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Role of Serum Cholesterol and Statin Usage in Predicting Nosocomial Surgical Site Infections after Gastrointestinal Surgery

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Abstract: *Total serum cholesterol levels and the use of statin medications are associated with incidence of complications after gastrointestinal surgery. low total serum cholesterol may contribute to the development of infections in induviduals undergoing surgery. It has been postulated that total cholesterol, VLDL, LDL, HDL can protect against endotoxin mediated sepsis.Cholesterol rich lipoproteins , they have the capacity to bind and detoxify bacterial lipopolysaccharide. Circulating cholesterol-rich lipoproteins and triglyceride-rich lipoproteins have the capacity to bind and detoxify bacterial lipopolysaccharide (LPS) . HDL has been shown to compete with lipopolysaccharide binding protein (LBP) for binding to lipopolysaccharide (LPS).*
The lipopolysaccharide-lipopolyscacharide binding protein (LPS-LBP) complex attaches to the cd-14 receptor on cells, which, in turn, stimulates TNF production, thus producing inflammation and infection. Secondly,cholesterol also affects gluconeogenesis and immune function.The transport forms namely the lipoproteins also serve as vehicles for anti-oxidants,fat soluble vitamins,drugsetc…Thus,high cholesterol might be protective ,possibly through a beneficial effect on the immune system.Based on these theories the nature of association between serum cholesterol and surgical site infections is to be evaluated under this study i.e is serum cholesterol a risk factor for the development of surgical site infections.

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I. Aim

- To determine if preoperative **serum cholesterol and statin usage** are associated with **higher risk of post-operative infections** in patients undergoing gastrointestinal surgery (abdominal surgery).
- **Is serum cholesterol a risk factor for the development of surgical site infections**

II. Materials and Methods

Study design: prospective study
Sample size: 80
INCLUSION CRITERIA: patients undergoing elective laparotomy & gastrointestinal surgery for benign and malignant disease

EXCLUSION CRITERIA:
1. Patients undergoing emergency surgeries.
2. Current smokers, current alcoholics, immunocompromised induviduals.
3. Hiv/Hbsag/Anti-Hcv positive induviduals
4. Age <15 years and >65 years.
5. History of long standing steroid abuse.
6. Patients with hypoalbuminemia are also excluded from this study.

- In this study patients are evaluated pre-operatively , data includes age ,gender, medications(statins),presence of surgical site infection, its category ,how surgical site infection was diagnosed.
- Current smokers and current alcoholics are excluded from this study.

- Patients who received a **statin medication more than 1 month before surgery** are included in the statin therapy group.
- A blood sample is taken under fasting conditions for serum cholesterol before surgery.
- **Serum cholesterol level is classified into 4 categories according to the American heart association guidelines (<159 , 160-199 , 200-239 , >240 mg/dl).**
- In this study post operative tissue and wound complications are defined as surgical site infections (ssi).
- Nosocomial surgical site infection surveillence is done **till 30 days** after surgery.
- We classify the study group into **2 categories ,8 sub-categories** & predict which group has the highest /lowest risk of surgical site infections, thus predicting whether serum cholesterol is a risk factor for surgical site infections.
- 2 categories- **statin therapy group** and **non-statin users**

Sub-categories

Non-statin users

1. S.cholesterol<159mg/dl
2.s.cholesterol 160-199mg/dl
3.s.cholesterol 200-239mg/dl
4.s.cholesterol >200mg/dl

Statin users

5. S.cholesterol<159mg/dl
6.s.cholesterol 160-199mg/dl
7.s.cholesterol 200-239mg/dl
8.s.cholesterol >200mg/dl

III. Results

AGE

- *In my study total population is 80 ,out of which SSI occurred in 21 induviduals.*
- *regarding age distribution of the population ,largest population belonged between 41-50 years of age (n=28).*
- *regarding age distribution of the population ,smallest population belonged between 61-70 years of age (n=4).*
- *regarding age distribution of the infected population (SSI) ,most infected population belonged between 41-50 years of age (n=8)*
- *regarding age distribution of the infected population (SSI) ,least infected population belonged between 21-30 years of age (n=8).*

GENDER

- *In total population out of 80 about 44(55%) were females*
- *In total population infected out of 21 infected about 11 (52.38%) were females*
- *So,in my study most common gender affected is females.*
- *77*

STATIN THERAPY GROUP AND SURGICAL SITE INFECTION:

- *Total number of induviduals in statin therapy group are 29.*
- *Total number of induviduals in non -statin group are 51.*
- *Total number of induviduals infected in statin therapy group are 7 (24.23%).*
- *Total number of induviduals infected in non -statin group are 14(27.45%).*

Thus indicating that there is no statistically significant difference in risk of surgical site infection between statin theray and non-statin group.

