AIMS

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OBJECTIVES
AIMS AND OBJECTIVE

To evaluate the impact of macrolides in acute coronary syndrome.

PATIENTS SELECTION

All acute coronary syndrome patients admitted to ICCU & medical wards in M.L.B. Medical College, Jhansi.

DIAGNOSIS CRITERIA:

- Typical anginal pain
- Classical ECG changes
- Enzymes- CPK-MB
  - Troponin
- 2 D Echo
- TMT as feasible

ACUTE CORONARY SYNDROME:

The spectrum of clinical presentations ranging from unstable angina through non-Q-wave MI to Q-wave MI are referred to as the acute coronary syndrome.
REVIEW
OF
LITERATURE
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Kahler J et al suggested that infection with C pneumonial increases the risk of coronary artery Disease by factor 2 or more. Sushussheim AE, Euster V. demonstrated that macroclide antibacterial treatment directed against C. pneumoniea reduces the risk resurrect coronary events.

Mehta JL, et al. Early trails with appropriate antibiotic agent in some pts with recent history of acute MI led to very salutary results.

Gurfinkel EP, Bozovich, EP, Bozovich G. The Roxis trail has shown some encouraging evidences for the potential role of intracellular pathogens in acute coronary syndrome.

Song YG, et al showed seropositive rate of Anti-Chlamydia pneumoniea IgG was higher in the disease group than in the negative control group.

Anderson JL, Muhelstein JB, Showed Azithromycin caused modest but significant reduction in markers of inflammation.
Fong IW, et al demonstrated with early treatment of C. pneumoniae infected rabbits with Azithromycin was highly effective (87%) in preventing atherosclerotic changes. They concluded that it is possible that longer or more aggressive antibiotic treatment may be needed to reverse preformed lesion or that antibiotics treatment may not be value once lesion have formed.

Gurfinkel E. questioned the role of infection in the instability of atherosclerotic plaques because of discrepancies in the results of clinical trials tested antibiotics in acute coronary syndrome.

Wong TK, et al advocated that the use of antibiotics in routine practice is not justified; large trails will help to elucidate the role of C pneumonia.

Ramirez JA cultured Chlamydia pneumonia from atherosclerotic plaques in one patient with severe coronary artery disease.

Frishman WH, Ismail AA, conducted that in high-risk patients; the results of most recent studies have not revealed any benefit of treatment with antibiotics.
Ismail, Khosravi H, Osion H, concluded that infectious agents including Chlamydia pneumoniae may play a role in atherosclerosis & its manifestation especially as they relate to CAD.

Danesh J, et al study, together with a meta-analysis of previous prospective studies, reliably excludes the existence of any strong association between C. pneumoniae & incidental coronary heart disease. Further studies are required to confirm or refute any modest association that may exist, particularly at younger ages.

Gleffers J, Solbach W, Maass M, Chlamydia pneumoniae strains have been recovered from arteriosclerotic coronary arteries, but their antibiotic susceptibility profiles have not yet been examined. We report in vitro susceptibility data for five cardiovascular C. pneumoniae isolates. These strains did not differ significantly from respiration strains in their pattern of susceptibility to azithromycin, erythromycin, roxithromycin ofloxacin, doxycycline, rifampin and penicillin G. Roxithromycin was the most active macrolide, and rifampin was the most effective drug overall.
Mirja Puolakkainen; San-Pin Wang, J. Thomas Grayston, and Lee Ann Campbell: a prospective study from Finland has indicated that chronic C. pneumoniae infection is significant risk factor for coronary heart disease.

Gupta S, Camm AJ. Recent evidence suggests that common chronic infections may contribute, either by direct or indirect mechanism, to the etiology and or progression of coronary atherosclerosis.

Persson K, Boman J. Newly published results of antibiotic treatment of vascular disease not only appear to provide further support for the infection hypothesis, but also suggest a quite different approach to the treatment of atheromatous cardiovascular disease.

Grayston JT, current knowledge of the relation of C. pneumoniae and atherosclerosis comes from observational and experimental studies. The limitations of the serologic studies of chronic infection are noted as is the conclusive demonstration of an association of C. pneumoniae and atherosclerosis by the repeated and frequent finding of the organism in atherosclerotic tissue.
Wong YK, Gallagher PJ, Ward ME, more evidence is required before C pneumoniae can be accepted as playing a role in atherosclerosis. Although use of antibiotics in routine practice is not justified, large-scale trials in progress will help to elucidate the role of C pneumoniae.

Behbahani R, Verme – Gibboney C, Romanelli AM. Conventional cardiovascular risk factors fail to explain completely the pathogenesis of atherosclerosis and coronary artery disease. “Innocent bystander” or whether antibiotic therapy has any role in the treatment of cardiovascular disease remains to be determined.

Dugan JP, Feuge RR, Burgers Ds. Established risk factors account for no more than 50% of coronary artery disease cases: therefore, the search continues for other modifiable risk factors. In recent years, there has been renewed interest in the infectious theory of atherosclerosis. Chlamydia pneumoniae has been implicated as a potential cause of atherosclerotic disease. C. pneumoniae antibodies are found in approximately 50% of middle-aged adults worldwide. These antibodies have been detected in atherosclerosis tissue.
Fortini A, Corti G, Cappelletti C. There is widespread consensus that atherosclerosis is an inflammatory disease. The organism has been identified in over 50% of atherosclerotic plaques examined by various histopathological techniques, while it has been only rarely found in normal artery tissues moreover; viable Chlamydia pneumoniae has recently been isolated from coronary and carotid atherosclerotic plaques.

