Pharmacological Management of the Cardiac Patient with Complex Comorbid Diseases
Case

- 78 year old male
- Presented with breathlessness and was diagnosed with acute coronary syndrome
- COPD
- Diabetes mellitus with CKD
- Dyslipidaemia
- Allergic to Aspirin
**Blood investigations**
CKD stage 3 – Creatinine 136 umol/L
eGFR 44 ml/min

**2D echocardiogram**
- Dilated LV
- Global Hypokinesia
- Poor LV systolic function
- LVEF 22%
- No clot
- Moderate to severe MR
- Moderate AR/AS
- Moderate TR

**Myocardial Perfusion Study**
- Moderate ischemia in mid and distal LAD and severe ischemia in distal RCA territory
- Global impairment of left ventricular function
Coronary Angiogram
LMS – Tight ostial and distal stenosis
LAD – Tight ostial and proximal stenosis
LCX – Tight ostial and distal stenosis; moderate stenosis at proximal segment
RCA – Total occlusion from proximal segment

CT Chest
Small bullae in right upper and middle lobes and left upper lobe
Nodule in right upper lobe posterior segment (3cm)
**List of medications**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>T. Plavix</td>
<td>75 mg daily</td>
</tr>
<tr>
<td>T. Bisoprolol</td>
<td>1.25 mg daily</td>
</tr>
<tr>
<td>T. Digoxin</td>
<td>0.125 mg daily</td>
</tr>
<tr>
<td>T. Rosuvastatin</td>
<td>10 mg on</td>
</tr>
<tr>
<td>T. Frusemide</td>
<td>40 mg daily</td>
</tr>
<tr>
<td>T. Spironolactone</td>
<td>12.5 mg daily</td>
</tr>
<tr>
<td>MDI Berodual (20/50mcg)</td>
<td>2 puffs tds</td>
</tr>
<tr>
<td>T. Clonazepam</td>
<td>1 mg on</td>
</tr>
<tr>
<td>T. Janumet (50/500 mg)</td>
<td>1 tab bd</td>
</tr>
<tr>
<td>S/C Lantus</td>
<td>14 units daily</td>
</tr>
</tbody>
</table>

What medications would you prescribe?

1. Antiplatelet
2. Lipid lowering medications
3. Diabetic medications
4. COPD medications
5. Antifailure medications
1. Dual antiplatelet therapy

Requires dual antiplatelet therapy but allergic to Aspirin
Recommendations

Clopidogrel or Ticagrelor alone (2012 ACC AHA Focused Update Guidelines)

Advised against combination of 2 P2Y12 receptor inhibitors (no data)

ACC of Chest Physician for primary and secondary prevention of cardiovascular disease recommend the phosphodiesterase inhibitor cilostazol\(^1,2\)

Lack of outcomes data

Contraindicated in patients with heart failure

References


2. Lipid lowering medications

Chronic Kidney Disease causes
1. Hypertriglyceridemia
2. Elevated LDL-cholesterol
3. Low HDL-cholesterol

Would you use statins?

1. May suffer increased adverse effect from statins
2. End stage renal failure did not benefit from intensive lipid lowering efforts in terms of CVD, MI and Stroke
3. Statins are safe and effective in treating hyperlipidaemia and preventing cardiac death in earlier stages of CKD

References
The effects of lowering LDL cholesterol with simvastatin plus ezetimibe in patients with chronic kidney disease (Study of Heart and Renal Protection): a randomised placebo-controlled trial


Summary

Background Lowering LDL cholesterol with statin regimens reduces the risk of myocardial infarction, ischaemic stroke, and the need for coronary revascularisation in people without kidney disease, but its effects in people with moderate-to-severe kidney disease are uncertain. The SHARP trial aimed to assess the efficacy and safety of the combination of simvastatin plus ezetimibe in such patients.
Methods This randomised double-blind trial included 9270 patients with chronic kidney disease (3023 on dialysis and 6247 not) with no known history of myocardial infarction or coronary revascularisation. Patients were randomly assigned to simvastatin 20 mg plus ezetimibe 10 mg daily versus matching placebo. The key prespecified outcome was first major atherosclerotic event (non-fatal myocardial infarction or coronary death, non-haemorrhagic stroke, or any arterial revascularisation procedure). All analyses were by intention to treat. This trial is registered at ClinicalTrials.gov, NCT00125593, and ISRCTN54137607.

