

Toll-Like-Receptor (TLR) 2 and 4 Responsiveness of Isolated Peripheral Blood Mononuclear Cells, in Young Women with Severe Dysmenorrhoea both on and off the Oral Contraceptive Pill.

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Introduction:

TLRs are a family of receptors found on the surface membrane of cells of the innate immune system that release cytokines including IL-1beta when stimulated. This paper investigates the role of the innate immune system in dysmenorrhoea-predominant pelvic pain, with particular reference to Toll-Like Receptors 2 and 4.

Patients and Methods:

56 young women with either severe or minimal dysmenorrhoea, and use or non-use of the oral contraceptive (OC) pill. Peripheral Blood Mononuclear Cells (PBMCs) were collected on Day 1-2 of the menstrual cycle ? a time of anticipated high pain, and Day 7-10 of her menstrual cycle ? a time of anticipated low pain. PBMCs were stimulated with either TLR2 (PAM) or TLR4 (LPS) agonists and IL ? 1B output determined.

Mixed - effects modelling and a linear regression model was used to compare IL-1 beta output and log TLR agonist concentrations for each group.

Results:

There was no difference in IL-1Beta output between groups using stimulation with LPS (Day 1-2 or Day 7-10), or with PAM on Day 1-2.

However, there were striking differences between those women on the OCP and women off the OCP for PAM stimulation on Day 7-10.

The response was three-fold (95%CI 1.4 - 6.7) greater in young healthy women with minimal or no dysmenorrhoea on the OC, than in similar women off the OC.

To determine the overall effect of the OC, regardless of pain status, all OC groups (with and without pain) were compared with all non-OC groups. There was a 2.0 fold greater (95% CI 1.4-3.3) response in the OC groups when compared to the non-OC group.

Young women, with and without pain, are highly reactive to TLR stimulation of PBMC's. This effect was more reliably apparent with TLR 2 (PAM) than TLR4 (LPS) stimulation.

Conclusions:

TLR responsiveness has previously been shown to differentiate patients with a chronic pain condition from healthy controls. This investigation provides disturbing evidence that OC use may be associated with enhanced TLR responsiveness of PBMC's, even in healthy women. As such, they may be primed for future persistent pain conditions.

Mots clefs : Toll-Like Receptor, Dysmenorrhoea, Pelvic Pain, Contraceptive Pill, Immune, Glia

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