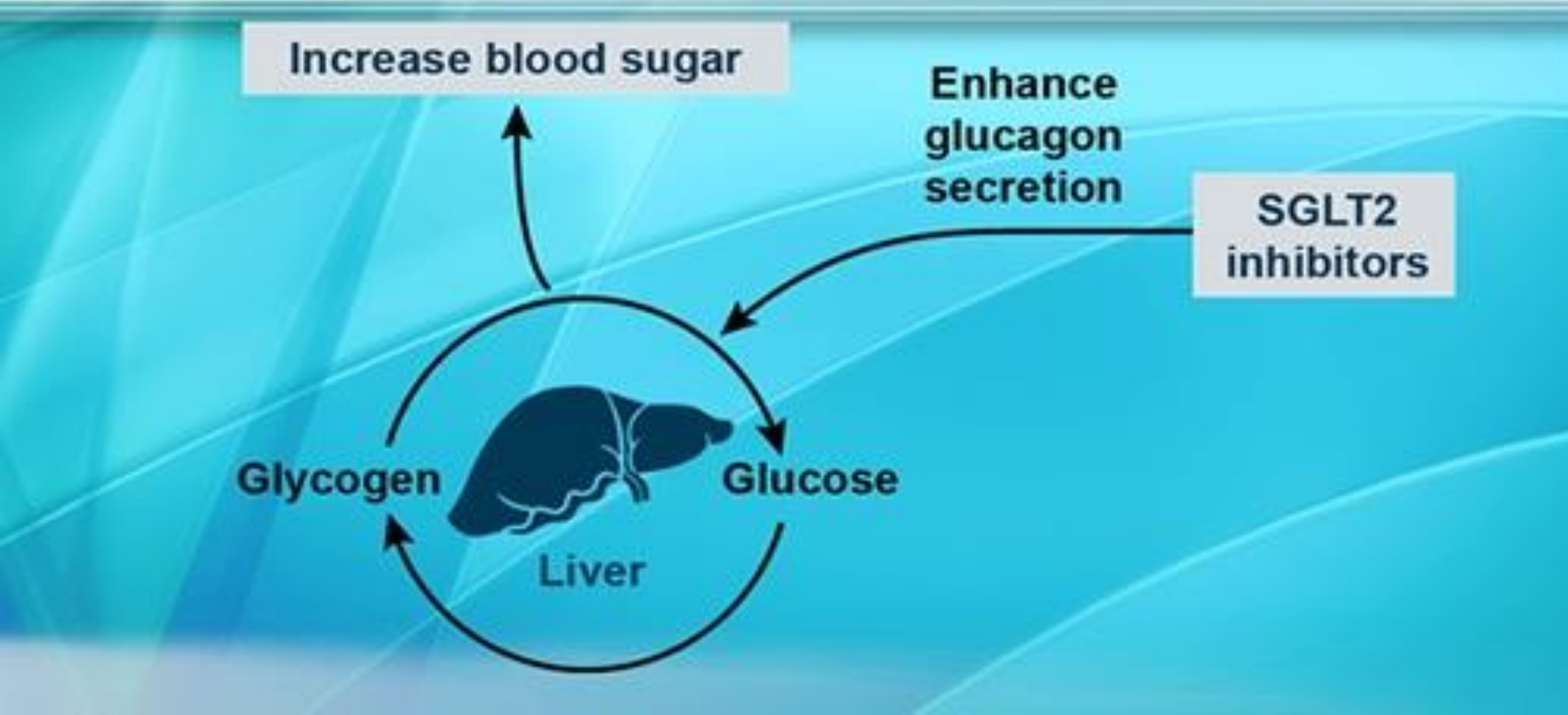
Figure 1: Mechanism of ketoacidosis with SGLT-2 inhibitors

2015 Indian Journal of Endocrinology and Metabolism

Dapagliflozin improves muscle insulin sensitivity but enhances endogenous glucose production

Aurora Merovci, Carolina Solis-Herrera, Giuseppe Daniele, Roy Eldor, Teresa Vanessa Fiorentino, Devjit Tripathy, Juan Xiong, Zandra Perez, Luke Norton, Muhammad A. Abdul-Ghani, and Ralph A. DeFronzo

SGLT2 Inhibitors: Mechanism of Action



Whole body Glu disposal..

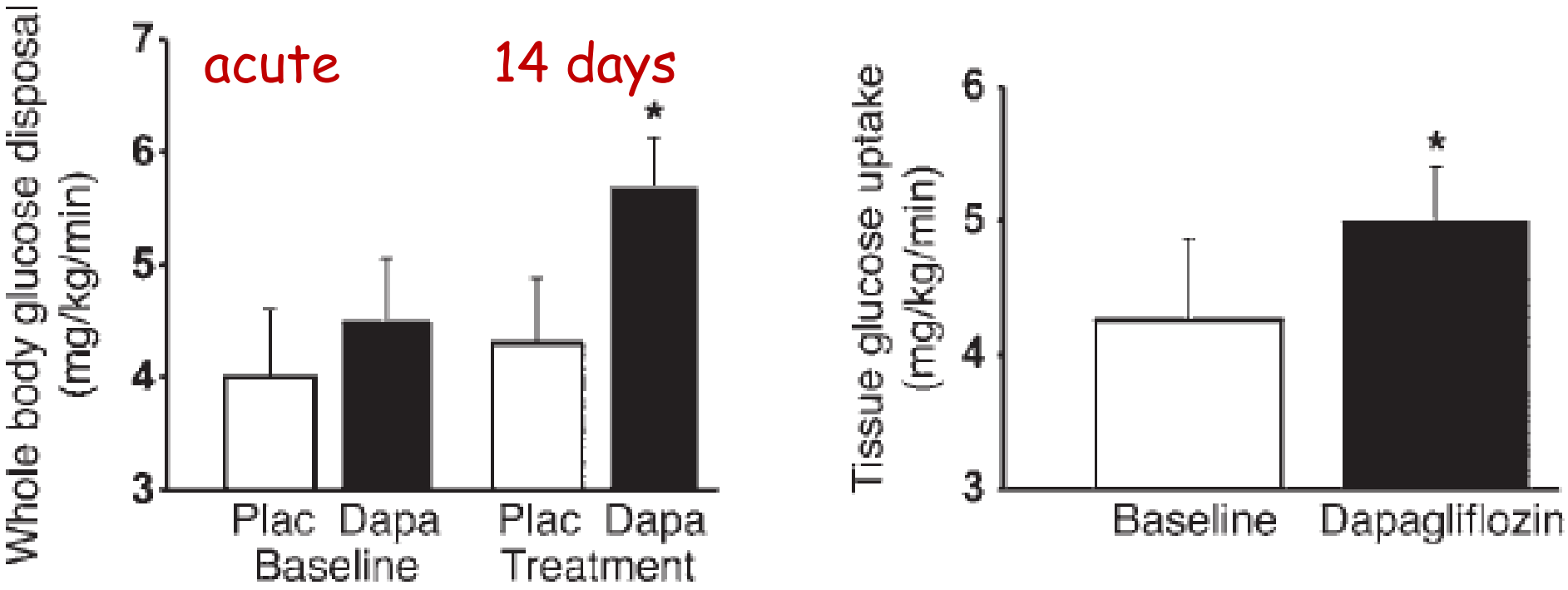


Figure 1

Whole body and tissue glucose disposal during the euglycemic insulin clamp studies performed in subjects with type 2 diabetes before (Baseline) and after 14 days of treatment with dapagliflozin (Dapa) or placebo (Plac). *$P < 0.05$.

