REVIEW ARTICLE

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The Influence of Low Molecular Weight Heparin and Early Enteral Nutrition on Immune, Coagulation, Inflammatory, and Nutritional Indicators in Hyperlipidemic Acute Pancreatitis: An In-Depth Analysis

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Abstract

Introduction: Hyperlipidemic acute pancreatitis (HLAP) is a growing and serious subtype of acute pancreatitis, involving a complicated interaction of metabolic imbalance, widespread inflammation, and clotting irregularities. The potential of low molecular weight heparin (LMWH) and early enteral nutrition (EEN) as supplementary treatments has attracted considerable attention for their ability to influence central disease mechanisms.
Methods: This detailed review integrates findings from clinical research, randomized controlled trials, and meta-analyses released between 2010 and 2024, gathered via systematic searches of PubMed, Embase, and Cochrane Library databases. Emphasis was placed on studies assessing how LMWH and EEN affect immune markers (IgA, IgG, IgM), clotting factors (PT, TT, APTT, FIB), inflammatory mediators (TNF-α, IL-6, IL-8, CRP), and nutritional indicators (TP, ALB, TRF) in HLAP patients.
Results: Current data suggest that using LMWH together with EEN produces better patient results than traditional care alone. Notable outcomes involve a marked decrease in inflammatory markers, better clotting function, higher antibody levels, and improved nutritional measures. This combined method is linked to reduced hospitalization time, quicker return of digestive function, and fewer complications like multiple organ failure.
Discussion: The complementary actions of LMWH and EEN tackle the diverse causes of HLAP. LMWH enhances blood flow in the pancreas while lowering excessive clotting and inflammation, whereas EEN protects intestinal lining and helps regulate immunity. Subsequent studies should aim to establish consistent treatment guidelines and determine which patients would gain the most from this dual therapy.

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Introduction

Hyperlipidemic acute pancreatitis (HLAP) has become an important clinical condition, currently identified as the second leading cause of acute pancreatitis after gallstone disease, responsible for about 4–10% of all cases [1]. The global increase in metabolic conditions like obesity, diabetes, and abnormal blood lipid levels has led to a corresponding rise in HLAP cases, imposing a considerable strain on healthcare systems [2]. Compared to other causes, HLAP is often linked to a more serious illness progression, greater frequency of systemic inflammatory response syndrome (SIRS), pancreatic tissue death, multiple organ failure, and a higher chance of recurrence [3].

The development of HLAP involves multiple factors, mainly caused by severely high triglyceride levels, often with blood triglyceride (TG) concentrations above 11.3 mmol/L [4]. Increased TGs are broken down by pancreatic lipase, producing a surplus of free fatty acids

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(FFAs) that damage pancreatic cells, trigger inflammation, and impair small blood vessel circulation in the pancreas through blockages and blood vessel injury [5]. This process initiates a strong body-wide inflammatory reaction, marked by the release of signaling molecules such as tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), and interleukin-8 (IL-8) [6]. At the same time, a tendency for increased blood clotting often occurs, shown by abnormal test results like longer prothrombin time (PT), thrombin time (TT), and activated partial thromboplastin time (APTT), leading to tiny blood clots and damage from reduced blood flow [7].

Standard care for HLAP usually involves vigorous fluid replacement, pain management, and quickly lowering blood TG levels [8]. However, consistent treatment plans are not well established. Recently, low molecular weight heparin (LMWH) has been studied not only for preventing clots but also for its possible anti-inflammatory and lipid-reducing effects [9]. By activating lipoprotein lipase, LMWH might speed up the removal of triglyceride-rich particles, directly tackling a main cause of HLAP [10].

At the same time, the importance of nutritional support has been reconsidered. The increased metabolic rate and tissue breakdown in severe acute pancreatitis worsen nutrient loss and weaken immune function [11]. Although intravenous feeding was once preferred to reduce pancreatic activity, current recommendations strongly support early enteral nutrition (EEN), started within 24–48 hours after hospital admission [12]. EEN helps protect the intestinal lining, prevents movement of bacteria, modifies the body's immune reaction, and enhances overall patient recovery [13].

This review aims to combine existing research on the joint use of LMWH and EEN in HLAP, with particular attention to their effects on a wide range of biomarkers—including antibodies, clotting factors, inflammatory signals, and nutritional measures. By analyzing these connected pathways, we aim to explain the combined mechanism of this multi-target strategy and its importance in enhancing outcomes for patients with this difficult illness.

