American Journal of Ethnomedicine, 4:2
DOI: 10.21767/2348-9502-C1-003

Cost-utility analysis of combination therapy of type 2 diabetes mellitus in Ukraine

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Background: Type 2 diabetes mellitus (T2DM) is a serious medical and social problem. T2DM has a severe and progressive course, complications, metabolic disorders and high disability, which significantly reduce the quality of life of patients.

Objectives: To evaluate the cost-utility of the therapy regimes with Metformin+Glibenclamide compared with Metformin+Glimepiride and Metformin+Gliclazide.

Methods: The decision tree model was used to estimate the incremental costs and quality-adjusted life expectancy in patients with T2DM by health economics methods. 150 questionnaires to determine the quality of life of patients with T2DM were used. These patients were treated in the endocrinology clinics of Podolsky region of Ukraine in 2011-2013. The quality of life of patients was determined by visual analogue scale adapted European questionnaire of quality of life EuroQol-5D. The patients were examined on the following parameters: age, duration of T2DM, body mass index, the average fasting plasma glucose, cost-utility ratios. It has been found that patients with Metformin+Glibenclamide regime were significantly older, with the largest T2DM duration, with the highest body mass index and highest levels of fasting plasma glucose, cheapest cost-utility ratio. In comparing patients with Metformin+Gliclazide and Metformin+Glimepiride regimes it was found no other significant differences ($p>0.05$). Calculations take into account the direct costs only. Treatment costs were estimated on the basis of average wholesale government drug price list as at 12.06.2014. To determine the stability of results sensitivity analysis was performed.

Results: The decision tree model predicted that Metformin+Glibenclamide therapy regime has cheapest cost-utility ratio; when compared Metformin+Glibenclamide therapy regime with Metformin+Glimepiride an incremental cost-utility ratio was 60 UAH and while gaining 0.11±0.04 quality-adjusted life-years (QALYs). Compared Metformin+Glibenclamide therapy regime with Metformin+Gliclazide an incremental cost-utility ratio was 318 UAH and while gaining 0.14±0.01QALYs.

Conclusions: Scheme of combined therapy Metformin+Glibenclamide has cost-utility advantages in comparison with other combined schemes of T2DM.

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Coronary flow regulation by adenosine it's signaling

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Adenosine acts through its receptors (A1, A2A, A2B, and A3) via G-proteins and causes an increase in Coronary Flow (CF) mostly through A2A AR. However, the role of other ARs in the modulation of CF is not well understood. Using KOs, we investigated the role for each AR in the regulation of CF. Using the isolated heart from A3 KO mice; we reported an increase in A2A-mediated CF. Similarly, we found an increase in CF in A1 KO mice with A2A agonist (CGS-21680). Also, in A2A KO mice, response to CGS was abolished. On the other hand, A2A KO mice showed a decrease in CF to NECA (non-selective agonist). BAY60-6583 (A2B selective agonist) was without an effect on CF in A2B KO mice; however, it increased CF significantly in A2A KO. CGS also caused a significant increase in CF in A2B KO mice. Also, exogenous adenosine-induced increase in CF in WT, A2A KO, and A2B KO mice were significantly reduced with catalase. BAY-induced increase in CF in WT was significantly inhibited with glibenclamide. Overall, our data support stimulatory roles for A2A and A2B and inhibitory roles for A1 and A3 in the regulation of CF; these observations provide new evidence for the presence of all four ARs in CF regulation. We propose, that activation of A2A/B may release H2O2 which then activates KATP channels, leading to vasodilation. These studies may lead to better understanding of the role of ARs in coronary disease and may lead to better therapeutic approaches.

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