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Evaluation of pharmacy to dose heparin protocol in neurological conditions

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OBJECTIVE

- The objective of this study was to assess the safety and efficacy of the current pharmacy to dose heparin protocol for neurological conditions.

BACKGROUND

- Heparin remains controversial in neurological patients, and there is no universally accepted dosing regimen[1].
- A recent study has shown a benefit in ischemic stroke lesion size with heparin use. This protocol had a median time to therapeutic aPTT was 14 hours[2].
- A review of Parkview's heparin protocols for non-neurological conditions showed a delay in achieving therapeutic aPTT in obese patients.
- Parkview's heparin protocol for neurological patients uses weight-based dosing and does not use bolus dosing.
  - Starting infusion rate: 11 units/kg/hour
  - Heparin drip is titrated by aPTT to a goal of 40-55 (rate may be changed up to 2 units/kg/hour).

METHODS

- **Study Design:** Retrospective chart analysis for all patients who received the pharmacy-to-dose heparin protocol for neurological conditions between June 2019 – June 2020
- **Inclusion criteria:**
  - At least 18 years of age
  - Received at least 1 aPTT while on therapeutic heparin
- **Exclusion criteria:**
  - Prescribed any pharmacy-to-dose heparin protocol for non-neurological conditions during the same admission
  - Any deviations from the pharmacy-to-dose heparin protocol for neurologic conditions
  - Heparin initiated outside of Parkview's Health
- **Primary outcome:** Frequency of initially therapeutic aPTT 6 hours post-heparin initiation
- **Secondary outcomes:**
  - Percent of initial therapeutic aPTT by BMI class as defined by the World Health Organization (WHO)
  - Mean time to cross therapeutic threshold
  - Mean heparin rate when first therapeutic aPTT achieved.
- **Safety outcomes:**
  - Frequency of hemoglobin drop over 3 g/dL post-heparin initiation
  - Frequency of major and minor bleed defined by the Bleeding Academic Research Consortium (BARC) [3]
  - Frequency of hemorrhagic conversion
  - Frequency of new thrombosis after heparin initiation

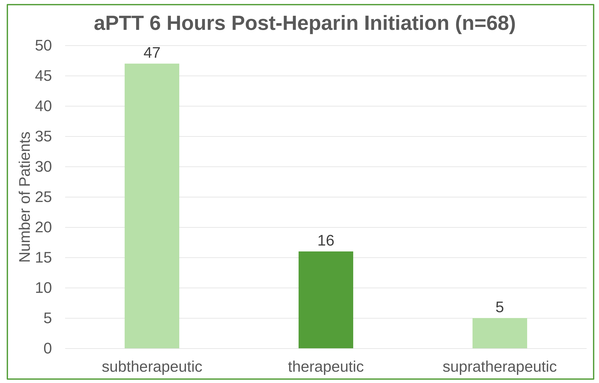
RESULTS

Demographics	(n=68)
Age	64.3 ± 14.8 years
Gender	
Male	39 (57.4%)
Female	29 (42.6%)
BMI	
Underweight (<18.5)	2 (2.9%)
Normal (18.5-24.9)	16 (23.5%)
Overweight (25-29.9)	26 (38.2%)
Class I (30-34.9)	12 (17.7%)
Class II (35-39.9)	8 (11.8%)
Class III (>40)	4 (5.9%)