J Clin Invest. 2014;124(2):509–514.

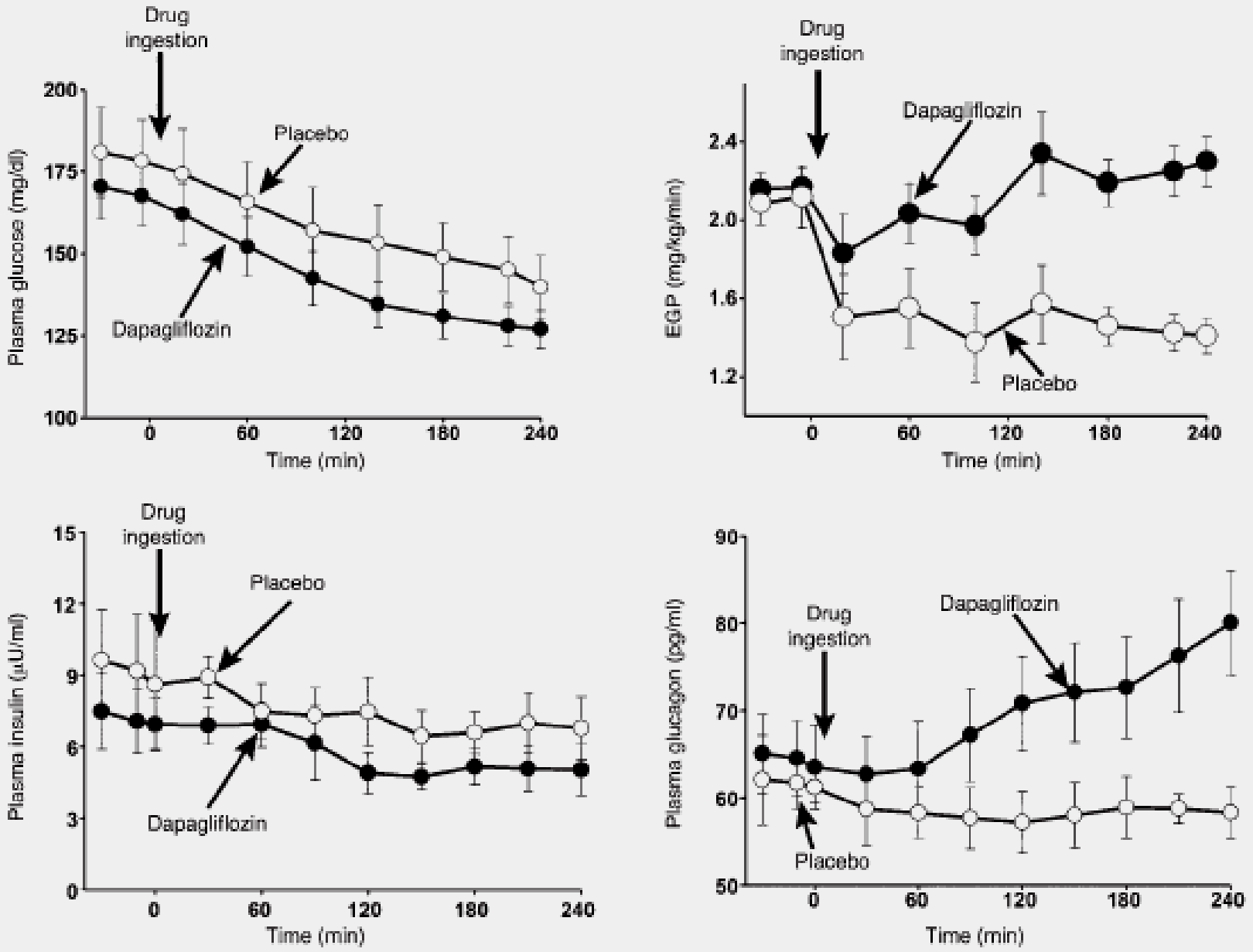


Figure 3

Plasma glucose, insulin, and glucagon concentrations and EGP in the study. On day 2, the ^{3}H-glucose infusion was started 3 hours before drug ingestion (time 0) and continued for 4 hours after drug ingestion (see Methods for more details).

