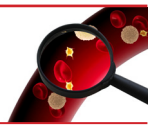
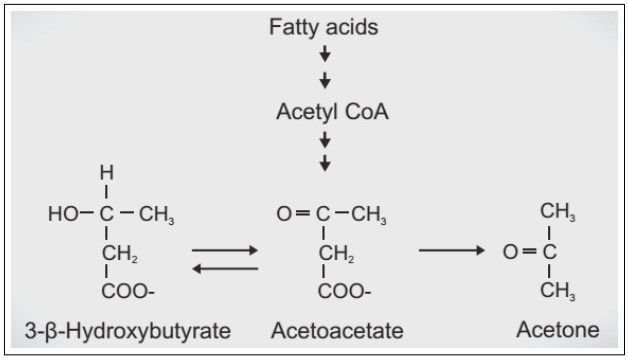
THE PATHCARE NEWS

β-Hydroxybutyrate at the Bedside



Diabetic ketoacidosis

Diabetic ketoacidosis (DKA) is a serious complication of diabetes mellitus, and consists of the biochemical triad of ketosis, hyperglycaemia and acidaemia. DKA usually occurs as a result of an absolute or relative insulin deficiency and an increase in counter-regulatory hormones, such as glucagon, cortisol, growth hormone and catecholamines. This hormone imbalance enhances glycogenolysis and gluconeogenesis, resulting in hyperglycaemia. Increased lipolysis increases free fatty acid levels, which are metabolised to ketones as an alternative energy source. This results in the accumulation of ketone bodies (acetoacetate (AcAc), β-hydroxybutyrate (β-OHB) and acetone) and a consequent metabolic acidosis. Acetone is formed by spontaneous decarboxylation of AcAc and is excreted by the lungs, and is responsible for the sweet odour on the breath of DKA patients. β-OHB is the dominant ketone in DKA.



Monitoring of ketones

It is now well recognised that elevated glucose in DKA is really only a surrogate for the underlying metabolic abnormalities, and the resolution of DKA depends upon suppression of ketosis. The measurement of ketones now represents best practice in monitoring response to treatment.[1] Indeed, some patients may present with "euglycaemic ketoacidosis", where glucose may not be particularly raised.

In DKA the highly reduced environment of mitochondria results in the accumulation of β-OHB to as much as 10 times more than AcAc,[2] from a ratio of 1:1 in health.[3] The widely used dipstix test for ketones only measures AcAc, which in untreated DKA is at a lower concentration than β-OHB. During recovery relatively more AcAc is produced, leading to the erroneous impression of worsening ketosis owing to increased concentration as measured by dipstix, which may lead to inappropriate treatment. The lack of a quantitative result is also a drawback of dipstix ketone measurement, particularly when monitoring response to therapy.

Quantitative ketone measurement at the bedside

Convenient access to blood gas and electrolyte analysis is relatively common, and bedside assessment of glucose, electrolytes, pH and bicarbonate is possible. Recent developments have allowed us to focus on ketosis, the underlying metabolic abnormality. Its measurement in blood using a portable ketone meter avoids the problems associated with dipstix measurement, and provides a result at the bedside. Guidelines have incorporated the use of bedside measurement of ketones into the management of DKA.[4] A recent South African study has shown the Abbott β-OHB portable quantitative ketone meter to be a reliable alternative to formal serum ketone measurement.[5]

Specimen requirements

Capillary whole blood.

Diagnosis of ketosis (Abbott β-OHB ketone meter)

β-OHB <1 mmol/L: No significant ketosis

β-OHB 1-3 mmol/L: Interpret with clinical findings and acid-base state

β-OHB >3 mmol/L: Unequivocal DKA in the presence of uncontrolled hyperglycaemia

In summary

- Ketones represent the underlying metabolic abnormality in DKA
- β-OHB is the dominant ketone in DKA
- Diagnosis of ketosis is made and treatment of DKA is monitored through the measurement of β-OHB
- Bedside quantitative measurement of β-OHB is now recommended

References

1) Wiggam, MI *et al.* (1997) Diabetes Care 20:1347-1352.
2) Sheikh-Ali, M *et al.* (2008) Diabetes Care 31:643-647.
3) Brewster, S *et al.* (2017) Pract. Diabetes 34:13-15.
4) Savage, MW *et al.* (2011) Diabet. Med. 28:508-515.
5) Coetzee, A *et al.* (2015) SAMJ 105:756-759.