Findings 4650 patients were assigned to receive simvastatin plus ezetimibe and 4620 to placebo. Allocation to simvastatin plus ezetimibe yielded an average LDL cholesterol difference of 0·85 mmol/L (SE 0·02; with about two-thirds compliance) during a median follow-up of 4·9 years and produced a 17% proportional reduction in major atherosclerotic events (526 [11·3%] simvastatin plus ezetimibe vs 619 [13·4%] placebo; rate ratio [RR] 0·83, 95% CI 0·74–0·94; log-rank p=0·0021). Non-significantly fewer patients allocated to simvastatin plus ezetimibe had a non-fatal myocardial infarction or died from coronary heart disease (213 [4·6%] vs 230 [5·0%]; RR 0·92, 95% CI 0·76–1·11; p=0·37) and there were significant reductions in non-haemorrhagic stroke (131 [2·8%] vs 174 [3·8%]; RR 0·75, 95% CI 0·60–0·94; p=0·01) and arterial revascularisation procedures (284 [6·1%] vs 352 [7·6%]; RR 0·79, 95% CI 0·68–0·93; p=0·0036). After weighting for subgroup-specific reductions in LDL cholesterol, there was no good evidence that the proportional effects on major atherosclerotic events differed from the summary rate ratio in any subgroup examined, and, in particular, they were similar in patients on dialysis and those who were not. The excess risk of myopathy was only two per 10 000 patients per year of treatment with this combination (9 [0·2%] vs 5 [0·1%]). There was no evidence of excess risks of hepatitis (21 [0·5%] vs 18 [0·4%]), gallstones (106 [2·3%] vs 106 [2·3%]), or cancer (438 [9·4%] vs 439 [9·5%], p=0·89) and there was no significant excess of death from any non-vascular cause (668 [14·4%] vs 612 [13·2%], p=0·13).

Interpretation Reduction of LDL cholesterol with simvastatin 20 mg plus ezetimibe 10 mg daily safely reduced the incidence of major atherosclerotic events in a wide range of patients with advanced chronic kidney disease.
Rosuvastatin and Cardiovascular Events in Patients Undergoing Hemodialysis

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ABSTRACT

BACKGROUND
Statins reduce the incidence of cardiovascular events in patients at high cardiovascular risk. However, a benefit of statins in such patients who are undergoing hemodialysis has not been proved.

METHODS
We conducted an international, multicenter, randomized, double-blind, prospective trial involving 2776 patients, 50 to 80 years of age, who were undergoing maintenance hemodialysis. We randomly assigned patients to receive rosuvastatin, 10 mg daily, or placebo. The combined primary end point was death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke. Secondary end points included death from all causes and individual cardiac and vascular events.

RESULTS
After 3 months, the mean reduction in low-density lipoprotein (LDL) cholesterol levels was 43% in patients receiving rosuvastatin, from a mean baseline level of 100 mg per deciliter (2.6 mmol per liter). During a median follow-up period of 3.8 years, 396 patients in the rosuvastatin group and 408 patients in the placebo group reached the primary end point (9.2 and 9.5 events per 100 patient-years, respectively; hazard ratio for the combined end point in the rosuvastatin group vs. the placebo group, 0.96; 95% confidence interval [CI], 0.84 to 1.11; P=0.59). Rosuvastatin had no effect on individual components of the primary end point. There was also no significant effect on all-cause mortality (13.5 vs. 14.0 events per 100 patient-years; hazard ratio, 0.96; 95% CI, 0.86 to 1.07; P=0.51).

CONCLUSIONS
In patients undergoing hemodialysis, the initiation of treatment with rosuvastatin lowered the LDL cholesterol level but had no significant effect on the composite primary end point of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke. (ClinicalTrials.gov number, NCT00240331.)
3. Diabetic medications

T. Janumet (50/500 mg)  1 tab bd
S/C Lantus       14 units daily
4. COPD medications

- Cardiac manifestations of COPD
  - Impairment of RV dysfunction and pulmonary vascular disease
  - Correlate inversely with survival
  - Co-existence of COPD and CAD frequent
- Management strategies of CAD similar as without COPD
- Arrhythmias common
- Betablockers with caution generally safe with cardioselective agents (cardioselective betablockers such as Atenolol, Metoprolol 1,2.
  Two meta-analyses with chronic betablockers treatment – no adverse respiratory effect 1,2
- Carvedilol may be used (non selective of alpha and betablockers)
- No evidence of adverse respiratory effects
- Betablockers should not be routinely withheld in patients with COPD

References

Cardiac Dysrhythmias

- Multifocal atrial tachycardia
- High mortality rate\(^1\)
- SVT common after CABG in COPD patients (commonly AF and MAT)
- May persist for a long period of time causing hypotension, systemic embolization, congestive heart failure and anxiety\(^2\)
- RCT post CABG amidarone prophylaxis reduces incidence of SVT, MAT as well as hospital and ICU related length of stay\(^2\)
- MAT – rate controlled with betablockers or diltiazem
- Alternative Amiodarone and high dose magnesium\(^1\)

References

Respiratory treatment and dysrhythmias

Beta$_2$ agonist used in COPD - meta-analysis of 18 randomized trials involving beta$_2$ agonist use in COPD