Methods

This in-depth review was performed to evaluate and combine published research on the impacts of LMWH and EEN in HLAP. A systematic search approach was used to find relevant English-language studies published from January 2010 to June 2024. The online databases searched included PubMed, Embase, Cochrane Central Register of Controlled Trials, and Web of Science.

The search used a mix of Medical Subject Headings (MeSH) terms and keywords: "hyperlipidemic acute pancreatitis," "hypertriglyceridemic pancreatitis," "low molecular weight heparin," "early enteral nutrition," "immunoglobulin," "coagulation," "fibrinogen," "inflammatory cytokines," "TNF-alpha," "IL-6," "IL-8," "nutritional status," "biomarkers," and "clinical outcomes." Boolean operators (AND, OR) helped combine search terms efficiently.

Inclusion and Exclusion Criteria

Studies were included if they: (1) involved adult human participants (≥18 years) diagnosed with HLAP; (2) examined LMWH and/or EEN as a treatment; (3) reported on at least one of the specified biomarker groups (immune, clotting, inflammatory, or nutritional); and (4) were clinical trials, cohort studies, case-control studies, or meta-analyses. Excluded were review articles, editorials, case reports with fewer than 10 patients, and non-English publications.

Data Extraction and Synthesis

Two reviewers independently screened titles and abstracts, then examined the full text of potentially relevant articles. Any disagreements were settled through discussion or by a third reviewer. Extracted data from each study included: lead author, publication year, study design, number of participants, patient details, treatment information (LMWH dose, EEN timing), comparison groups, and main findings related to the biomarkers of interest. Because of expected differences in study designs and reported outcomes, a narrative summary was conducted instead of a meta-analysis. Results were grouped by theme to address the review's goals, focusing on changes in specific biomarker pathways.

Results

Impact on Clinical Recovery and Digestive Function

Several studies consistently show that combining LMWH and EEN greatly speeds up clinical improvement in HLAP patients. A key clinical trial by Zhang et al. (2023) noted that patients receiving both treatments had a much shorter duration until abdominal pain and bloating subsided (3.2 ± 0.8 days vs. 5.1 ± 1.2 days in the control group, $p<0.01$) [14]. Similarly, time to resume oral intake, regain normal bowel movements, and restore normal bowel sounds were all notably shorter. Hospital stay was also reduced in the treatment group (7.5 ± 2.1 days vs. 10.8 ± 3.4 days, $p<0.01$). These results are supported by a meta-analysis by Li & Wang (2022), which found that EEN alone could shorten hospital stay by an average of 3.2 days [15].

Changes in Inflammatory and Clotting Biomarkers

The anti-inflammatory impact of the combined therapy is strong. After treatment, levels of C-reactive protein (CRP), TNF-α, IL-6, and IL-8 were considerably

lower in patients given LMWH and EEN compared to those on standard care [16]. For example, a study by Chen et al. (2024) reported a 60% greater decrease in IL-6 levels in the combination therapy group. LMWH is thought to block the release of pro-inflammatory signals from white blood cells and blood vessel cells [17].

Clotting function also shows clear improvement. LMWH treatment corrects the excessive clotting tendency typical of HLAP, resulting in normalization of PT, TT, APTT, and Fibrinogen (FIB) levels [18]. This better clotting profile is closely associated with improved pancreatic blood flow and less injury from poor blood supply [19].

Improvement in Nutritional and Immune Status

Nutritional indicators, including Total Protein (TP), Albumin (ALB), and Transferrin (TRF), show significant enhancement with EEN [20]. By supplying key nutrients directly to the intestinal lining, EEN aids protein production and reverses the state of tissue breakdown. Additionally, immune-modulating effects are visible in the increased levels of antibodies IgA, IgG, and IgM in patients receiving the combined treatment [21]. This points to a strengthening of the antibody-based immune defense, which is often weakened in severe pancreatitis.

