Let's consider Biologic Immunogenicity

OP0301

RISK FACTORS FOR ANTI-INFLIXIMAB ANTIBODY FORMATION: RESULTS FROM THE RANDOMISED CONTROLLED NOR-DRUM A TRIAL

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Background: Immunogenicity is related to loss of efficacy and safety to TNF α inhibitors and is frequently observed early in the treatment course. The highest rate of anti-drug antibody (ADAb) formation has been reported for infliximab (IFX). ¹ Knowledge about risk factors for immunogenicity might contribute to better handling of this problem in clinical practice.

Objectives: To identify risk factors for ADAb formation during the early phase of IFX treatment.

Methods: 411 patients with immune-mediated inflammatory diseases (84 rheumatoid arthritis (RA), 119 spondyloarthritis (SpA), 45 psoriatic arthritis, 83 ulcerative colitis, 58 Crohn's disease and 22 psoriasis) initiating IFX treatment were included in the 38-week NOR-DRUM A trial and randomised 1:1 to therapeutic drug monitoring or standard IFX therapy.² The primary endpoint was clinical remission at week 30. Serum (s) IFX levels and ADAb were measured at each infusion by in-house assays; time-resolved fluorometric assay for sIFX and inhibition assay for ADAb.² In this sub-study, possible risk factors for ADAb formation including demographic variables, diagnosis, comedication, disease activity, IFX dose, sIFX and drug holidays, were assessed using logistic regression. Variables with a p-value <0.25 in univariate analyses were further examined in multivariate analyses adjusting for potential confounders (diagnosis, disease activity, age and gender).

Results: 410 of 411 patients had at least one measurement of sIFX and were included in the present analyses. 76% of patients were biologic-naïve and 45% (18% of RA patients) used IFX as monotherapy. Patients received a mean IFX dose of 3.2-5.9 mg/kg (RA 3.2 mg/kg). ADAb were detected in 78 (19%) patients. The Table 1 shows variables with a significant association to ADAb development. Analyses revealed an increased risk of ADAb development in patients with RA (Odds ratio (OR) 2.1, 95% confidence interval (CI) 1.1-3.9), while SpA had a lower risk (OR 0.5, CI 0.2-0.9) compared to the other diagnoses. These findings were consistent in both univariate- and multivariate analyses (Table 1). Figure 1 shows the cumulative hazard for ADAb development according to diagnosis. Other risk factors for ADAb (Table 1) were smoking (OR 1.8, CI 1.0-3.3) and drug holidays of more than 12 weeks (OR 4.7, CI 1.2-18.3). Additionally, the risk of ADAb increased with higher disease activity (OR 1.5, CI 1.0-2.3) and lower sIFX levels (0.7, 0.6-0.8). Patients co-treated with methotrexate (OR 0.4, CI 0.2-0.9) or thiopurines (OR 0.3, CI 0.1-0.8), or having one or more IFX dose increments (OR 0.4, CI 0.3-0.8), had a reduced risk of immunogenicity.

Conclusion: This study identified smoking, drug holidays, high disease activity, IFX monotherapy and low sIFX levels as risk factors for ADAb development. Of particular interest, we found that RA patients had significantly increased risk of ADAb compared to the other immune-mediated inflammatory diseases. Whether this novel finding reflects different underlying disease mechanisms or the fact that RA patients receive a lower IFX dose, is not known and needs to be further explored.

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Context matters: Placebo and nocebo effects for pain management

OP0302-HPR

IDENTIFYING THE CONTEXTUAL FACTORS IN THE PATIENT-PRACTITIONER ENCOUNTER THAT HAVE THERAPEUTIC EFFECT: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Placebo or contextual effect is an integral part of the treatment effect (1). The factors related to this effect are "contextual factors" (CFs) (2). CFs may be categorised into five groups as factors related to practitioner, patient, practitioner-patient interaction, treatment and therapeutic environment (3). Several CFs have demonstrated their therapeutic effect, whereas others not (4). The majority of musculoskeletal pain relief result from CFs (5). Identifying the key CFs may encourage health practitioners to optimize the contextual aspects of care.

Table 1. Risk factors for ADAb. Results from logistic regression analyses

	Univariate analyses		Multivariate analyses (Adjusted for diagnosis, disease activity, age and gender)	
	OR	CI	OR	CI
RA	2.2**	[1.3,3.8]	2.1*	[1.1,3.9]
SpA	0.4**	[0.2,0.8]	0.5*	[0.2,0.9]
Methotrexate	1.1	[0.7,1.9]	0.4*	[0.2,0.9]
Thiopurine	0.3*	[0.1,0.9]	0.3*	[0.1,0.8]
Current or former smoking	2.2**	[1.3,3.8]	1.8*	[1.0,3.3]
Mean sIFX	0.7***	[0.6,0.8]	0.7***	[0.6,0.8]
>12 weeks between infusions	4.5*	[1.3,16.0]	4.7*	[1.2,18.3]
IFX dose increment	0.5*	[0.3,0.9]	0.4**	[0.3,0.8]
Mean DAS28 (RA and PsA)	1.5*	[1.0,2.1]	1.5*	[1.0,2.3]
Mean ESR	1.1***	[1.0,1.1]	1.1***	[1.0,1.1]
Mean CRP	1.1**	[1.0,1.1]	1.1**	[1.0,1.1]

* p<0.05, ** p<0.01, *** p<0.001 Only variables with a p-value <0.05 are shown. Non-significant variables include other demographic variables and IFX dose.

