Preoperative phytonadione supplementation for mitral valve intervention hemostasis

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Background

Cardiac Procedures & Hepatic Dysfunction

- Per ACC/AHA guidelines, surgical or percutaneous interventions are recommended for severe degenerative mitral valve disease, which are associated with various degree of body organ dysfunction, likely due to systemic inflammatory response and oxidative stress.
- In high-risk surgeries, 10% of patients experience hepatic injury, increasing complications related to degree of coagulopathy, including bleeding events, thromboembolic events, and valve thrombosis.
- Blood transfusions secondary to bleeding events during or following cardiac operations has been shown to worsen short- and long-term outcomes for patients.

Phytonadione

- One proposed hemostatic strategy includes the prophylactic use of phytonadione (Vitamin K), a fat-soluble vitamin which catalyzes the hepatic synthesis of blood-clotting factors II, VII, IX, and X.
- Phytonadione is available in several formulations (PO, IV, IM, SQ) and is commonly utilized as a safe and effective method for the reversal of warfarin therapy.
- Based on the proposed mechanism of hepatic dysfunction and pathophysiology of patients undergoing mitral valve intervention, a local surgeon implemented this theory into practice in effort to advance patient care and outcomes.
- Supporting evidence regarding utilization of phytonadione as surgical prophylaxis prior to mitral valve intervention is currently limited.

Objectives

Primary

- Compare the rate of post-operative major bleeding events in patients who received phytonadione administration prior to surgical valve intervention

Secondary

- Compare the rates of antithrombotic utilization, hemostatic agents and blood product utilization, length of stay, and time to therapeutic INR
- Compare rates of mortality, re-admission, or re-intervention within 30 days of hospital discharge

Methodology

- Single-center, single-surgeon retrospective chart review study at a large tertiary medical center
- Inclusion criteria
  - ≥18 years of age
  - Underwent mitral valve replacement (MVR) between January 2018 and June 2021
- Exclusion criteria
  - Received phytonadione for warfarin reversal
  - Emergent procedures
  - IV phytonadione administered
  - Severe renal impairment
  - Potentially vulnerable populations
- Statistical analysis completed using t-test or Wilcoxon rank sum test for continuous variables and chi-square or Fisher exact test for categorical variables

Results

Patient Baseline Characteristics

Characteristics on admission	Phytonadione	No Phytonadione
Age, mean±SD	68.5±10.7	66.3±12.6
Female	6 (75.0%)	12 (66.7%)
Previous valve intervention	2 (25.0%)	3 (16.7%)
INR, median (IQR)	1.1 (1.0-1.2)	1.0 (1.0-1.0)
Hematocrit (%), median (IQR)	38.0±8.4	41.6±4.2
Hemoglobin (g/L), median (IQR)	11.8±2.7	13.5±1.6
CrCl, mean±SD	60.2±34.6	70.3±29.6
Co-morbidities		
Atrial fibrillation	2 (25.0%)	7 (38.9%)
Chronic heart failure	3 (37.5%)	4 (22.2%)
Chronic kidney disease	2 (25.0%)	2 (11.1%)
Coronary artery disease	3 (37.5%)	3 (16.7%)
Diabetes mellitus	5 (62.5%)	4 (22.2%)
History of endocarditis	1 (12.5%)	2 (11.1%)
History of Stroke	1 (12.5%)	2 (11.1%)
History of PE/DVT	0 (0.0%)	1 (5.6%)
Hypertension	5 (62.5%)	15 (83.3%)

Table 1. Baseline characteristics; IQR = interquartile range

Anticoagulation & Antiplatelets

Medications	Phytonadione	No Phytonadione
Anticoagulation prior to admit		
Warfarin	0 (0.0%)	2 (11.1%)
Apixaban	2 (25.0%)	5 (27.8%)
Rivaroxaban	0 (0.0%)	2 (11.1%)
None	6 (75.0%)	9 (50.0%)
Antiplatelet prior to admit		
Aspirin	3 (37.5%)	7 (38.9%)
Clopidogrel	2 (25.0%)	1 (5.6%)
None	3 (37.5%)	10 (55.6%)
Discharge anticoagulation		
Warfarin	2 (25.0%)	5 (27.8%)
Apixaban	3 (37.5%)	6 (33.3%)
Rivaroxaban	0 (0.0%)	3 (16.7%)
None	3 (37.5%)	4 (22.2%)
Discharge antiplatelets		
Aspirin	6 (75.0%)	16 (88.9%)
Clopidogrel	1 (12.5%)	3 (16.7%)
None	1 (12.5%)	1 (5.6%)

Table 2. Anticoagulants and antiplatelets received before and after surgery

Surgical and Phytonadione Characteristics

Operational Information	Phytonadione (n=8)	No Phytonadione (n=18)	p-value
Elective surgery	6 (75.0%)	15 (83.3%)	0.628
Bio-prosthetic valve	7 (87.5%)	15 (83.3%)	>0.999
Re-intervention	2 (25.0%)	3 (16.7%)	0.628

Table 3. Mitral valve surgical characteristics reported as number of patients (%)

