Evaluation and Monitoring of Anticoagulation in Pediatric Patients Receiving Unfractionated Heparin on Regular Hemodialysis

Thesis

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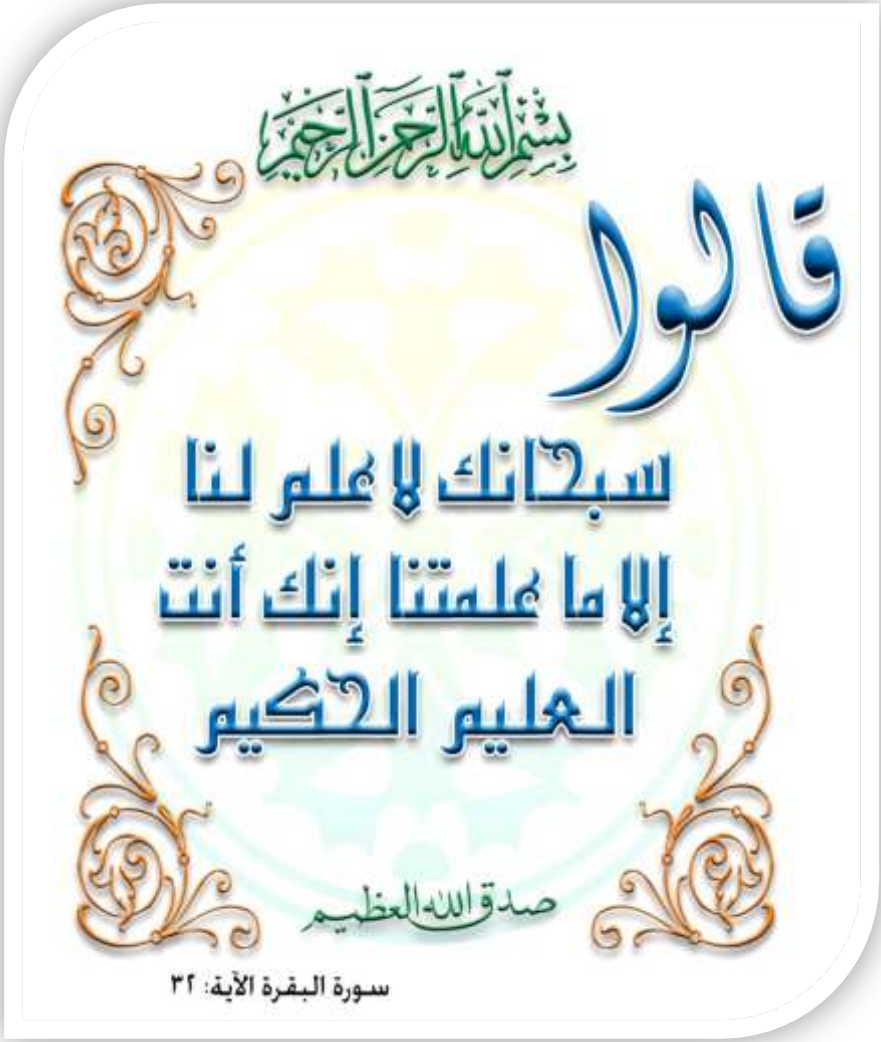
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سبحانك لا علم لنا
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Ahmed Hosam El-Din Baranek

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List of Abbreviations

Abbr.	Full-term
ACT	**:** Activated clotting time
ADP	**:** Adenosine diphosphate
AF	**:** Atrial fibrillation
aPTTr	**:** Activated partial thromboplastin time ratio
AT	**:** Antithrombin
β2M	**:** β2 microglobulin
CDCA	**:** Clinically detected coagulation abnormalities
CI	**:** Confidence interval
CKD	**:** Chronic kidney disease
COX	**:** Cyclooxygenase
DRA	**:** Dialysis related amyloidosis
DVT	**:** Deep venous thrombosis
ECC	**:** Extracorporial circuit
ECMO	**:** Extracorporeal membrane oxygenation
ESRD	**:** End-stage renal disease
FDA	**:** Food and Drug Administration
GP	**:** Glycoprotein
HD	**:** Hemodialysis
HDF	**:** Hemodiafiltration

