中文題目：療效與風險：慢性腎臟病人使用 Metformin 引起之乳酸中毒

英文題目：Weighing Risks and Benefits: Metformin Associated Lactic Acidosis in A Patient with Stage 3 Chronic Kidney Disease

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Background:

After the first Biguanide derivative, Phenformin was introduced on market in the 1950s and withdrawn in the 1970s, the strong correlation between Biguanide and increasing risk of lactic acidosis was discovered. As Metformin become the drug of choice for first line anti-diabetic agent nowadays, the concern of metformin associated lactic acidosis (MALA) arises besides its benefit, especially in patient with impaired renal function.

Case presentation:

A 80 years old male was brought to our ER due to sudden onset chest tightness and vomiting for 2 times for one day.

He has the history of type 2 DM, CKD stage 3(baseline creatinine 1.8mg/dl, eGFR 36ml/min/1.73m2), hypertension and old CVA. He previously took Glimet (Glimepiride2mg/Metformin500mg) 1 tab QD, Glucophage (Metformin 850mg) 1 tab QD and Trajenta (Linagliptin 5mg) 1 tab QD for DM control. However, the dose of Glimet was titrated to 1.5 tab QD 3 weeks ago, resulting in daily Metformin dose increased from 1350mg/day to 1600mg/day.

Soon after his arrival at ER, loss of consciousness occurred. His heart rate was 38/min, and blood pressure was unmeasurable. EKG revealed 3rd degree AV block. Atropine, Dopamine pump, transcutaneous pacemaker and endotracheal intubation were administered right away. Arterial gas analysis showed severe metabolic acidosis (pH 7.113, PCO2 17.8mmHg, HCO3 8.1mEq/L, BE -21.9), with high anion gap [Na 132mEq/L – Cl 103mEq/L - HCO3 8.1mEq/L +2.5*(4- Alb 3.9g/dl) =21].
Further laboratory data showed hyperkalemia 7.4mmol/L, deteriorated renal function (Creatinine 4.0mg/dl, eGFR 14ml/min/1.73m2), and elevated lactate 13.1mmol/L.

He was then admitted to ICU under the impression of 1. Shock, favor cardiogenic (3rd degree AV block), caused by lactic acidosis and hyperkalemia, and 2. Acute kidney injury. Emergent hemodialysis with CVVH was arranged after failed sodium bicarbonate treatment to correct acidosis.

We sent blood sample (obtained before CVVH) to the poison center in TPEVGH to evaluate the plasma Metformin level, which revealed an extremely high level of

12.427μg/ml, while the therapeutic range is 1-2μg/ml.

Final diagnosis:

Cardiogenic shock, metformin associated lactic acidosis and/or hyperkalemia induced

Discussion:

Metformin was recommended for first-line medication for type 2 DM due to its relatively low cost, and potential benefit effect on cardiovascular risk. However, MALA, the rare but potentially life-threatening adverse effect, causes a dilemma for its use in patients with impaired renal function.

The risk factor of MALA including conditions related to increase production or reduce clearance of lactate, e.g. sepsis, decompensated heart failure, hypoxia, shock and hepatic/renal impairment. A plasma Metformin level > 5μg/ml also increase the risk of MALA, as the therapeutic dose is 1-2μg/ml.

Despite lack of solid evidence, hemodialysis was recommended for the treatment of MALA. It not only corrects the acidosis, but also efficiently eliminates metformin from plasma.

In patient presented with lactic acidosis, as in this patient, medication history should be clarified, to recognize the potential development of MALA.

關鍵字: 二甲雙胍，乳酸中毒，第二型糖尿病，慢性腎臟病

Key words: Metformin associated lactic acidosis, Biguanide, Type 2 Diabetes Mellitus, Chronic kidney disease