The Egyptian Journal of Hospital Medicine (October 2017) Vol. 69 (5), Page 2455-2458

Prognosis of Unfractioned Heparin versus Low Molecular Weight Heparin in Pumlonary Embolism: Review Article

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ABSTRACT

Anticoagulation is the mainstay treatment of pulmonary embolism. Using low molecular weight heparin versus unfractionated heparin remains a matter of debate. **Objectives**: the aim of this review is to study the prognosis of using low molecular weight versus unfractionated heparin in treatment of pulmonary embolism. **Methods:** PubMed and Cochrane library were searched for articles comparing the efficacy of low molecular weight heparin and unfractionated heparin in management of pulmonary embolism. Ten related results were selected for review. **Results:** Literatures studies indicated that low molecular weight heparin was effective in therapeutic treatment of acute sub-massive and massive pulmonary embolism. It was as effective as intravenous unfractionated heparin. It was not associated with higher risk of major, minor bleeding, or thrombocytopenia. Low molecular weight heparin was as effective as unfractionated heparin in prophylaxis of deep venous sinus thrombosis as well as pulmonary embolism. **Discussion:** Low-molecular-weight heparin seemed to be as effective safe as intravenous unfractionated heparin for the treatment as well as prophylaxis of pulmonary embolism. It was also safe with no major bleeding risk or higher risk of thrombocytopenia. **Conclusion**: Both low molecular weight and unfractionated heparin had similar efficacy and safety in management of PE.

Keywords: Pulmonary embolism, low molecular weight heparin, unfractionated heparin, outcome.

INTRODUCTION

Anticoagulation is the mainstay treatment of pulmonary embolism. It had significantly decreased the pulmonary embolism-related mortality[(1)]. Recently, two forms of heparin are available for treating pulmonary embolism; low molecular weight heparin (LMWH) and unfractionated heparin (UFH). Unfractionated heparin had long been used for therapeutic management of pulmonary embolism. However, with the introduction of low molecular weight heparin in 1980, the role of unfractionated heparin in deep venous thrombosis (DVT) and pulmonary embolism (PE) began to diminish[(2)]. Low molecular weight heparin was proved to be superior to unfractionated heparin in prevention of deep venous system thrombosis[(3)]. However, unfractionated heparin is still widely used in treatment of pulmonary embolism[(4)].

Study rationale and objectives: To date, clear-cut data are unavailable about the superiority of any of the two available types of heparin in prevention and management of pulmonary embolism. Data from different studies are conflicting. Thus, this review was conducted to review different literature articles about the effect and prognosis of both medications.

METHODS

For achieving this aim, PubMed and Cochrane library were searched for articles comparing the efficacy of low molecular weight heparin and unfractionated heparin in management of pulmonary embolism. Ten related results were selected for review. Studies evaluating the efficacy of both agents on prophylactic as well as therapeutic management of pulmonary embolism were reviewed. Of various search results, ten of them

Received: 13 / 8 /2017
Accepted: 22 /8 /2017
DOI : 10.12816/0041693

were closely related to the research point, so they were well inspected and included within the review data. The study was done after the approval of ethical board of Alfaisal university.

RESULTS

Upon reviewing the published literatures studies, many researchers had explored the difference between unfractionated and low molecular weight heparin in prophylactic and therapeutic management of pulmonary embolism. **SenturkA *et al.*[5]**prospectively studied 249 patients with massive and sub-massive pulmonary embolism to explore whether low molecular weight heparin (LMWH) would be preferred to unfractionated heparin or not. They found that the mortality rate after 1 month was 8.2% among patients who received LMWH and 17.3% among patients who received unfractionated heparin (p=0.031). Major as well as minor hemorrhages were more associated with LMWH. Similarly, **Khor YH *et al.*[6]**, in a retrospective study in 211 patients with pulmonary embolism (PE) stated that the mortality rates did not significantly differ between LMW heparin and UFH (28% and 29%). However, Unfractionated hemorrhage had a longer time to reach therapeutic range. Similarly, **Mayer*et al.*[, 7]Quinlan*et al.*[3], Simonneau G*et al.*[9] and FindikS *et al.*[8]** reported no difference between the therapeutic effect of LMWH and UFH in patients with sub-massive pulmonary embolism.

As regards the side effects of heparin, a meta-analysis was conducted in the year 2007 on 5275 patients to study the incidence of heparin-induced thrombocytopenia among patients receiving UFH in comparison patients receiving LMWH. Results from this meta-analysis indicated that here were no statistically significant differences in heparin-associated thrombocytopenia in patients receiving LMWH (1.2%) and those receiving UFH (1.5%) (p=0.246).Heparin-induced thrombocytopenia could not be evaluated due to very low incidence[9].