HIT : Heparin-induced thrombocytopenia

IL : Interleukin

KDIGO : Kidney Disease Improvement of Global Outcomes

LMWH : Low molecular weight heparin

NO : Nitric oxide

OAC : Oral anticoagulation

PAI-1 : Plasminogen activator inhibitor-1

PCI : Percutaneous coronary intervention

PMN : Polymorph-nuclear cells

PFA : Platelet function analyzer

PTT : Partial thromboplastin time

RCA : Regional Citrate Anticoagulation

RR : Risk ratio

SBP : Systolic blood pressure

SD : Standard deviation

SLE : Systemic lupus erythmatosis

SPSS : Statistical package for social science

TAT : Thrombin antithrombin complex

TGF β_1 : Transforming growth factor β_1

TF : Tissue factor

TFPI : Tissue factor pathway inhibitor

TM : Thrombomodulin

TNF **:** Tumor necrosis factor

tPA **:** Tissue plasminogen activator

UFH **:** Unfractionated heparin

vWF **:** von Willebrand factor

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Abstract

Background: The dialysis population represents the only group of patients to receive heparin three times per week, with a potential long-term cumulative effect associated with an increased risk of osteoporosis, aldosterone suppression and hyperkalemia, and a deterioration of lipid profile and endothelial function. **Aim of the Work:** to evaluate the adequacy of heparin therapy used for anticoagulation in pediatric patients receiving regular hemodialysis sessions, at pediatric dialysis unit, children`s hospital, Ain Shams University hospitals, during period from January 2018 to December 2018. **Patients and Methods:** This interventional study **was conducted on 48** pediatric hemodialysis patients who were attending dialysis setting, Pediatric Dialysis Unit, Children's Hospital, Ain Shams University during a period of 12 months. **Results:** Eleven patients (23%) had clinically detected coagulation abnormalities, bleeding in 6 cases (12.5%), 3 of them had bleeding with high ACT reading predialysis, 1 of them showed defective platelet functions by platelet function analyzer PFA which was repeated following phase II was normal. Clotting was detected in 4 cases (8%) and both bleeding and clotting were detected in 1 case (2%). **Conclusion:** CDCA occurred in 23% of the studied patients, among these bleeding was more prevalent. ACT as a bedside rapid test of anticoagulation adequacy during HD sessions did not offer predictive benefit over clinical evaluation, which is still considered a more accurate method. Moreover, HDF is proved beneficial in decreasing CDCA over conventional HD.

Key words: anticoagulation, children, unfractionated heparin, regular hemodialysis

Introduction

Anticoagulation in hemodialysis is targeted to prevent activation of coagulation cascade during the procedure **(Kalra and Roy, 2012).** Appropriate anticoagulation for hemodialysis (HD) requires a subtle balance between under- and over-heparinization to prevent extracorporeal circuit (ECC) clotting and bleeding, respectively **(Kessler et al., 2015).**

Maintaining full patency in ECC during HD sessions is a prerequisite for optimal HD quality **(Suranyi and Chow, 2010).** A complex disturbance of the coagulation system is commonly encountered in patients at the terminal stage of chronic kidney disease (CKD), leading to considerable morbidity and mortality **(Jalal et al., 2010).**

Heparin is the most commonly used anticoagulant as it is easy to administer, has a short half-life and low cost **(Kalra and Roy, 2012).**

Of interest, the dialysis population represents the only group of patients to receive heparin three times per week, with a potential long-term cumulative effect associated with an increased risk of osteoporosis, aldosterone suppression and hyperkalemia, and a deterioration of lipid profile and endothelial function **(Lavainne et al., 2014).**

Unfractionated heparin (UFH) is metabolized by hepatic and vascular endothelial heparinases, in a dose dependent manner. Half-life can be modified by nonspecific binding to the endothelium, leukocytes and plasma proteins **(Chan et al., 2004).** UFH is highly charged and therefore nonspecific binding to plastic tubing and dialyzer membrane surfaces can occur altering its pharmacokinetics **(Kalra and Roy 2012).**

Anticoagulant management in HD patients is not evidence-based, and can therefore be challenged. Individual tailoring of anticoagulant treatment at any time remains difficult in daily practice. Given that a routine bedside biological monitoring protocol is not currently available, dialysis units have developed their own standard strategies to avoid both bleeding and clotting by pragmatically and empirically adjusting doses according to extracorporeal circuit (ECC) visual inspection and monitoring compression time at needle puncture site at the end of HD sessions **(Kessler et al., 2015).**

The use of biological monitoring is not clearly defined in routine clinical practice. The ideal test would be a rapid bedside whole-blood test that is accurate enough for quantifying the level of anticoagulation, and identifying under- or over-heparinization during HD. Different coagulation tests can be used, but their availability and the delay with obtaining results may differ from one dialysis center to another **(Herrero- Calvo et al., 2012).**

Aim of the Work

Objective evaluation of the adequacy of heparin therapy used for anticoagulation in pediatric patients receiving regular hemodialysis sessions, at pediatric dialysis unit, children`s hospital, Ain Shams University hospitals, during period from January 2018 to December 2018.

Chapter 1
Hemostasis in ESRD and Hemodialysis

INTRODUCTION

End-stage renal disease (ESRD) is associated with profound effects on hemostasis ranging from thrombosis to bleeding complications. The pathogenesis of uremic bleeding is multifactorial. It has been attributed to platelet dysfunction, particularly platelet-platelet and platelet-vessel wall interactions. Renal replacement therapy has helped reduce bleeding episodes, but the risk of morbidity and mortality due to hemorrhage remains **(Goluza et al., 2011)**.

Abnormalities of blood coagulation and fibrinolysis predispose uremic patients to hypercoagulable state carrying the risk of cardiovascular disease and thrombotic complications such as thrombosis of the vascular access wall **(Li et al., 2016).**

Interestingly, the dialysis population represents the only group of patients to receive heparin three times per week, with a potential long term cumulative effect associated with an increased risk of osteoporosis, aldosterone suppression and hyperkalemia, and a deterioration of lipid profile and endothelial function **(Lavainne et al., 2014).**