Majority of the trials - long acting beta$_2$ agonist

Increased incidence of tachycardia and hypokalemia - ? increased cardiovascular death

TORCH (TOwards a Revolution in COPD Health) Study
- 6,000 patients with COPD
- Randomized to Salmeterol, Fluticasone, combination Salmeterol – Fluticasone, or placebo
- Conclusion: overall mortality, cardiovascular mortality and cardiovascular related adverse events were no greater in the salmeterol group compared with any of the other groups
Respiratory treatment and dysrhythmias (cont)

High dose steroid >7.5 mg/d – development of AF (reason unknown)

Proposed mechanism – potassium efflux, mineralocorticoid effect leading to hypertension, development of late potentials, vasodilation and possible anaphylaxis

Theophylline – predispose to tachyarrythmias even in the absence of elevated serum drug levels. Short term use increased arrhythmias, AF

Conclusions

Spectrum of CAD with COPD broad

Unique challenge in management of patients with COPD and CAD which appears to be additive with regard to morbidity and mortality
5. Antifailure medications

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TAKE HOME MESSAGES

Pharmacological Management of the Cardiac Patient with Complex Comorbid Diseases

1. Multidisciplinary team approach
   - Endocrinologist
   - Nephrologist
   - Respirologist
   - Cardiologist
   - General Physician
   - Geriatrician
   - Pharmacist

2. Polypharmacy with drug interactions should be avoided

3. Medications to be adjusted with progression of comorbid diseases

4. Optimal pharmacological multidisciplinary management to improve quality of life and reduction of long term MACE
Comparison of Physician and Computer Diagnostic Accuracy

The Institute of Medicine recently highlighted that physician-diagnostic error is common and information technology may be part of the solution.1 Given advancements in computer science, computers may be able to independently make accurate clinical diagnoses.2 While studies have compared computer to physician performance for reading electrocardiograms,3 the diagnostic accuracy of computers vs. physicians remains unknown. To fill this gap in knowledge, we compared the diagnostic accuracy of physicians with computer algorithms called symptom checkers.

Symptom checkers are websites and apps that help patients with self-diagnosis. After answering a series of questions, the user is given a list of rank-ordered potential diagnoses generated by a computer algorithm. Previously, we evaluated the diagnostic accuracy of 23 symptom checkers using 45 clinical vignettes.4 The vignettes included the patient’s medical history and had no physical examination or test findings. In this study, we compared the diagnostic performance of physicians with symptom checkers for those same vignettes using a unique online platform called Human Dx.

Methods: Human Dx is a web- and app-based platform on which physicians generate differential diagnoses for clinical vignettes. Since 2012, Human Dx has been used by over 27,000 physicians and trainees from 41 countries who have addressed over 100,000 vignettes.

Results: Of the 244 physicians who solved at least 1 vignette, 21 (50%) were in internal medicine and 41 (50%) were fellows or residents (Table 1). Physicians listed the correct diagnosis first more often when compared with symptom checkers (72.3% vs. 54.5%, P = .001) as well as in the top 3 diagnoses listed (84.3% vs. 51.2%, P = .001 (Table 2)).

### Table 1. Physician Diagnostic Accuracy Stratified by Physician Characteristic

<table>
<thead>
<tr>
<th>Physician Characteristic</th>
<th>Listed (%)</th>
<th>Listed in top 3 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All Physicians</strong></td>
<td>72.3</td>
<td>84.3</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>72.3</td>
<td>84.3</td>
</tr>
<tr>
<td>Female</td>
<td>72.3</td>
<td>84.3</td>
</tr>
<tr>
<td><strong>Area of practice</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>General medicine</td>
<td>72.3</td>
<td>84.3</td>
</tr>
<tr>
<td>Internal medicine</td>
<td>72.3</td>
<td>84.3</td>
</tr>
<tr>
<td><strong>Years in practice</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Under 10 years</td>
<td>72.3</td>
<td>84.3</td>
</tr>
<tr>
<td>10-20 years</td>
<td>72.3</td>
<td>84.3</td>
</tr>
<tr>
<td>21+ years</td>
<td>72.3</td>
<td>84.3</td>
</tr>
<tr>
<td><strong>Board Certification</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Board certified</td>
<td>72.3</td>
<td>84.3</td>
</tr>
<tr>
<td>Board not certified</td>
<td>72.3</td>
<td>84.3</td>
</tr>
<tr>
<td><strong>Residency program</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>National residency</td>
<td>72.3</td>
<td>84.3</td>
</tr>
<tr>
<td>Local residency</td>
<td>72.3</td>
<td>84.3</td>
</tr>
</tbody>
</table>

Includes resident or equivalent only.

* Including vignettes completed outside of this system as determined in the study.

| Columns: P-value unless otherwise indicated. |
Thank you!