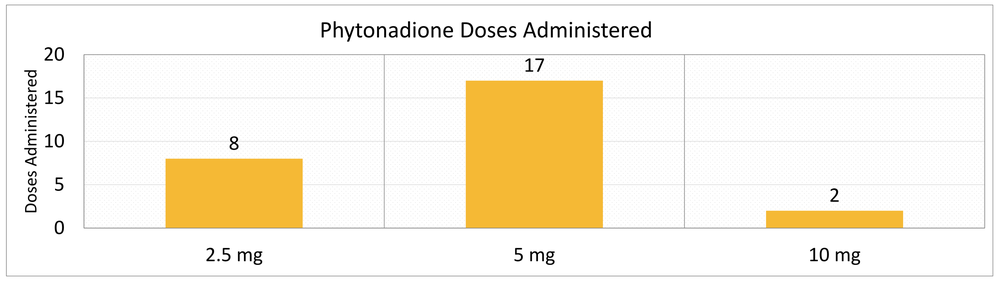

Figure 1. Total doses (#) of oral phytonadione ordered and administered

Primary Outcome	Phytonadione (n=8)	No Phytonadione (n=18)	p-value
Post-op bleeding, no (%)	1 (12.5%)	4 (22.2%)	>0.999

Table 4. Post operative bleeding rates in patients that receive phytonadione versus those who did not

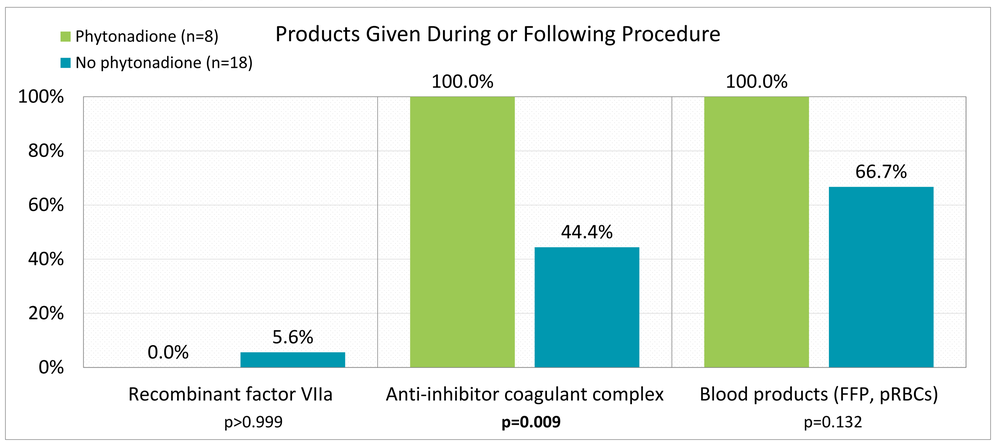

Figure 2a-c. Percentages of patients that received recombinant factor VIIa, anti-inhibitor coagulant complex and/or blood products during or following procedure; FFP = fresh frozen plasma, pRBC = packed red blood cells

Secondary Outcomes	Phytonadione	No Phytonadione	p-value
Re-admission within 30 days for bleeding	1 (66.7%)	4 (33.3%)	0.683
Re-intervention within 30 days	0 (0.0%)	3 (16.7%)	0.529
Mortality within 30 days	1 (12.5%)	0 (0.0%)	0.308
Therapeutic INR obtained during admission	1 (50.0%)	3 (40.0%)	>0.999
LOS, median (IQR)	17.0 (14.8-21.0)	9.0 (8.0-14.0)	**0.02**
POLOS, median (IQR)	12.0 (9.0-16.8)	8.0 (8.0-13.8)	0.4

Table 5. Secondary outcomes; INR = international normalized ratio, LOS = length of stay, POLOS = post-op length of stay, IQR = interquartile range

Discussion

Patient Population

- 26 patients met inclusion and exclusions criteria
- The average study patient was a 68-year-old female (69.2%) who underwent elective bio-prosthetic MVR as their first valvular intervention

Phytonadione Administered

- On average, oral phytonadione was supplemented with a strength of 5 mg for 3.4 doses prior to MVR

Primary Outcome

- Patients who had received phytonadione supplementation (n=8), compared to those who did not (n=18), were found to have less postoperative bleeding events (12.5% vs. 22.2%, p>0.999)

Secondary Outcomes

- Phytonadione study group significantly received more anti-inhibitor coagulant complex during admission (100% vs. 44.4%, p=0.009) and had longer length of stay (17 days vs. 9 days, p=0.02)
- Mortality, re-admission rates due to bleeding, re-intervention rates, and time to therapeutic INR were similar between both groups

Study Limitations

- Retrospective, non-randomized single-center study
- Small sample size
- Variations in phytonadione doses administered
- Inconsistencies in electronic medical record documentation of bleeding outcomes
- Presence of hepatic disorders were not identified

Conclusion

- In patients undergoing mitral valve replacement, phytonadione supplementation did not significantly decrease the rate of postoperative bleeding events and was associated with an increase in anti-inhibitor coagulant complex utilization and longer hospitalization length of stay.

Future Considerations

- Given study limitations, benefit of prophylactic phytonadione cannot be completely ruled out.
- Considerations for future research include a larger, prospective, multi-center, randomized study with standardized phytonadione dosing and defined criteria of patients who would be eligible for supplementation.

References

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