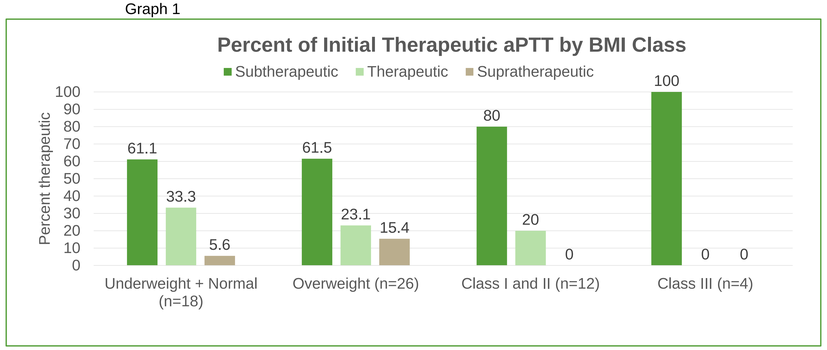
Table 1

Indication	(n=68)
Cerebrovascular Accident	49 (72.1%)
Dural Venous Thrombus	2 (2.9%)
Glioblastoma	1 (1.5%)
Internal Carotid Occlusion	1 (1.5%)
Other Clot with Recent Bleed	6 (8.8%)
Sinus Thrombus	3 (4.4%)
Subdural Hematoma	1 (1.5%)
Transient Ischemic Attack	3 (4.4%)
Traumatic Brain Injury	1 (1.5%)
Vertebral Artery Dissection	1 (1.5%)

Table 2



Graph 1



Graph 2

	(n=68)
Average Time on Heparin	84.0 ± 83.8 hours
Average Time to Reach Therapeutic Threshold (n=52)	26.6 ± 23.6 hours
Underweight + Normal	25.0 ± 25.7 hours
Overweight	20.6 ± 23.4 hours
Class I and II	31.4 ± 19.3 hours
Class III	27.3 ± 14.9 hours

Table 3

Never Reached Therapeutic Threshold	16 (23.5% of study- population)
Age	60.3 ± 15.5 years
Average Time on Heparin	22.8 ± 7.7 hours
Underweight + Normal	4 (25%)
Overweight	4 (25%)
Class I and II	6 (37.5%)
Class III	2 (12.5%)

Table 4

RESULTS

- 159 consults were identified, and 68 met inclusion criteria.
- **Outcomes:**
  - 16 patients (24%) had an initially therapeutic aPTT.
  - 47 patients (69%) had an initially subtherapeutic aPTT.
  - 52 patients reached therapeutic aPTT.
  - Initially therapeutic aPTT was highest in patients with normal or underweight BMI (33.3%).
  - Class III obesity patients had the highest frequency of initially subtherapeutic aPTT.
  - Mean time to cross therapeutic threshold was 26.6 hours (n=52).
  - Mean heparin rate at first therapeutic aPTT was 13.6 units/kg/hour (n=52).
- **Safety:**
  - 9 patients (13.2%) had a hemoglobin drop greater than 3 g/dL.
  - 5 patients experienced a bleed (3 of these were noted before heparin initiation).
  - There were no newly reported cerebral hemorrhages post-heparin initiation.
  - There were no new thrombotic events.

DISCUSSION & CONCLUSIONS

- The current protocol at Parkview Health is relatively conservative; this may place patients at increased risk of clot expansion.
  - Risk of clot expansion may be driven by the delay in achieving therapeutic anticoagulation.
  - Mean heparin rate at first therapeutic aPTT was 13.6 units/kg/hour, but this value is likely understated as it did not include patients that never achieved therapeutic anticoagulation.
- There were no reports of new thrombotic events. However, these patients were likely screened out since this study excluded patients that received heparin under a different protocol.
- Bleeding frequency was relatively low, but 13.2% of patients experience a hemoglobin drop greater than 3 g/dL.
- There is an opportunity for Parkview's pharmacy-to-dose protocol for neurological conditions to be adjusted to achieve therapeutic anticoagulation more rapidly.

REFERENCES

1. Powers WJ, et. al. Guidelines for the Early Management of Patients with Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke. *Stroke.* 2019; 5-: 344-418
2. Rocha EA, et. Al. Reduced Ischemic Lesion Growth with Heparin in Acute Ischemic Stroke. *Journal of Stroke and Cerebrovascular Disease.* 2019; 28 (6): 1500-8
3. Mehran R, et. al. Standardized Bleeding Definitions for Cardiovascular Clinical Trials. *Circulation.* 2011; 123 (23): 2736-47.

Disclosure
The authors of this presentation have the following to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation:
Leslie Siegel: Nothing to disclose | Tim Johnston: Nothing to disclose | Karen Dunkelberger: Nothing to disclose |