

Current Advance of Management in Vascular Disease

16:20-16:40 Anti-Inflammatory Strategies for Preventing Cardiovascular Events

김응주/고려의대 순환기내과

항염증 치료와 심혈관질환 간에는 두 가지 측면이 있다.

하나는 그간 많은 이슈가 되었던 non-aspirin NSAIDs 의 심혈관계 위험에 관한 것이고, 다른 한가지는, 죽상동맥경화 병태생리에 관여하는 염증이론에 기반한 항염증 치료이다.

본 강좌에서는 위 두 측면에 대해 정리해 보고자 한다.

아래는 미국 식품의약품안전처의 홈페이지에 게시되어 있는 현재까지의 증거들 기반 non-aspirin NSAIDs의 심혈관계 위험에 관한 입장으로 참고할 만 하다 [1].

FDA Drug Safety Communication: FDA strengthens warning that non-aspirin nonsteroidal anti-inflammatory drugs (NSAIDs) can cause heart attacks or strokes

Based on our review and the advisory committees' recommendations, the prescription NSAID labels will be revised to reflect the following information:

- The risk of heart attack or stroke can occur as early as the first weeks of using an NSAID. The risk may increase with longer use of the NSAID.
- The risk appears greater at higher doses.
- It was previously thought that all NSAIDs may have a similar risk. Newer information makes it less clear that the risk for heart attack or stroke is similar for all NSAIDs; however, this newer information is not sufficient for us to determine that the risk of any particular NSAID is definitely higher or lower than that of any other particular NSAID.
- NSAIDs can increase the risk of heart attack or stroke in patients with or without heart disease or risk factors for heart disease. A large number of studies support this finding, with varying estimates of how much the risk is increased, depending on the drugs and the doses studied.
- In general, patients with heart disease or risk factors for it have a greater likelihood of heart attack or stroke following NSAID use than patients without these risk factors because they have a higher risk at baseline.
- Patients treated with NSAIDs following a first heart attack were more likely to die in the first year after the heart attack compared to patients who were not treated with NSAIDs after their first heart attack.

- There is an **increased risk of heart failure** with NSAID use.

LDL 콜레스테롤 저하 치료 외에, 죽상동맥경화의 염증과정을 표적으로 하는 항염증 또는 면역조절 치료에 관한 연구는 아직도 매우 초기단계이며 대규모 임상연구를 통해 그 효과가 입증된 바는 없다. 그러나, 아래와 같이 염증이론에 기반한 치료의 시도들이 다양하게 이뤄지고 있는 만큼 [2], 조만간 항염증 치료의 심혈관 위험 감소에 대한 해답이 제시될 것으로 예상된다.

Clinical trials of anti-inflammatory therapy in cardiovascular disease

Drug	Target	Trial	Size	Sponsor	Status
A. Agents impacting on the IL-6 signalling pathway					
Canakinumab	IL-1 β	CANTOS	10 000	Novartis	Enrolling
Methotrexate	IL-6, TNF	CIRT	7 000	NHLBI	Enrolling
Anakinra	IL-1Ra	IL-HEART	190	UK-MRC	Completed
Colchicine	multiple	LoDoCo	532	HRS, Aus	Positive
Tocilizumab	IL-6	Entracte	3 000	Hoffmann	Enrolling
Etanercept	TNF	Entracte	3 000	Hoffmann	Enrolling
B. Agents impacting on alternative inflammatory pathways					
Succinobucol	Ox-LDL	ARISE	6 144	AtheroGenics	Negative
Varespladib	sPLA ₂	VISTA-16	5 000	Anthera	Negative
Darapladib	Lp-PLA ₂	STABILITY	15 000	GSK	Enrolled
Darapladib	Lp-PLA ₂	SOLID-TIMI-52	13 000	GSK	Enrolled
Inclacumab	P-Selectin	SELECT-ACS	544	Roche	Completed
Inclacumab	P-Selectin	SELECT-CABG	380	Roche	Enrolled

1. FDA Drug Safety Communication: FDA strengthens warning that non-aspirin nonsteroidal anti-inflammatory drugs (NSAIDs) can cause heart attacks or strokes. 2015 Jul [https://www.fda.gov/Drugs/DrugSafety/ucm451800.htm].

2. Ridker PM, Lüscher TF. Anti-inflammatory therapies for cardiovascular disease. Eur Heart J. 2014;35:1782-91.