"Nonsteroidal anti-inflammatory drugs exacerbated respiratory disease as an asthma endotype - clinical and immunological characterization"

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Introduction:
Airway disease exacerbated by NSAIDs (NERD) is a syndrome that occurs in nearly a dozen percent of asthma patients, more often in the group of patients with severe and uncontrolled asthma. The spectrum of N-ERD symptoms includes bronchial asthma, chronic sinusitis with polyps, and hypersensitivity to NSAIDs.The underlying cause of this disease are, possibly genetically determined, disturbances in the metabolism of arachidonic acid manifested by excessive synthesis of proinflammatory mediators, especially cysteinyl leukotrienes,and a deficit in the production of protective eicosanoids. Infectious, viral and bacterial agents play an important role in inducing and maintaining this process. Studies conducted in recent years (Bochenek et al. 2014, Kim et al. 2018) indicate that patients with N-ERD are diverse in terms of their clinical picture, and probably in terms ofthe characteristics ofthe inflammatory background in the airways.
Understanding the clinical (subphenotypes) and pathogenetic (endotypes) heterogeneity may be the basis for the implementation of individualized treatment (including biological drugs).

Research subject and methodology:
Selectiontion of the study group of 42 patients with bronchial asthma diagnosed according to the GINA2018 criteria with a history of NSAID hypersensitivity (in some cases confirmed by a positive exposure test with aspirin), meeting the inclusion criteria and not meeting the exclusion criteria. Conducting: questionnaire (including demographic data, medical history, family history of allergic diseases, environmental exposure), ACT, SNOT 22, smell test, spirometry according to ERS recommendations, spirometry after bronchodilator, FeNO according to ATS recommendations, PTS in the study group. Selection of a control group consisting of 21 NSAID tolerant patients with bronchial asthma and 11 patients without bronchial asthma, selected in terms of meeting similar demographic (age, gender) and clinical (asthma severity) criteria for the study group, meeting the inclusion criteria and not meeting the exclusion criteria. Performing tests in the control group, such as in the test group.

Pilot study - search for biomarkers:
In order to find biomarkers collected using minimally invasive methods (blood, NasosorptionTM), cytokines were screened in the collected material in 13 controls, 33 patients with asthma, tolerant of NSAIDs (ATA) and 14 patients with N-ERD. The Bio-Plex Pro Human Cytokine 27-Plex Immunoassay panel (27 cytokines) was used.

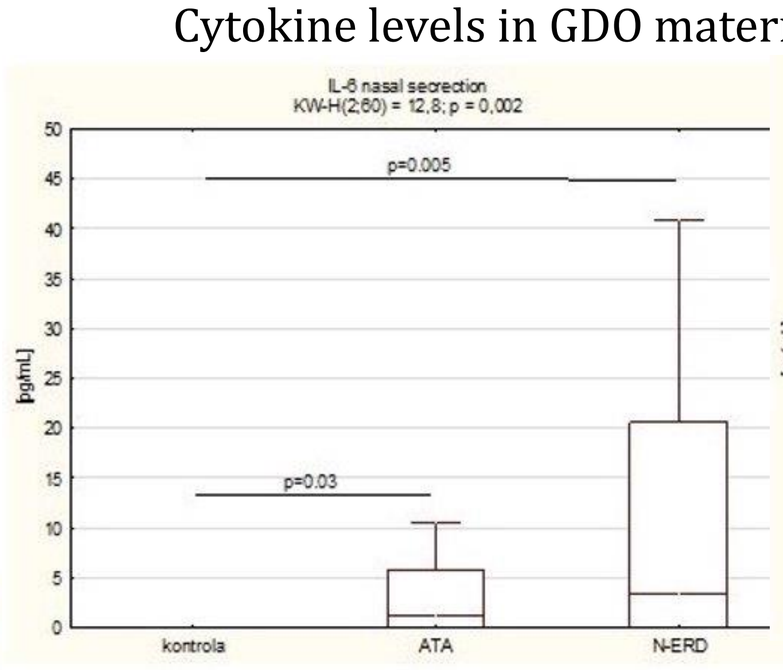
Results:

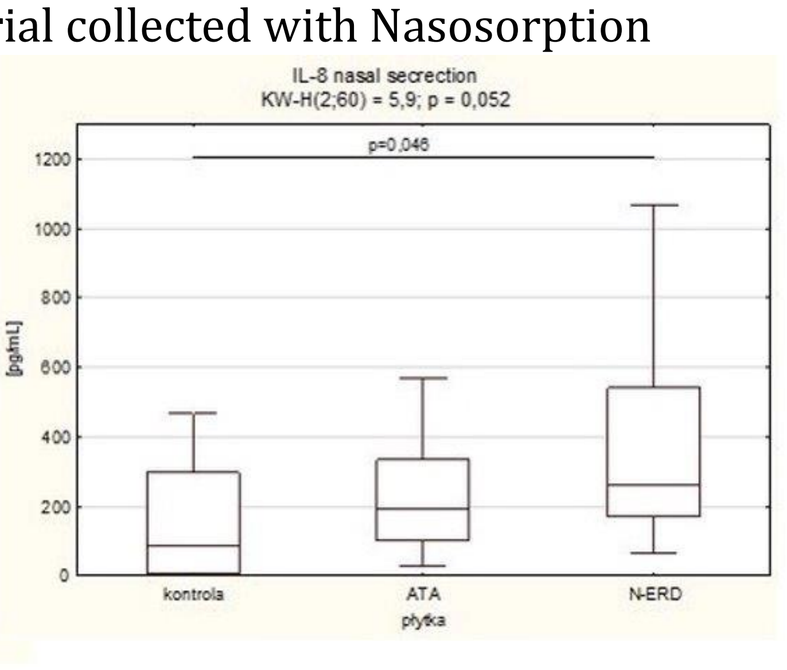
NS (n=60)		Serum, n=53	
Basic FGF (44)	21/60 (35%)	Basic FGF (44)	23/53 (43,4%)
Eotaxin (43)	52/60 (86,7%)	Eotaxin (43)	52/53 (98,1%)
G-CSF (57)	40/60 (66,7%)	G-CSF (57)	51/53 (96,2%)
GM-CSF (34)	1/60 (1,7%)	GM-CSF (34)	1/53 (1,9%)
IFN-gamma (21)	49/60 (81,7%)	IFN-gamma (21)	13/53 (24,5%)
IL-10 (56)	16/60 (26,7%)	IL-10 (56)	0/53 (0%)
IL-12(P70) (75)	0/60 (0%)	IL-12(P70) (75)	1/53 (1,9%)
IL-13 (51)	12/60 (20%)	IL-13 (51)	3/53 (5,7%)
IL-15 (73)	2/60 (3,3%)	IL-15 (73)	0/53 (0%)
IL-17 (76)	11/60 (18,3%)	IL-17 (76)	1/53 (1,9%)
IL-1beta (39)	50/60 (83,3%)	IL-1beta (39)	1/53 (1,9%)
IL-1ra (25)	56/60 (93,3%)	IL-1ra (25)	10/53 (18,9%)
IL-2 (38)	0/60 (0%)	IL-2 (38)	0/53 (0%)
IL-4 (52)	7/60 (11,7%)	IL-4 (52)	47/53 (88,7%)
IL-5 (33)	13/60 (21,7%)	IL-5 (33)	0/53 (0%)
IL-6 (19)	26/60 (43,3%)	IL-6 (19)	1/53 (1,9%)
IL-7 (74)	17/60 (28,3%)	IL-7 (74)	9/53 (17%)
IL-8 (54)	59/60 (98,3%)	IL-8 (54)	31/53 (58,5%)
IL-9 (77)	40/60 (66,7%)	IL-9 (77)	53/53 (100%)
IP-10 (48)	59/60 (98,3%)	IP-10 (48)	53/53 (100%)
MCP-1 (53)	42/60 (70%)	MCP-1 (53)	53/53 (100%)
MIP-1alfa (55)	52/60 (86,7%)	MIP-1alfa (55)	45/53 (84,9%)
MIP-1beta (18)	35/60 (58,3%)	MIP-1beta (18)	53/53 (100%)
PDGF-BB (47)	8/60 (13,3%)	PDGF-BB (47)	53/53 (100%)
RANTES (37)	20/60 (33,3%)	RANTES (37)	53/53 (100%)
TNF-alfa (36)	19/60 (31,7%)	TNF-alfa (36)	52/53 (98,1%)
VEGF (45)	1/60 (1,7%)	VEGF (45)	3/53 (5,7%)