Table (1): Literatures survey comparing LMWH to UFH

No.	Author	Year	Patients	Type of study	Aim	Comments
1	**Senturk *et al.*** [5]	2016	249	Prospective, Observational multicenter tria	LMWH versus UFH in severe pulmonary embolism (PE)	LMWH was safer than UFH
2	**Khor YH *et al.*** [6]	2011 - 2012	211	Retrospective	LMWH versus UFH in PE	UFH was suboptimal
3	**Morris TA *et al.*** [9]	2007	5,275	Meta-analysis	LMWH versus UFH in PE and DVT as regards incidence of HIT	No difference between LMWH and UFH as regards thrombocytopenia
4	**Quinlan DJ *et al.*** [3]	2004	2110	Meta-analysis	LMWH versus UFH in treatment of acute PE	Same effect No bleeding complications
5	**Findik S *et al.*** [8]	2002	95	Prospective	Enoxaparin versus UFH in treatment of PE	Enoxaparin is as effective as UFH
6	**Bounameaux *et al.*** [2]	1998	----	Meta-analysis	UFH versus LMWH in venous thrombosis	LMWH is more safe than unfractionated heparin
7	**Simonneau G *et al.*** [10]	1997	312	Prospective	Tinzaparin versus UFH in treatment of PE	Tinzaparin as effective as UFH No risk of bleeding
8	**Avikainen V *et al.*** [11]	1995	167	Prospective	LMWH versus UFH in prophylaxis of DVT and PE after hip replacement	No significant difference
9	**Meyer G *et al.*** [7]	1995	60	Open pilot randomized study	LMWH versus UFH in sub massive PE	No significant difference
10	**Théry C *et al.*** [12]	1992	101	Prospective	SC Fraxiparine and IV UFH in massive PE	Fraxiparine at a dose of 400 anti-Xa Institute Choay units/kg was as effective and safe as UFH

Henri Bounameaux *et al.*[2] reported in their meta-analysis in 1998 that the LWWH had safer profile than unfractionated heparin, so that it is preferable in both prophylactic and therapeutic management of venous thrombosis.

Furthermore, LMWH was as safe as UFH in prophylaxis of deep venous sinus thrombosis as well as pulmonary embolism in a prospective study held on 167 patients after hip replacement. Proximal DVT occurred in 1.2% of patients on LMWH and 4.8% in patients on UFH ($p > 0.05$). Pulmonary embolism occurred in 1.2% of patients on UFH[11].

Théry *et al.*[12] prospectively studied 101 patients with massive pulmonary in 1992. They found that the Fraxiparine at a dose of 400 anti-Xa Institute Choay units/kg was as effective and safe as unfractionated heparin.

DISCUSSION

Low molecular weight heparin has witnessed a considerable concern during the past few decades. Since its introduction in 1980, many researchers conducted various studies to compare the efficacy as well as the safety of the low molecular weight heparin to the unfractionated heparin. Most of the results were promising. Low molecular weight heparin was successful in head to head comparison in multiple clinical situations particularly pulmonary embolism and deep venous thrombosis. It was shown to be effective in both prophylactic as well as therapeutic management, and it had a safe profile. Along with easier dosing system without close laboratory monitor, LMHW had become preferred by many physicians.

As regards the safety profile, low molecular weight heparin (LMWH) was safer compared to unfractionated heparin (UFH) in different literature articles. It was associated with less mortality rate(5), less major and minor hemorrhagic complications[5], Additionally, unfractionated heparin showed a delayed therapeutic response in some studies[6] and difficulty in adjusting the therapeutic range.

On the contrary, some studies did not report a significant difference between the mortality rates among patients on LMWH and UFH[6], no difference between the incidence of heparin-associated thrombocytopenia[9],

As regards the therapeutic efficacy, Subcutaneous LMWH at a dose of 400 anti-Xa Institute Choay units/kg was as effective and safe as unfractionated heparin in one study[12]. Similarly, LMWH was as effective as UFH in therapeutic treatment of massive and sub-massive pulmonary embolism[3,5,7,8,10,13].

As regards the prophylactic efficacy, LMWH was as safe and effective as UFH in prevention of deep venous sinus thrombosis as well as pulmonary embolism in patients who had hip replacement surgery[11].

The safe profile of the LMWH, and the better benefit-to-risk ratio, is mainly attributed to its mechanism of action on anti-factor Xa and anti-thrombin activity, its unique pharmacological properties allowing less frequent dosing, and its low risk for bleeding diathesis. Furthermore, it does not require laboratory monitoring of coagulation profile[2].

In spite of the promising effects of LMWH, it could not yet replace unfractionated heparin in certain clinical situations particularly myocardial infarction and arterial thrombosis[2].

CONCLUSION

In conclusion, Low-molecular-weight heparin seemed to be as effective safe as intravenous unfractionated heparin for the treatment of pulmonary embolism as well as a prophylaxis agent. It was also safe with no major bleeding risk or higher risk of thrombocytopenia.

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