Acute day 2

***J Clin Invest.* 2014;124(2):509–514.**

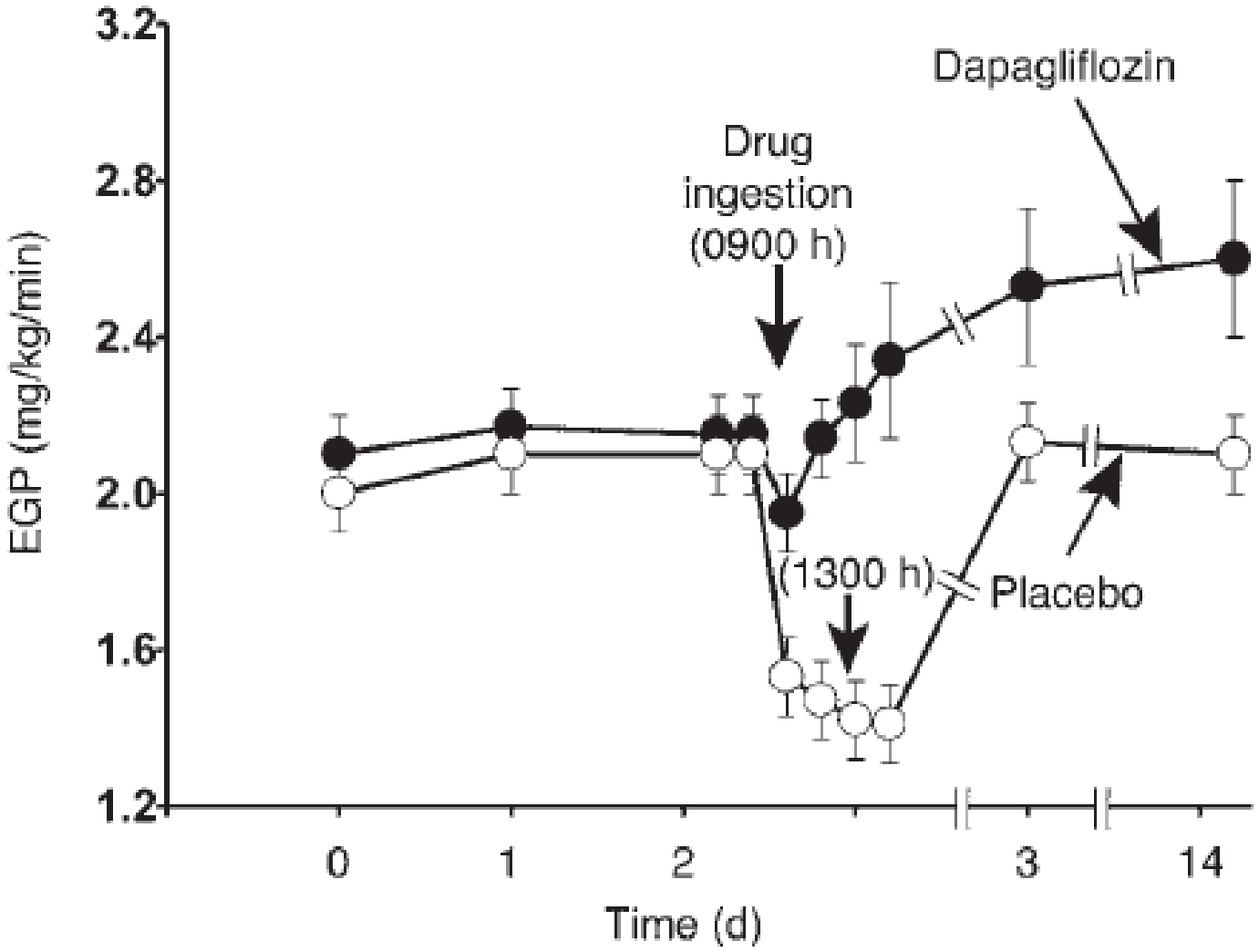
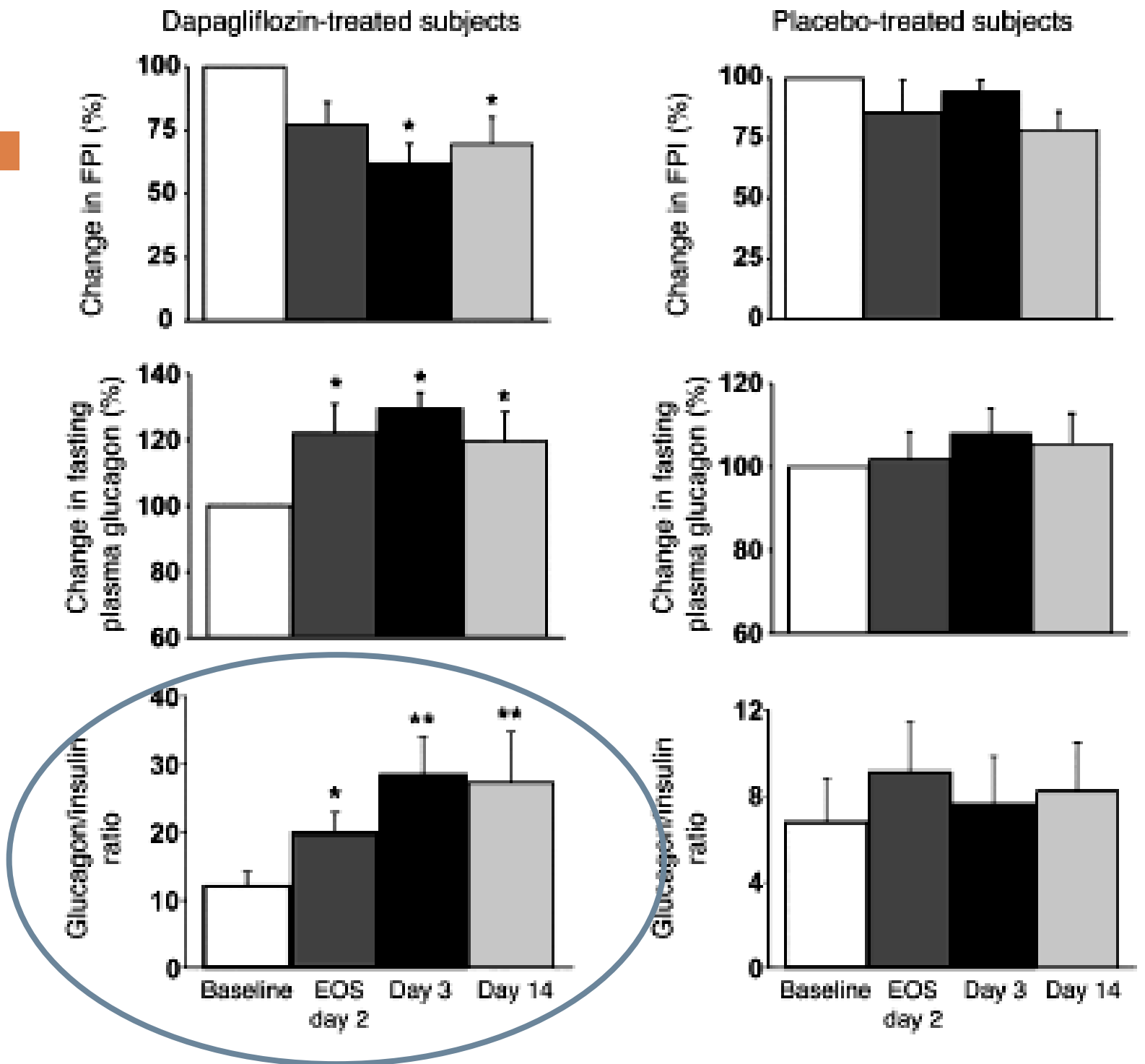


Figure 2

Basal EGP before and after ingestion of dapagliflozin or placebo EGP was measured on day 0 with the euglycemic clamp, on days 1 and 2 before subjects ingested dapagliflozin or placebo, and on days 2, 3, and 14 during dapagliflozin treatment. Note the break in the time scale (*x* axis) between days 2 and 3 and between days 3 and 14.

J Clin Invest. 2014;124(2):509–514.