Better Lipid Control and Pancreatic Enzyme Levels

As anticipated, LMWH directly influences fat metabolism. Studies indicate a quicker drop in blood TG, Total Cholesterol (TC), and Low-Density Lipoprotein Cholesterol (LDL-C) levels, along with a rise in High-Density Lipoprotein Cholesterol (HDL-C), in groups receiving LMWH [22]. This is due to heparin-induced activation of lipoprotein lipase. At the same time, blood and urine amylase levels return to normal faster, suggesting a speedier reduction of pancreatic inflammation and cell damage [23].

Decrease in Complication Rates

The occurrence of major problems, including stomach or intestinal bleeding, infections, and progression to multiple organ failure, is significantly lower in patients treated with LMWH and EEN. A combined analysis by Wang et al. (2023) reported an overall complication rate of 6–8% in the intervention groups versus 20–25% in conventional treatment groups [24]. This highlights the protective role of this multi-faceted approach against the most severe effects of HLAP.

Discussion

This review brings together strong evidence that combining LMWH and EEN provides a synergistic, multi-target treatment strategy for HLAP, effectively addressing its complex disease process. The advantages seen across clinical, inflammatory, clotting, nutritional, and immune areas emphasize how these systems are interconnected in HLAP.

LMWH's effectiveness goes well beyond its traditional clot-preventing role. Its capacity to activate lipoprotein lipase directly tackles the main metabolic problem in HLAP—severe high triglycerides [25]. By increasing clearance of triglyceride-rich fats, LMWH reduces the material for harmful FFA production in the pancreas. Moreover, its anti-inflammatory qualities, such as inhibiting white blood cell activation and reducing cytokine release (e.g., TNF-α, IL-6), help lessen the damaging body-wide inflammatory response [26]. The simultaneous improvement in clotting measures highlights its role in fixing the pro-clotting state that adds to pancreatic blood flow problems [27].

EEN serves as a fundamental part of supportive care by opposing the breakdown crisis and maintaining gut barrier function [28]. Delivering nutrients through the digestive tract supports the health and structure of the intestinal lining, thereby decreasing bacterial movement and the resulting gut-related inflammation [29]. This is reflected in the lower pro-inflammatory cytokine levels and higher nutritional protein and antibody levels seen in patients receiving EEN. The recovery of antibody levels (IgA, IgG, IgM) is especially important, as it signals regained immune strength, which is vital for preventing additional infections [30].

The synergy between LMWH and EEN likely comes from their complementary actions. While LMWH reduces inflammation and improves small blood vessel circulation throughout the body, EEN works from within the gut to stabilize the intestinal barrier and adjust the immune system [31]. This combined effect creates a more favorable internal setting for pancreatic healing, leading to faster symptom resolution, shorter hospital stays, and fewer complications.

Limitations of Current Evidence

Although current findings are encouraging, several limitations must be recognized. Many existing studies have relatively small participant numbers, and there is variation in the protocols used for both LMWH (dose, length) and EEN (timing, type of formula). Furthermore, most studies are single-center, which may restrict how widely the results can be applied.

Clinical Implications and Future Directions

The results support incorporating LMWH and EEN as a standard additional protocol in HLAP management. Clinicians should consider starting EEN within 48 hours of admission and think about using LMWH, especially in patients with very high triglycerides or signs of a systemic inflammatory reaction.

However, several questions remain. The best dose and length of LMWH therapy for HLAP are not yet standardized [32]. Future large, multi-center randomized controlled trials (RCTs) are needed to create clear guidelines. Research should also focus on finding predictive biomarkers that can identify patients who would benefit most from this intensive combined therapy [33]. Investigating the molecular mechanisms behind the immune-modulating effects of both LMWH and EEN will further improve our understanding and use of this treatment approach. Long-term follow-up studies are also necessary to evaluate the impact of this combined therapy on HLAP recurrence rates.

Conclusion

In summary, the combination of low molecular weight heparin and early enteral nutrition marks a significant change in managing hyperlipidemic acute pancreatitis. This review shows that this multi-target approach effectively addresses the core disease pathways—high blood lipids, excessive inflammation, increased clotting tendency, and immune-nutritional deficiency. The outcome is a marked improvement across a wide range of biomarkers, which leads to real clinical benefits: faster recovery, fewer complications, and shorter hospital stays. Adopting this synergistic strategy offers substantial promise for improving outcomes in patients with this severe and complex condition.

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Authors Contributions

The authors contributed to the data analysis. Drafting, revising and approving the article, responsible for all aspects of this work.

Conflict of Interest

None

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