SERUM CHOLESTEROL LEVELS AND SURGICAL SITE INFECTION

- *Among 80 patients in this study, the highest number of patients belonged to the serum cholesterol range of >240mg/dl(n=26 ,32.5%)*
- *the lowest number of patients belonged to the serum cholesterol range of 200-239mg/dl(n=15 , 18.8%)*
- *Among 21 patients having surgical site infections in this study,*

- *78 the highest number of infected patients belonged to the serum cholesterol range of <159mg/dl(n=10 ,47.61%)*
- *the lowest number of infected patients belonged to the serum cholesterol range of 200-239mg/dl(n=2, 19.52%)*
- *this signifies that increased incidence of SSI's is seen in patients with low serum cholesterol levels i.e,* ***LOW***

SERUM CHOLESTEROL IS A RISK FACTOR FOR NOSOCOMIAL SURGICAL SITE INFECTIONS AFTER GASTOINTESTINAL SURGERY(ABDOMINAL SURGERY).

IV. Discussion

Hypercholesterolemia has been associated with an increased incidence of coronary heart disease ,respiratory disease atherosclerotic occlusive vascular disorders .Hypocholesterolemia has been related to the development of organ dysfunction and morbidity and mortality in numerous patients .Very low levels of total cholesterol are more frequently found in polytrauma patients,after extensive surgeries, in life threatening infections and hypovolemic shock. Hypocholesterolemia is associated with severely ill patients. Neverthless it is not known whether it is a secondary manifestation of a disease or whether it actively contributes to worsening of the disease. Hypocholesterolemia is common in severely ill patients. Lipids have been found to play an important role in the reaction of the organisms to inflammation and in immune functions.

Their role in neutralization of bacterial lipopolysaccharides, i.e., endotoxins, is of particular importance. Low cholesterol levels reduces competition for binding of lipopolysaccharide (LPS) to lipopolysaccharide-binding protein (LBP), leading to ligation of the CD14 complex and activation of mononuclear cells. Conversely, binding of lipopolysaccharides to lipoproteins facilitates delivery of lipopolysaccharides to hepatocytes for detoxification, which if insufficient may leads to increased mononuclear cell activation.

Lipoproteins, especially High Density Lipoprotein(HDL), they bind to and neutralize lipopolysaccharide (LPS). Reconstituted HDL (rHDL), which consists of purified apolipoprotein A1 and phosphatidylcholine is even more effective in neutralizing the endotoxin toxicity. In rabbits, administration of recombinant HDL reduced tumor necrosis factor (TNF) production in response to lipopolysaccharide (LPS) and reduced tumor necrosis factor (TNF) production and acidosis after E. coli, but not Staphylococcus aureus bacteremia .

In another study ,Lipoprotein phospholipids were administered prophylactically in a porcine model of intraabdominal infection. Pretreatment with liposaccharides decreased serum endotoxin and TumorNecrosisFactor concentrations and preserved cardiac output and left ventricular ejection fraction. It also attenuated increases in systemic and pulmonary vascular resistances. Of extraordinary importance has been the experimental finding that administration of reconstituted HDL lipoprotein to septic animals significantly increased their survival.

Apart from the effect of HDL and rHDL on Lipopolysaccharide toxicity, HDL can also influence the fibrinolytic pathway and platelet function directly. Humans also have a high circulating level of HDL ,thus have higher tissue-type plasminogen activator and plasminogen activator inhibitor concentrations than subjects with low HDL levels. HDL affects platelet function by interacting with the glycoprotein IIb-IIIa complex, and thereby competing with the binding of fibrinogen to platelets and results in inhibition of platelet aggregation.