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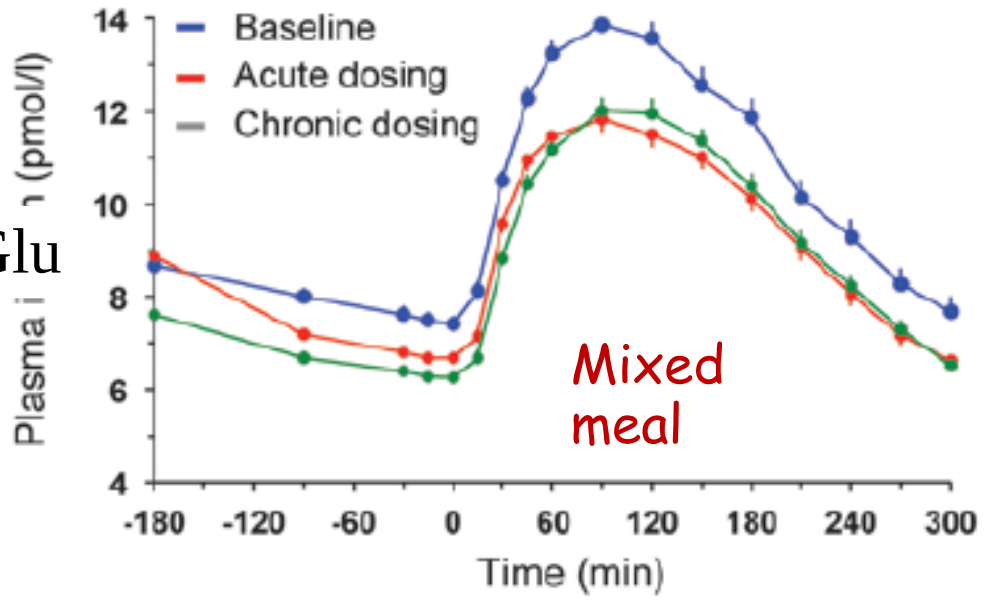
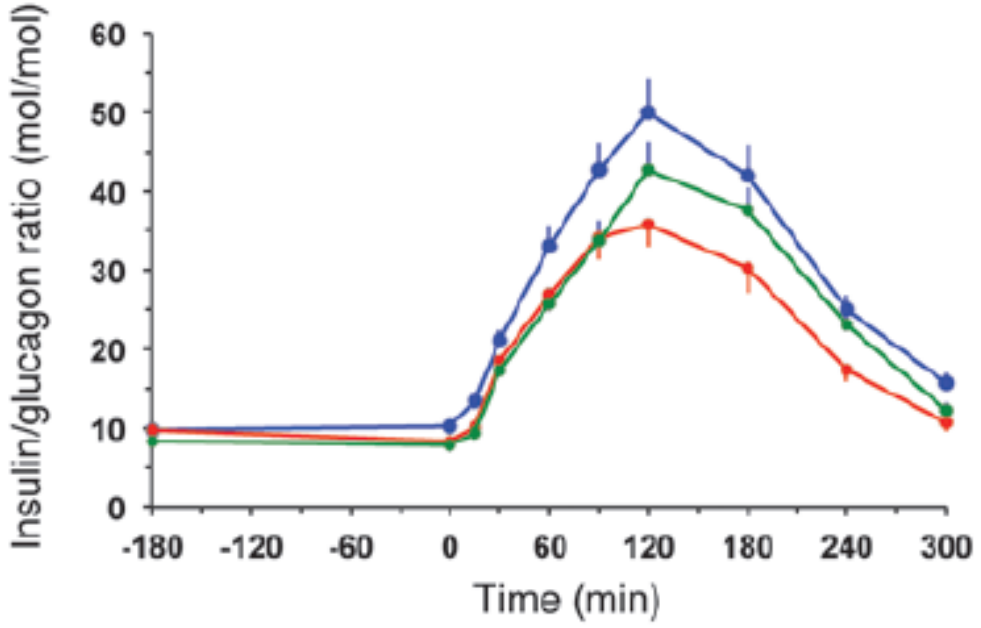
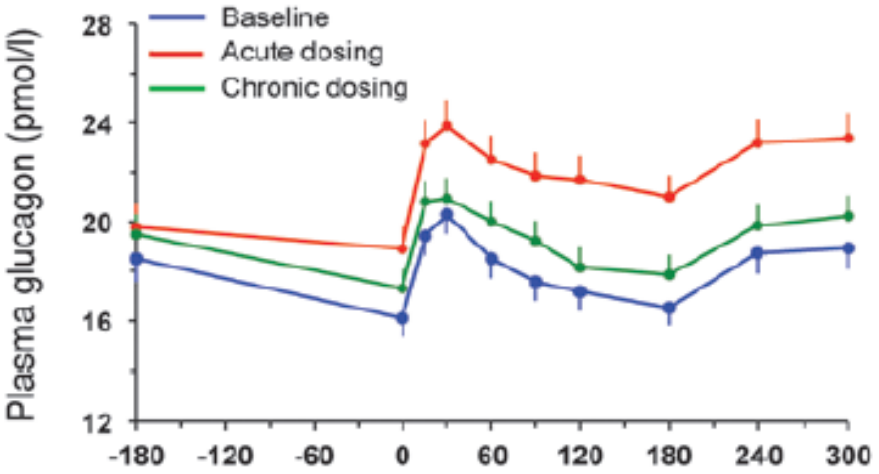
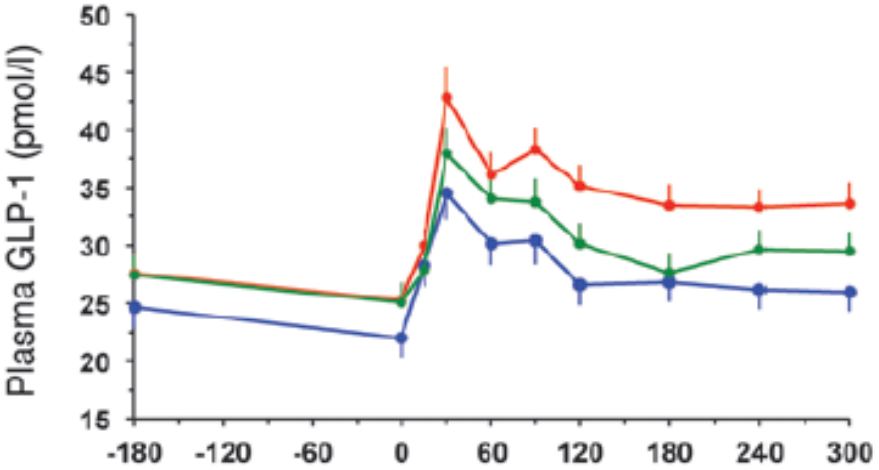
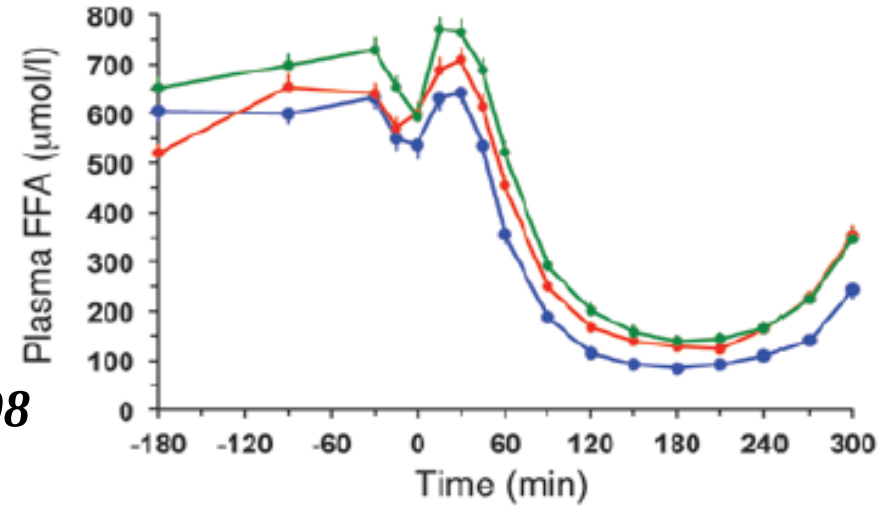
Glu