In conclusion, while the association between Chlamydia pneumoniae and atherosclerosis seems to be established, it is still uncertain whether or not the organism plays a causal role in atherosclerosis and its complications.

Girard SE, Temesgen E. Data from three interventional studies in humans have suggested that treatment with antibiotics decreases inflammatory markers and perhaps influences the anti-C pneumoniae antibody titers; At present antimicrobial therapy for atherosclerosis is not advocated outside of well – controlled research settings.

Maass M. Serological response to chlamydia pneumoniae statistically indicates an increased risk of coronary artery disease and myocardial infarction. This surprising relation is
corroborated by the presence of chlamydial structures and even viable chlamydia pneumoniae in atherosclerotic plaques. These finding have already resulted in initial studies on the potential benefit of antimicrobial therapy in coronary heart disease.

**Fong TW.** Support but do not prove that C pneumoniae can cause atherosclerosis.

**Cambell LA, Kuo CC. Grayston JT.** The association of C pneumoniae with atherosclerosis is corroborated by the presence of the organism in atherosclerotic lesions throughout the arterial tree and the near absence of the organism healthy arterial tissues, C. pneumoniae has also been isolated from coronary and carotid atheromatous plaques.

**Larsen MM. Morn B, Andersen PL, Ostergaard LJ.** Chlamydia pneumoniae could be associated with the risk of developing atherosclerosis and an increased risk of thromboembolic complication. The effect of antibiotic treatment in cardiovascular disease has been explored in epidemiologic studies and in randomized controlled trials. Data suggest a protective but short – lasting effect of macrolide antibiotics on cardiovascular disease. The effect could be the result of anti-
bacterial as well as anti-inflammatory properties. Currently, there is no indication for treating cardiovascular disease with antibiotics.

**Carlisle SS, Natha MC.** Numerous reports have suggested an association between chronic CP and CAD. CP has been seroepidemiologically linked to CAD. The organism has also been isolated from atherosclerotic lesions. Two reports in Humans and one report in animals have shown that macrolide therapy (azithromycin or roxithromycin) may decrease the risk of adverse cardiovascular events. Evidence seems to support an association between CP infection and an increased incidence of CAD.

**Higgins JP.** Infectious agents such as chlamydia pneumoniae have been alleged to be activators information that may contribute to atherosclerosis and thus coronary artery disease (CAD) and its associated complications. A logical pneumoniae extension of this theory whether treating C. pneumoniae infection with antibiotics and / or modulating inflammatory processes can effect CAD and its sequelae.
Grayaton JT, Kuo CC, Campbell LA, Benditt EP. Infection with chlamydia pneumoniae, strain TWAR, has been associated with atherosclerotic cardiovascular disease in two types of investigations, seroepidemiological and morphological – molecular. A series of seroepidemiological studies from Finland and the United States have shown a statistically significant association between several types of TWAR antibody, including immune complexes, and atherosclerotic disease of the coronary and carotid arteries. Presence of the organism in atheroma has been demonstrated by electronmicroscopy, immunocythemical staining with TWAR-specific monoclonal antibody and by the polymerase chain reaction for TWAR-specific DNA.

Stille W, Stephen C. Atherosclerosis can be apparently the result of ultrachronic persistent infection by Chlamydia pneumoniae and not the results of heterogeneous risk factors. The main arguments for the chlamydial genesis are: Correlation of coronary heart disease and other atherosclerotic disease and antibodies against Chlamydia pneumoniae. The reduction of
incidence of atherosclerotic disease since the 1960s, probably due to advanced antibiotic therapy.

Anderesen JJ. Chlamydia-specific antibodies and circulating immune complex are found more often in patients than in controls. The organism can often be shown in atherosclerotic plaques from coronary, carotid, iliac and femoral arteries as well as from the aorta, but is seldom demonstrated in arteries without atherosclerosis.

Leinonen M. C. pneumoniae infections are more common in smokers than in nonsmokers, suggesting that smoking predisposes to the development of chronic infection. Infections may also affect lipid metabolism. In persons with acute pneumonia caused by C. pneumoniae, high-density lipoprotein (HDL) values are lower and triglyceride values higher than seen in pneumonia caused by viruses and other bacteria. Furthermore, chronic C. pneumonia infection is associated with elevated triglyceride and lower HDL levels in healthy Finnish men.

Epstein SE, Zhou YF, Zhu J. Although definitive proof of a causal role of infection contributing to atherogenesis is
lacking, multiple investigations have demonstrated that infectious agents evoke cellular and molecular changes supportive of such a role.

Monno R, Di Biase M, Costi A, De Nicolo T, Correale M, Bolognese P, Losacco G. There is increasing body of evidence that links Chlamydia pneumoniae infections to atherosclerosis and the clinical complications of unstable angina, Myocardial infarction and stroke. Several epidemiologic reports indicate an association between the presence and titer of Chlamydia pneumoniae antibodies and atherosclerosis and its complications. Other studies show the presence of Chlamydia pneumoniae, Chlamydial antigens or nucleic acid in atherosclerotic plaques.