Evaluating the use of heparin derivatives in overweight and obese pediatric patients: a review

Michael P. Garner, PharmD Candidate; Chimnonso P. Onuoha, PharmD Candidate;
Norman E. Fenn III, PharmD, BCPS
University of Texas at Tyler - Fisch College of Pharmacy

BACKGROUND

- According to the CDC, one in five minors in the United States are described as obese.[1]
- Obese children are at higher risk of a hypercoagulable event, such as venous thromboembolism, compared to healthy weight children.[2]
- Concerns exist with the narrow therapeutic window of anticoagulants in general, and especially with children.[3]
- The use of low molecular weight heparins (LMWHs) in anticoagulation prophylaxis in overweight and obese children has been sparsely studied.

OBJECTIVES

- Evaluate and describe current available literature on the use of heparin derivatives in overweight and obese pediatric patients
- Assess efficacy and safety parameters of heparin derivatives in overweight and obese pediatric patients

METHODS

- A comprehensive literature search of PubMed, SCOPUS, Cumulative Index of Nursing and Allied Health, Academic Search Complete, PsycInfo, Cochrane Library, and Web of Science databases was conducted.
- Search terms used were “LMWH OR low molecular weight heparin OR enoxaparin OR dalteparin OR tinzaparin OR fondaparinux,” AND “pediatric OR child OR children,” AND “obese OR obesity OR overweight.”
- No limits or timeline restrictions were imposed.
- Studies were included if they contained pediatric patients who were overweight or obese and received either enoxaparin, dalteparin, tinzaparin, or fondaparinux.
- Exclusion criteria: Duplicate studies; off-topic studies; adult studies; inaccessible full articles; non-English studies; animal trials.

RESULTS

Figure 1: Number of evaluated studies retrieved

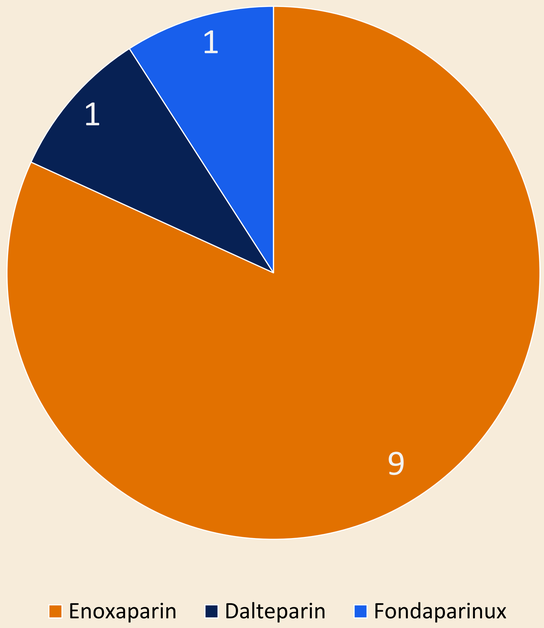


Figure 2: Changes in enoxaparin doses to reach therapeutic anti-factor Xa measurements

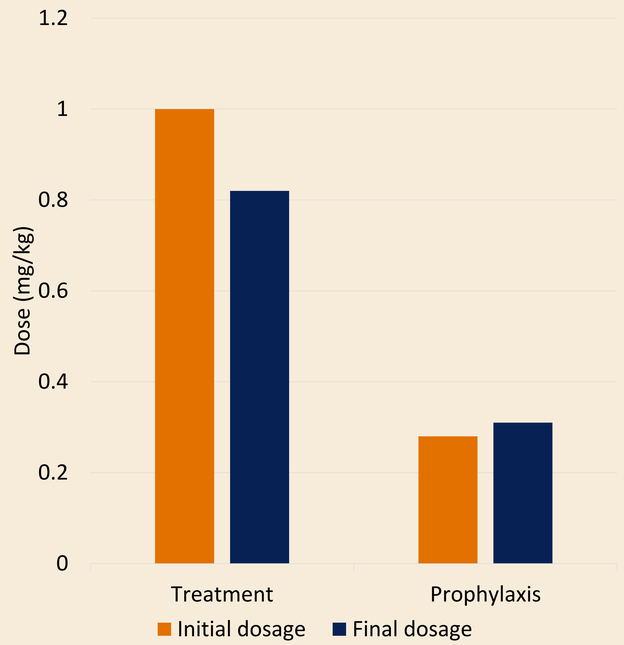
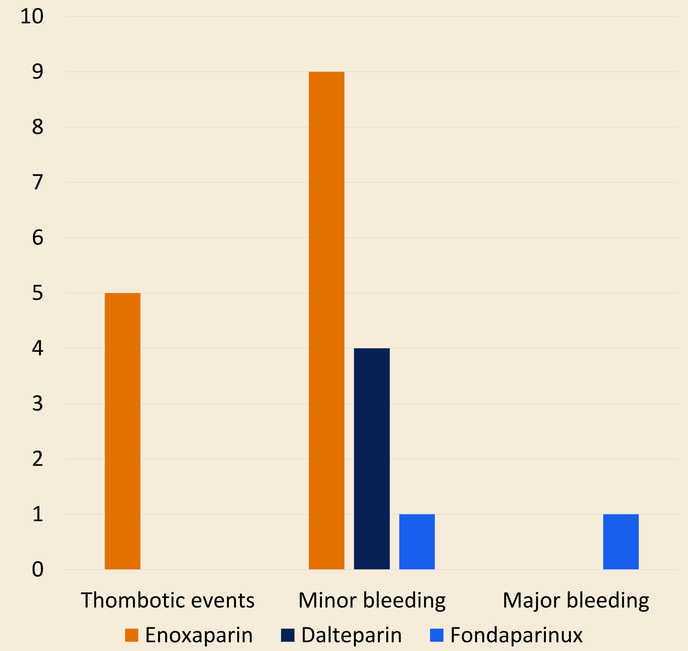


Figure 3: Number of safety events



RESULTS

- Enoxaparin was the most studied heparin derivative in obese pediatric patients.
- Evidence for dalteparin and fondaparinux were limited; no studies using tinzaparin in this population were retrieved.
- Enoxaparin dose reductions of 13% to 37% occurred from baseline within the treatment studies.
- Prophylactic dose increases of enoxaparin from baseline ranged from 0% to 27.3%.
- Monitoring of anti-factor Xa measurements was inconsistently performed or reported by investigators.
- Fourteen minor bleeding events were reported in the literature along with one major bleeding event.
- Three thrombus extensions and two new thrombotic formations were described.

DISCUSSION

- The observed decrease seen from the enoxaparin treatment studies suggests that obese pediatric patients may be receiving supratherapeutic dosing initially.
- Prophylactic doses of enoxaparin were unchanged in two of three studies regardless of monitoring due to study protocol.
- Minor bleeding events were the most commonly reported safety parameter, with only one incidence of a major bleed inferred in the literature.
- The observed lack of monitoring is concerning due to the narrow therapeutic window of these agents, potentially placing patients at greater risk for safety concerns.
- Presently, there is no sub-stratification of obesity in pediatric patients, which could have a dramatic influence on future dosing of heparin derivatives.

CONCLUSIONS

- Enoxaparin is the most frequently described anticoagulant in the obese pediatric literature.
- Monitoring should be performed using anti-factor Xa measurements, although controversy does exist with the use of these measurements.
- Larger, long-term randomized controlled trials are needed to determine optimized treatment strategies on the heparin derivatives for better clinical outcomes in the overweight or obese pediatric population.

REFERENCES

For the full list of references, abstract, and more information use this QR code