Ferrannini, J Clin Invest. 2013;124(2):499–508

Metabolic response to sodium-glucose cotransporter 2 inhibition in type 2 diabetic patients

Ele Ferrannini,[1] Elza Muscelli,[1] Silvia Frascerra,[1] Simona Baldi,[1] Andrea Mari,[2] Tim Heise,[3] Uli C. Broedl,[4] and Hans-Juergen Woerle[4]

Table 2

Glucose, hormones, and FFA during the meal[A]

	Baseline	Acute	Chronic	P^B	P^C
AUC_G ($g \cdot dl^{-1} \cdot h$) [IQR]	57 [16]	51 [11]	51 [10]	<0.0001	<0.0001
AUC_I ($nmol \cdot l^{-1} \cdot h$) [IQR]	93 [65]	80 [59]	76 [59]	<0.0001	<0.0001
AUC_{Glg} ($nmol \cdot l^{-1} \cdot h$)	1.07 ± 0.32	1.33 ± 0.42	1.15 ± 0.36	<0.0001	0.0005
Meal I/Glg ratio (mol/mol) [IQR]	29 [19]	22 [17]	24 [19]	<0.0001	<0.0001
$AUC_{GLP\text{-}1}$ ($nmol \cdot l^{-1} \cdot h$)	8.7 ± 4.1	10.4 ± 3.9	9.2 ± 3.9	0.0013	NS
AUC_{GIP} ($nmol \cdot l^{-1} \cdot h$)	38.3 ± 38.4	39.8 ± 43.7	36.5 ± 43.1	NS	NS
AUC_{FFA} ($mEq \cdot l^{-1} \cdot h$)	68 ± 23	86 ± 29	94 ± 33	<0.0001	<0.0001
Insulin MCR ($l \cdot min^{-1} \cdot m^2$)	1.20 ± 0.42	1.32 ± 0.46	1.43 ± 0.53	<0.0001	<0.0001

Table 4

Glucose fluxes in the fasting state and during the meal (5 hours)[A]

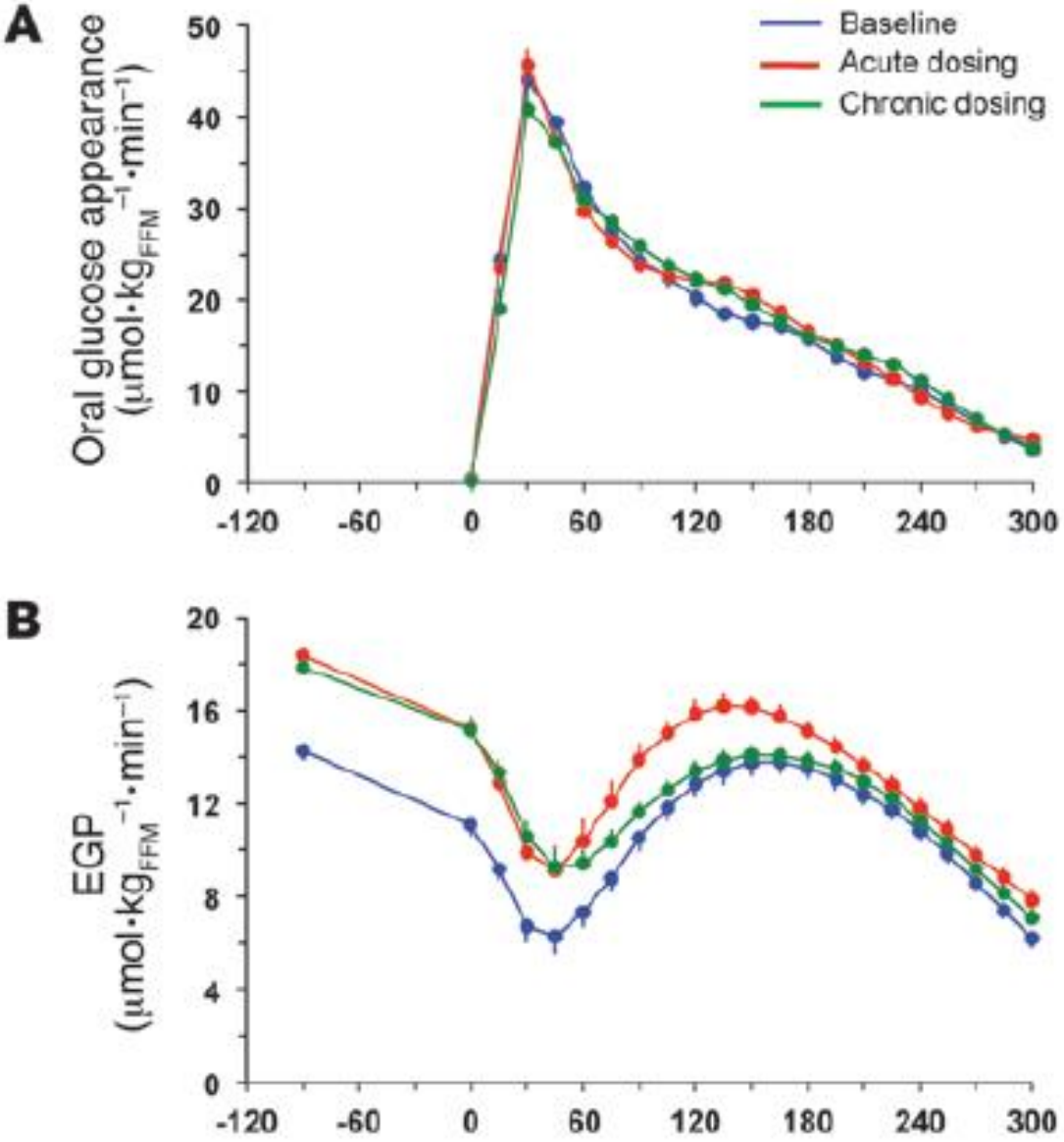
	Baseline	Acute	Chronic	P^B	P^C
Fasting EGP ($\mu mol \cdot kg_{FFM}^{-1} \cdot min^{-1}$) [IQR]	13.8 [5.2]	17.6 [4.8]	17.5 [4.1]	<0.0001	<0.0001
Fasting TGD ($\mu mol \cdot kg_{FFM}^{-1} \cdot min^{-1}$) [IQR]	14.9 [5.4]	14.8 [5.2]	12.9 [4.5]	NS	<0.0001
RaO_{AUC} (g) [IQR]	61 [14]	62 [15]	63 [12]	NS	NS
EGP_{AUC} (g) [IQR]	34 [11]	40 [14]	37 [11]	<0.0001	0.0028
RaT_{AUC} (g) [IQR]	95 [15]	102 [12]	98 [12]	<0.0001	0.0033
Rd_{AUC} (g) [IQR]	95 [18]	102 [16]	99 [13]	<0.0001	NS
TGD_{AUC} (g) [IQR]	93 [18]	75 [16]	70 [21]	<0.0001	<0.0001
Insulin sensitivity ($ml \cdot kg_{FFM}^{-1} \cdot min^{-1} \cdot nM^{-1}$)	8.2 [5.8]	9.1 [6.7]	8.6 [8.0]	0.0226	NS