In a double-blind, placebo-controlled crossover study, LPS was injected following an infusion of rHDL or placebo into healthy male and female volunteers. In this experiment, rHDL significantly reduced LPS-induced activation of coagulation and fibrinolysis and collagen
stimulated platelet aggregation.

Hypocholesterolemia has also been associated with the development of nosocomial infections, mostly in the postoperative period.

Leardi et al. found the risk of postoperative infection to be 73 % among patients with a total cholesterol concentration of <2.7 mmol/L, compared with an incidence of infection of 35 % ($p< 0.001$) with a higher cholesterol concentration. These researchers also noted that the cholesterol level fell at the onset of infection, and that a fall in cholesterol was more predictive of infection than an increase in the white cell count. The degree of hypocholesterolemia reproduces, in a parallel manner, the seriousness of the inflammatory response and metabolic dysregulation, abnormalities in cytokine level, gravity of illness and organ dysfunction.

In a large cohort of hospitalized patients who had cholesterol levels < 2.6 mmol/L, a ten-fold higher mortality was reported, which correlated with low cholesterol levels. Low serum cholesterol levels on admission to a surgical Intensive care unit has been found to be associated with a higher APACHE III and Multi-Organ

Dysfunction Score (MODS), longer length of hospital stay, and higher morbidity and mortality. Those data suggestted that although total and HDL cholesterol levels fall with acute illness, the low cholesterol levels may predispose severly ill patients to endotoxemia, sepsis and MODS.

An important clinical observation has been that in severly ill patients with hypocholesterolemia there is progressive increase in cholesterol concomitantly with general improvement of the patients clinical condition; therefore repeated cholesterol determinations may provide useful information about the course of the disease. In this context it is also interesting that pre-operative hypocholesterolemia in surgical patients might also be connected with higher post-operative risk of septic complications.

As hypocholesterolemia is associated with a poor outcome during severe illness, it could be postulated that patients who receive statins (3-hydroxy-3-methylglutaryl Coenzyme A reductase inhibitors) (HMG-CoA) have a poor outcome when severely ill. Emerging data, however, is suggesting that statins may improve the outcome of patients with sepsis. This effect of improving the condition of severely ill patients is independent of the effect of statins on the lipid profile. Statins have diverse anti-inflammatory and immunomodulating properties.

The HMG-CoA reductase inhibitor simvastatin has been shown to significantly improve the survival in a murine model of sepsis. In a prospective observational study treatment with a statin for greater than one month before the onset of an acute bacterial infection was found to be associated with a reduced rate of severe sepsis and , despite the fact that the patients receiving statins had a significantly higher frequency of comorbidities. Additional studies, however, are required before statins are recommended for the treatment of sepsis

Hypocholesterolemia is commonly observed in critically ill patients and in other acute or chronic conditions. In these patients, it is often an index of a pathophysiological frailty and impending danger. It may also reflect incapacity of the organism to increase cholesterol availability, to meet increased requirements in critical illness.

Nevertheless, it is not known whether it is a secondary manifestation of disease, or whether it actively contributes to deterioration of the disease. Cholesterol seems to be a potentially essential component of nutrition, particularly in critically ill patients, where, due to the absence of cholesterol in parenteral nutrition, its exogenous supply is discontinued. However, the extent of contribution of impaired endogenous synthesis to hypocholesterolemia is not yet well-defined. The relationship between plasma cholesterol levels and severity of illness is also important.

In many hospital wards, progressive reversal of hypocholesterolemia is considered a marker of reversal of critical illness, and of patient recovery; likewise, severe persistent hypocholesterolemia, or further extreme drop in cholesterol, is a strongly unfavourable prognostic sign.

Although the contribution of hypocholesterolemia to mortality is modest compared with known risk factors such as increased severity of illness and the development of nosocomial infection, low serum lipid concentration represent a potential therapeutic target in sepsis. What remains unclear is whether treatment which increases HDL or total cholesterol prevents or limits complications and improves the outcome of critically ill patients.At present, the only concrete consequence of hypocholesterolemia is the imperative and rapid resolution of the underlying illness. The enrichment of fat emulsions used in parenteral nutrition with cholesterol may be a new promising tool to influence hypocholesterolemia and the related undesirable effects in critically ill patients.

Bibilography

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