Compiled by

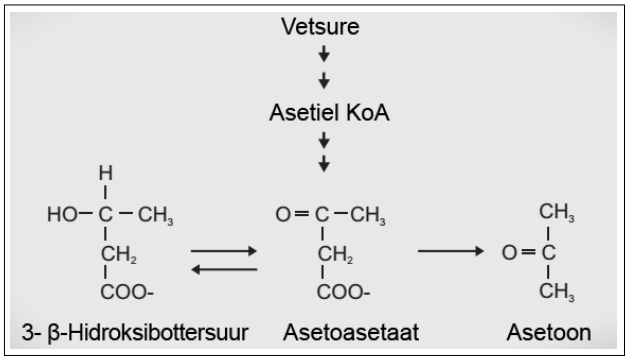
Dr Philip Fortgens (Chemical Pathologist), PathCare, Cape Town

DIE PATHCARE NUUS

Sykamerondersoek vir β-Hidroksibottersuur

Diabetiese ketoasidose

Diabetiese ketoasidose (DKA) is 'n ernstige komplikasie van diabetes mellitus en bestaan uit die biochemiese triade van ketose, hiperglisemie en asidemie. DKA ontstaan gewoonlik as gevolg van 'n absolute of relatiewe insulientekort en 'n toename in teenregulerende hormone, soos glukagon, kortisol, groeihormoon en katesjolamiene. Hierdie hormoonwanbalans verhoog glikogenolise en glukoneogenese, wat hiperglisemie tot gevolg het. Verhoogde lipolise verhoog vry vetsuurvlakke, wat afgebreek word tot ketone as 'n alternatiewe energiebron. Dit veroorsaak die ophoping van ketoonliggame (asetoasetaat (AsAs), β-hidroksibottersuur (β-OHB) en asetoon) en 'n gevolglike metaboliese asidose. Asetoon word gevorm deur spontane dekarboksilering van AsAs en word deur die longe uitgeskei. Dit is die rede dat DKA-pasiënte se asem 'n soet reuk het. β-OHB is die dominante ketoon in DKA.



Monitering van ketone

Daar word nou algemeen aanvaar dat verhoogde glukose in DKA in werklikheid slegs 'n surrogaat vir die onderliggende metaboliese abnormaliteite is, en dat die resolusie van DKA afhanklik is van die onderdrukking van ketose. Die meting van ketone word tans beskou as beste praktyk om die respons op behandeling te moniteer.[1] Trouens, sommige pasiënte mag met "euglisemiese keto-asidose" presenteer, waar glukose nie noemenswaardig verhoog mag wees nie.

In DKA veroorsaak die hoogs gereduseerde mitochondria-omgewing die ophoping van β-OHB tot soveel as 10 keer meer as AsAs,[2] teenoor 'n verhouding van 1:1 in gesondheid.[3] Die doopstokkie-toets vir ketone wat algemeen gebruik word, meet slegs AsAs, wat in onbehandelde DKA 'n laer konsentrasie het as β-OHB. Tydens herstel word relatief meer AsAs geproduseer. Dit gee die foutiewe indruk van verergerende ketose te wyte aan verhoogde konsentrasie soos deur die doopstokkie-toets gemeet, en mag tot ontoepaslike behandeling lei. Die afwesigheid van 'n kwantitatiewe resultaat is 'n verdere nadeel van doopstokkie-meting van ketone, veral wanneer die respons op behandeling gemoniteer word.

Kwantitatiewe ketoonmeting as sykamerondersoek

Die beskikbaarheid van bloedgas- en elektrolietbepaling is relatief algemeen, en sykamerondersoeke vir glukose, elektroliete, pH en bikarbonaat kan uitgevoer word. Onlangse ontwikkelings stel ons in staat om die aandag op die onderliggende metaboliese abnormaliteit, naamlike ketose, toe te spits. Die meting van ketone in bloed met behulp van 'n draagbare ketoonmeter oorkom die probleme wat met doopstokkie-meting verband hou, en maak sykamerondersoeke moontlik. Riglyne sluit die gebruik van sykamermeting van ketone in die hantering van DKA in.[4] 'n Onlangse Suid-Afrikaanse studie dui aan dat Abbott se draagbare kwantitatiewe β-OHB ketoonmeter 'n betroubare alternatief tot formele serumketoonmeting bied.[5]

Monstervereistes

Kapillêre heelbloed.

Diagnose van ketose (Abbott se β-OHB ketoonmeter)

β-OHB <1 mmol/L: Geen beduidende ketose

β-OHB 1-3 mmol/L: Interpreteer met kliniese bevindings en suur-basis status

β-OHB >3 mmol/L: Bevestigde DKA in die teenwoordigheid van ongekontrolleerde hiperglisemie

Ter opsomming

- Ketone verteenwoordig die onderliggende metaboliese abnormaliteit in DKA
- β-OHB is die dominante ketoon in DKA
- Diagnose van ketose word gemaak en die behandeling van DKA word gemoniteer deur β-OHB te meet
- Kwantitatiewe sykamermeting van β-OHB word tans aanbeveel

Verwysings

1) Wiggam, MI *et al.* (1997) Diabetes Care 20:1347-1352.

2) Sheikh-Ali, M *et al.* (2008) Diabetes Care 31:643-647.

3) Brewster, S *et al.* (2017) Pract. Diabetes 34:13-15.

3) Savage, MW *et al.* (2011) Diabet. Med. 28:508-515.

4) Coetzee, A *et al.* (2015) SAMJ 105:756-759.

Saamgestel deur

Dr Philip Fortgens (Chemiese Patoloog), Pathcare, Kaapstad