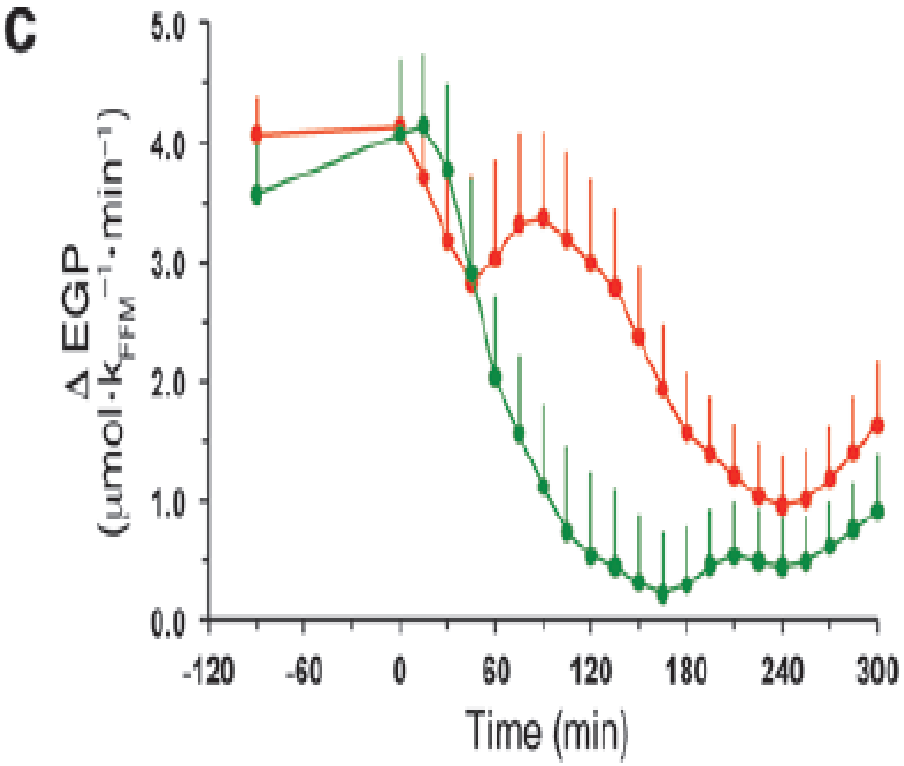
[A]Data are median [IQR]; correspondingly, *P* values are from Wilcoxon signed-rank testing (P^B = acute vs. baseline, P^C = chronic vs. baseline). RaT, rate of total glucose appearance.

J Clin Invest. 2013;124(2):499–508

Metabolic response to sodium-glucose cotransporter 2 inhibition in type 2 diabetic patients

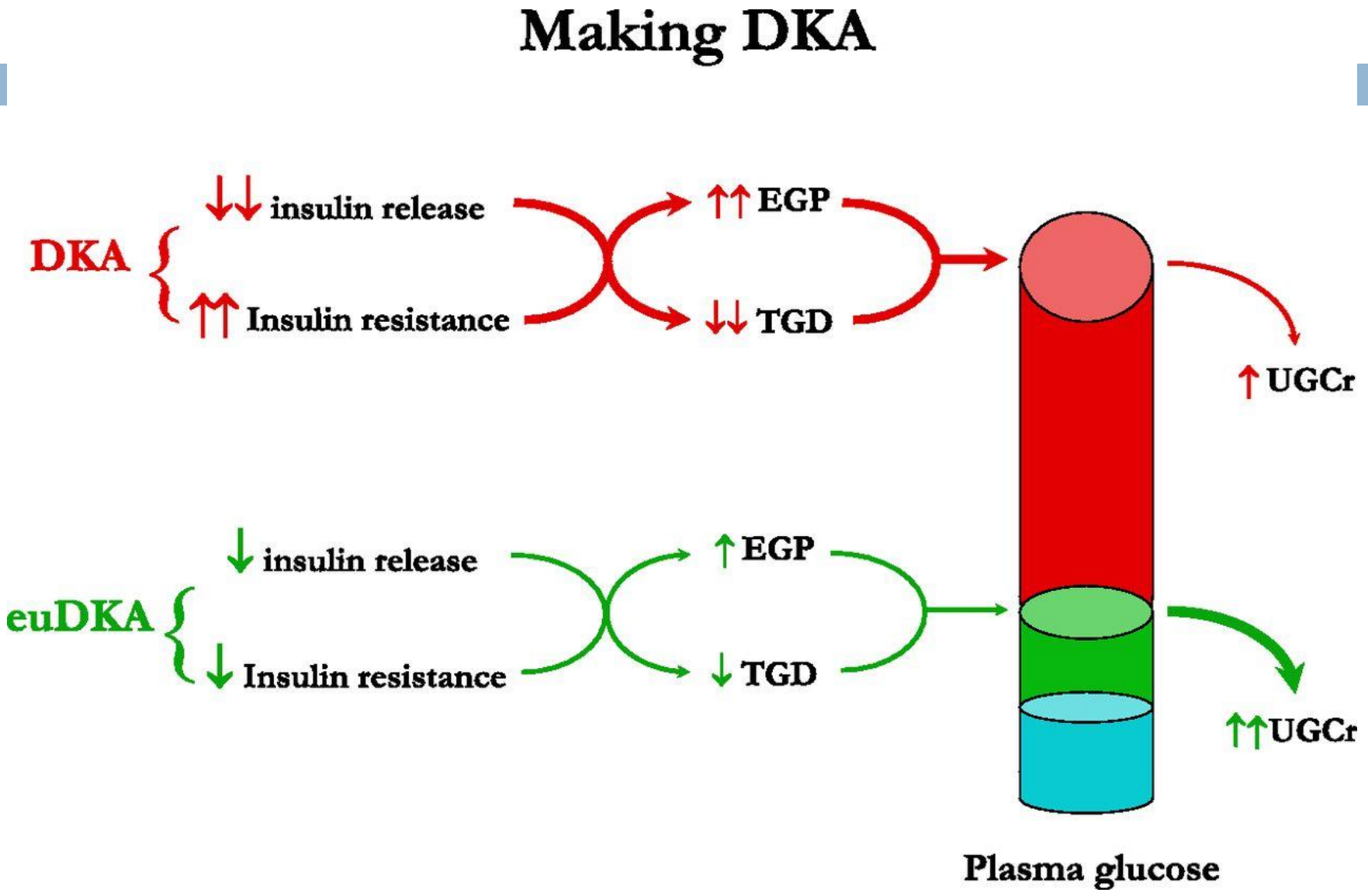
Ele Ferrannini,[1] Elza Muscelli,[1] Silvia Frascerra,[1] Simona Baldi,[1] Andrea Mari,[2] Tim Heise,[3] Uli C. Broedl,[4] and Hans-Juergen Woerle[4]