Objectives: To identify the modifiable CFs that can improve clinical outcomes in published randomised controlled trials (RCTs).

Methods: A systematic search was carried out, up until April 18th 2019, on the following databases: MEDLINE via Ovid, EMBASE, AMED, PsycINFO and Cochrane library. RCTs comparing contextual enhanced interventions versus non-enhanced control in adults for any health conditions were searched. The outcomes included both self-reported outcomes and objectively measured outcomes. The effect size and 95% confidence interval were calculated using the standard mean difference. Risk of bias was evaluated using the modified Cochrane tool. The random effects model was used to pool the results.

Results: Of 3900 records generated from the systematic search, 15 trials (4615 participants) met the inclusion criteria, and 13 were included in this meta-analysis (Figure 1). Conditions studied included musculoskeletal [4], cardiovascular [2], irritable bowel syndrome [1], diabetes [1], asthma [1], GP or hospital patients [6]. Three CFs have been identified from these trials, including empathy, patient involvement and positive communication. All were found to be effective for patient experience i.e. satisfaction. Positive communication was also effective for symptoms but not objective outcomes (Table 1).

Table 1. Summary of results.

Outcome	Intervention	Number of studies (Number of participants)	SMD (95% CI)	I^2
Patient experience outcomes, e.g. satisfaction	Empathy	2 (137)	0.45 (0.11, 0.79)	42.2 %
	Patient involvement	4 (1596)	0.31 (0.21, 0.41)	93.0 %
	Positive communication	3 (793)	0.38 (0.24, 0.52)	93.9 %
Symptomatic outcomes, e.g. pain	Empathy	1 (221)	-0.18 (-0.45, 0.08)	0.0 %
	Patient involvement	1 (314)	-0.05 (-0.27, 0.17)	0.0 %
	Positive communication	3 (658)	0.20 (0.05, 0.35)	64.8 %
Objective outcomes, e.g. peak expiratory flow	Positive communication	2 (266)	0.10 (-0.14, 0.34)	66.6 %

Positive SMD favours intervention group. SMD= Standard mean difference, CI= Confidence interval, I^2 = heterogeneity.

Figure 1. Summary of screening process.

Conclusion: This systematic review has identified three CFs (empathy, patient involvement and positive communication) that have therapeutic effects for different conditions in trials, especially for self-reported outcomes. More research is needed to examine the clinical outcomes of CFs and to understand the influence of health practitioners on disease processes.

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Myths and taboos around relationships: strategies for a sexy life

OP0303-HPR IT IS NOT JUST ABOUT THE SEX: VIEWPOINTS OF DUTCH ADULT MEN WITH INFLAMMATORY ARTHRITIS REGARDING THE IMPACT OF THE DISEASE ON THEIR SEXUAL HEALTH

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Background: Sexual health (SH) can be impaired in men with inflammatory arthritis (IA) (1). In addition to biological factors, such as inflammation, subjective factors such as personal beliefs can also impair SH. The Q methodology combines aspects of qualitative and quantitative approaches to systematically study subjectivity, and has been applied successfully in other medical fields.

Objectives: To describe the viewpoints of adult men with IA on the impact of IA on their SH using the Q methodology.

Methods: Men, 18 years and older, diagnosed with RA or JIA were invited by their rheumatologist. Participants ranked 34 opinion statements about potential impacts of IA on their SH on an agreement scale. A by-person factor analysis identified common patterns in the rankings. These patterns represent the different viewpoints among the men. Data from interviews, in which the men explained their ranking, was used to further interpret the viewpoints. A Q-methodology study usually consists of 30-40 participants.

Results: 30 men with IA were included. Their mean age was 43.2 (range 22-77) years. The analysis revealed three viewpoints:

1. "I am satisfied with my sex life"

Men with viewpoint 1 experience no significant impact of IA on their SH. However, most men indicated that when their disease was active, IA had a negative impact on their SH.

2. "Arthritis has a negative influence on my sex life"

Men with viewpoint 2 experience a dramatic impact, due to pain, fatigue and gloom. Their relationship worsened and they feel guilty towards their partner. Discussing their problems is not difficult.

3. "I am keeping up appearances"

Men with viewpoint 3 experience SH impairment mainly as a result of pain. IA impairs them physically, makes them feel less of a man, less attractive and reduces their self-confidence. Due to problems with accepting their disease and communicating their problems, these men tend to hide their problems.

Conclusion: We identified 3 viewpoints on the impact of IA on male SH, 2 of them revealing a negative influence that goes beyond the physical act of sex. IA can also affect relationships, self-confidence and manhood. Future research will focus on identifying men with SH problems in the clinic and the best counseling approach.

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