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Metformin's sidekick? The magical powers of SGLT-2 inhibitors in the management of type 2 diabetes mellitus

Summary by Edgar G. Dorsey-Trevino MD MMSc and Diana Othón-Martínez MD

Given that type 2 diabetes mellitus (T2DM) is one of the most prevalent diseases worldwide, the mention of first-line treatment should immediately invoke thoughts of metformin. However, what transpires when metformin alone proves insufficient? Which second-line agent should be prescribed to patients to maintain optimal blood sugar levels?

While sodium-glucose cotransporter 2 inhibitors (SGLT-2i) are garnering attention from primary care physicians due to their broad effects, the evidence supporting their use often includes participants who may not reflect the typical patient seen in everyday clinical practice, making it challenging to apply these results to real-life patients.

To address this gap, Bidulka and colleagues embarked on the challenge of using observational data to emulate a pragmatic randomized controlled trial utilizing a large database and advanced epidemiological methods. They enrolled 75,739 patients already on metformin who later received either SGLT-2i, sulfonylureas, or dipeptidyl peptidase-4 inhibitors (DPP-4i) as part of their treatment for uncontrolled hyperglycemia. The primary objective was to observe changes in HbA1c levels after one year. Additionally, they examined BMI, systolic blood pressure, kidney function, and a combination of renal and cardiac events.

Their sophisticated statistical analysis found that SGLT-2i significantly outperformed sulfonylureas and DPP-4i in lowering HbA1c, reducing systolic blood pressure, and mitigating the risk of hospital readmission due to heart failure and worsening kidney function. In contrast, other clinical parameters did not show significant differences.

Although some may criticize this study for its observational nature, it nevertheless provides valuable insights for primary care physicians managing patients with T2DM. This research suggests that SGLT-2i could offer significant clinical benefits in the routine management of real-world patients compared to other common oral antidiabetic drugs added to metformin.

Image 1. AI-generated image depicting the clash between T2DM therapeutic options. Clinical results demonstrated some significant changes favoring SGLT2 against sulfonylureas and DPP-4i, as well as some similarities.

For more information, visit:
https://doi.org/10.1136/bmj-2023-077097

Prolonged infusions of β-lactam antibiotics. The future of sepsis management?

Summary by Ramon Elizondo, MD

A recent study investigated whether prolonged infusions of β-lactam antibiotics improve survival in critically ill adults with sepsis or septic shock compared to standard intermittent-shorter doses. Sepsis and septic shock are serious conditions with high mortality rates, so finding the best antibiotic strategy is crucial. The goal was to determine if longer infusions of β-lactam antibiotics lower the chances of dying within 90 days compared to shorter, intermittent doses.

The research included a systematic review and meta-analysis of randomized clinical trials that compared prolonged and intermittent infusions of β-lactam antibiotics. The study analyzed data from 18 trials with 9,108 critically ill adults, with a median age of 54 years, and 65% of them were men.

The intervention involved administering β-lactam antibiotics either continuously or for an extended period, compared to the standard intermittent method. The primary outcome measured was 90-day all-cause mortality, with secondary outcomes including ICU mortality, clinical cure rates, microbiologic cure, adverse events, and ICU length of stay.

Key findings were:

- Prolonged infusions reduced 90-day mortality with a risk ratio of 0.86, showing a high certainty of benefit (99.1% probability).
- Reduced ICU mortality with a risk ratio of 0.84.
- Increased clinical cure rates with a risk ratio of 1.16.
- No significant differences were observed in microbiologic cure, adverse events, and ICU length of stay.

Strengths of the study included its robust methodology, large participant pool, and diverse data sources, enhancing the reliability and generalizability of the findings. Weaknesses involved heterogeneity in trial designs and implementation, possible insufficient statistical power in subgroup analyses, and variability in outcome assessment across trials.

In conclusion, longer β-lactam infusions significantly reduce the 90-day death rate in critically ill patients with sepsis or septic shock compared to intermittent infusions. This evidence supports using prolonged infusion as a standard practice to improve survival and clinical outcomes. More research is needed to fine-tune treatment protocols for specific patient subgroups.

For more information, visit:
https://jamanetwork.com/journals/jama/fullarticle/10.1001/jama.2024.9803?utm_campaign=articlePDF%26utm_medium=articlePDFlink%26utm_source=articlePDF%26utm_content=jama.2024.9803

The battle of antiplatelet therapy: Extended Clopidogrel Monotherapy vs DAPT in Patients With ACS

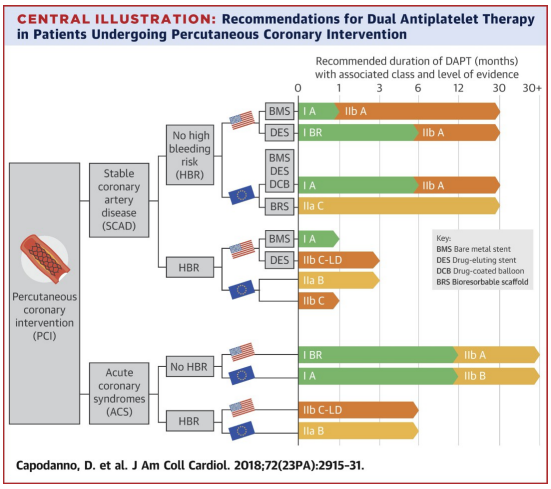
Summary by: Eunbee Cho MD and Jian García-Cruz MD

Introduction of DAPT

According to the ACC/AHA and ESC (European Society of Cardiology), the standard duration of DAPT after PCI with DES (drug-eluting stent) implantation is at least 6 months to 12 months in most clinical settings (class I recommendation). However, what happens beyond that period? The OPT-BIRISK trial was conducted to determine the optimal strategy for patients who have high risks of both bleeding and ischemic events.

Study End-points

The study primary endpoint: BARC (Bleeding Academic Research Consortium) types 2, 3, 5 bleeding. The secondary endpoint MACCE (the incidence of major adverse cardiac and cerebral events).



Result of DAPT

The study found that extended clopidogrel monotherapy reduced bleeding compared to continued DAPT without further ischemic events. Among 7758 patients in the study, 3.3% of patients assigned to DAPT had BARC types 2, 3, or 5 bleeding compared to 2.5% allocated to clopidogrel monotherapy. The incidence of MACCE was 3.5% in the DAPT compared to 2.6% for monotherapy.

The results of this trial indicate that, among high bleeding and ischemic risk patients who had successfully completed 9-12 months of DAPT with aspirin and clopidogrel following DES PCI for an ACS presentation, clopidogrel monotherapy is superior to continued DAPT for an additional 9 months; reductions were noted in both ischemic and bleeding events. This result indicates that monotherapy with clopidogrel is equally effective and safer when compared to continuing DAPT.

For more information, visit:
https://jamanetwork.com/journals/jama/fullarticle/10.1001/jamacardio.2024.0534?utm_campaign=articlePDF%26utm_medium=articlePDFlink%26utm_source=articlePDF%26utm_content=jamacardio.2024.0534

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