J Clin Invest. 2013;124(2):499–508

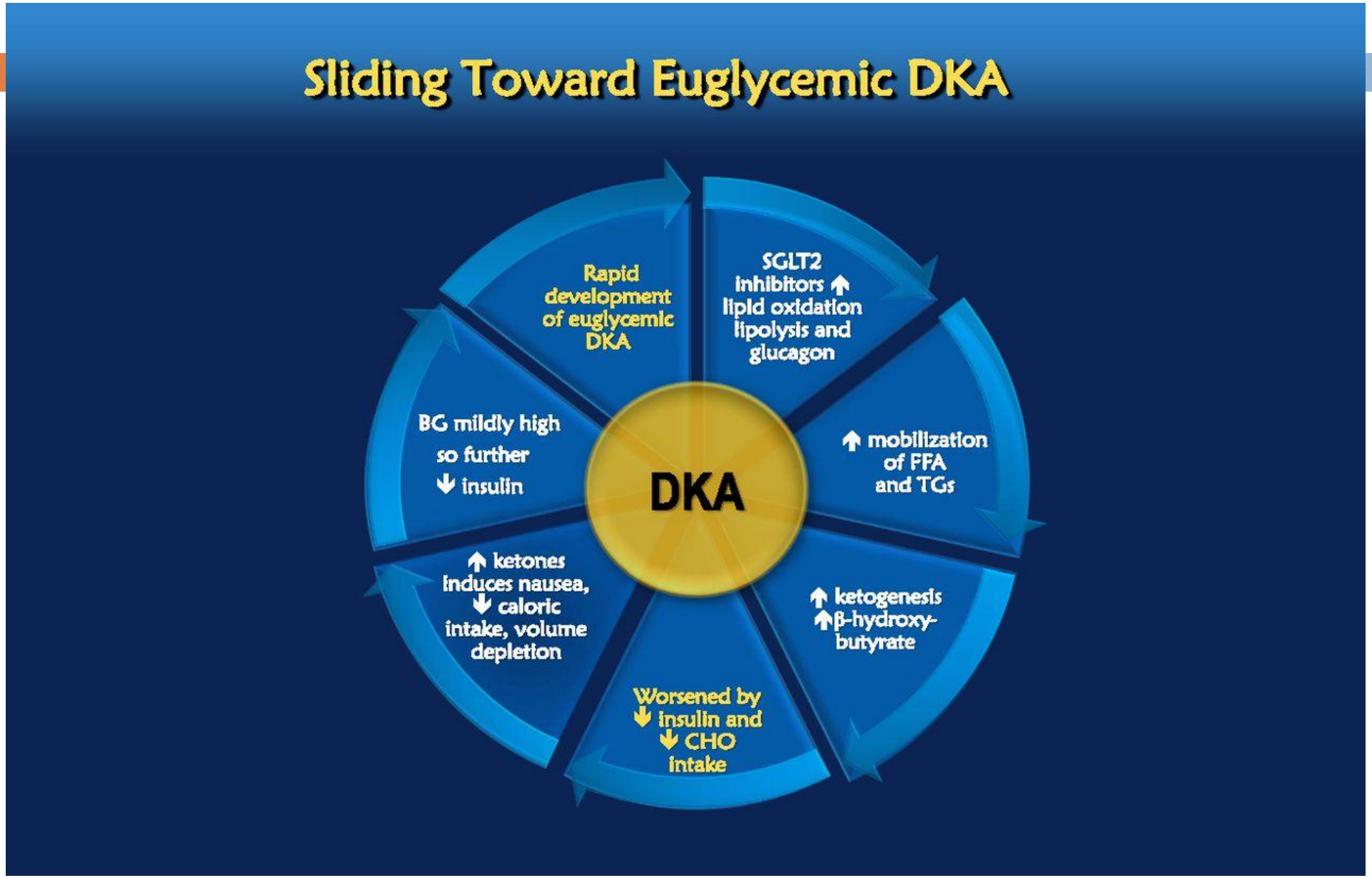
Essential pathophysiology of DKA and euDKA consequent of the use of SGLT2 inhibitors.



Julio Rosenstock, and Ele Ferrannini
Dia Care 2015;38:1638-1642

American Diabetes Association.

Demonstration of the cascade of clinical events and metabolic changes that contribute sequentially to progressive clinical deterioration and development of full-blown episodes of euDKA.



Julio Rosenstock, and Ele Ferrannini Dia Care 2015;38:1638-1642

American Diabetes Association.

Some do, some don't

Explaining why, of the estimated 40,000 patients taking these medications, only a small proportion ever manifest euDKA is obscure. One possible mechanism ***involves alterations in the metabolism of these drugs through genetic mutations***. The normal metabolic pathway for the SGLTinhs involves UGT1A9 producing inactive metabolites. However, ***known polymorphisms of UGT1A9*** (potentially allele *3 and *22) may alter the expression of genes coding UGT1A9 and alter its metabolic activity. **The end result being active drug accumulation leading to profound glucosuria, insulin secretion depression and subsequently FFA oxidation.** Although the clinical implications of this polymorphism aren't known and pharmacogenomic research rarely leads to cost effective screening methods to prevent given adverse events.