%
0-20
20-40
40-60
60-80
80-100

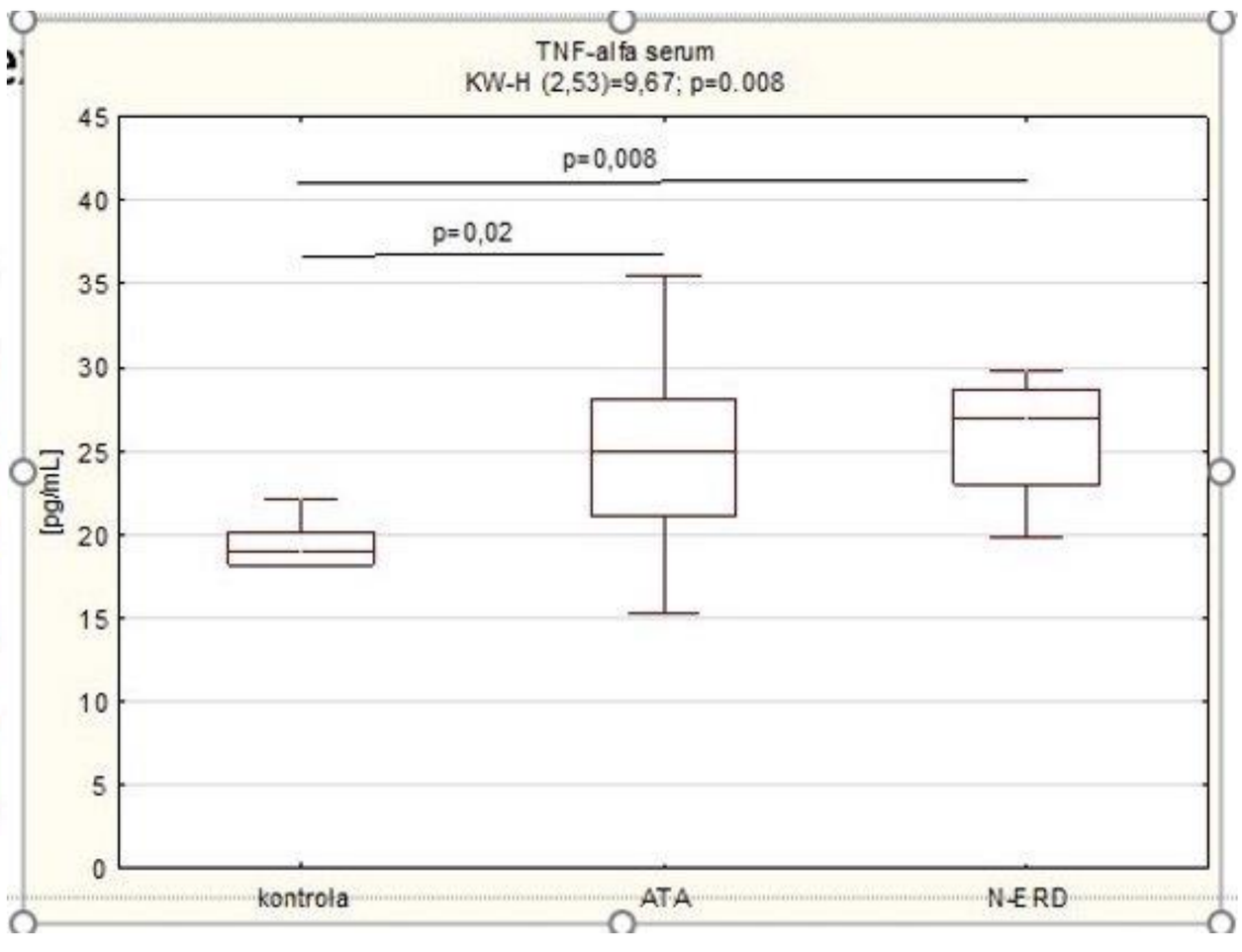
% of positive results in samples taken

Cytokine levels in GDO material collected with Nasosorption





Serum cytokine levels



Conclusions:
The pilot study showed that among the tested cytokines, none met the criteria of the NERD biomarker (no cytokine differentiating both controls and ATA).

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