Αντιμετώπιση

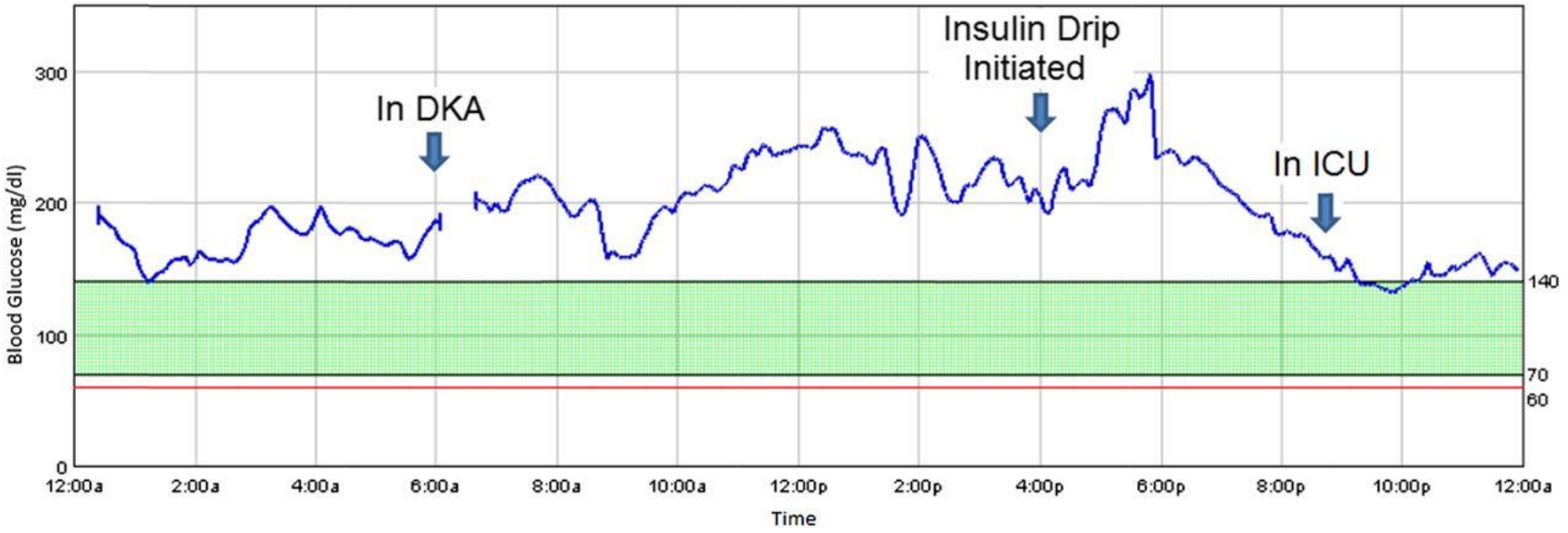
- In terms of management, these patients ***should be treated as any other DKA patient would.***
- Failure to start insulin with dextrose will cause the outlined mechanism to persist and potential worsening of the metabolic picture. That may mean starting an insulin drip at 0.1 unit/kg/hr with D10W on a patient with a glucose of 130 mg/dL. These patients should be responsive to insulin/dextrose since the pathophysiology does not involve exacerbated insulin resistance. ***there is no evidence suggesting lower insulin doses should be substituted for conventional dosing for DKA.***
- When considering the patient's home diabetes regimen, they should no longer receive any of the SGLT2inh since the manifestation of euDKA should be considered a class effect.

One-day CGM reading of case patient #3 on the day of admission to the ICU in euDKA.

Anne L. Peters et al. Dia Care 2015;38:1687-1693

American Diabetes Association.

One-day CGM reading of case patient #7 the day of admission to the ICU in euDKA.



Anne L. Peters et al. Dia Care 2015;38:1687-1693

American Diabetes Association.

Περιστατικό αντιμετώπιση

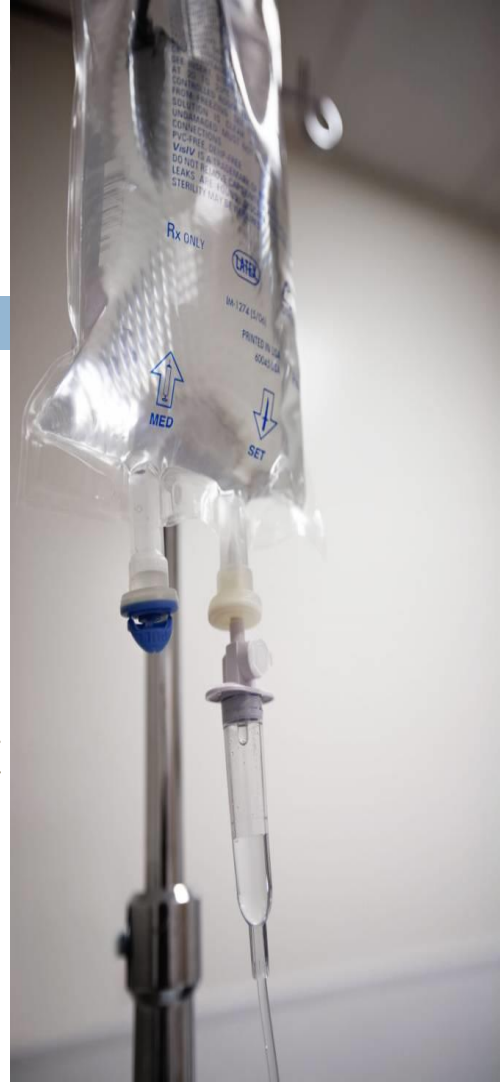
- Διακοπή N/S. Απαξ χορήγηση NaHCO3 44meq
- Ετέθη D/W 10% + 3NACl στα 120ml/h

και παράληλα αντλία ινσουλίνης με ρυθμό 5iu/h.

5 ώρες μετά ο ασθενής άρχισε να αισθάνεται καλύτερα και μπόρεσε να σιτιστεί με υδατάνθρακα + rapid acting insulin επιπλέον

Χρειάστηκαν 48 ώρες για να αποκατασταθεί στο φυσιολογικό η οξεοβασική ισορροπία, με τιμές σακχάρου <130 και D/W 10% + 3Na+3K συνεχώς.

Ο ασθενής έλαβε οδηγίες που δεν περιελάμβαναν γλιφλοζίνη στο εξής



DIABETIC KETOACIDOSIS ORGANIZATION

Management of DKA

- Resolve ketosis[a]
  - IV glucose or saline
  - IV insulin
  - Monitor potassium level
  - Assess need for bicarbonate drip
- Potential DKA triggers[b]
  - Infection
  - Acute illness changes (eg, urinary tract infection, gastroenteritis, influenza, or trauma)
  - Urosepsis
  - Reduced caloric or fluid intake
  - Reduced insulin dose

a. Kitabchi AE, *Diabetes Care*. 2004;27:S94-S102.[8]
b. FDA website.[4]

Take-Away Points

- Patients on SGLT2 inhibitors need to be educated on the risks of DKA
- Healthcare providers need to be aware of the signs and symptoms of DKA in order to make a prompt diagnosis, and treat accordingly
- DKA presents atypically: high anion gap metabolic acidosis with elevated urine or serum ketones

Peters AL, et al. *Diabetes Care.* Jun 15. [Epub ahead of print][5]

Benefits of SGLT- Inhibitors