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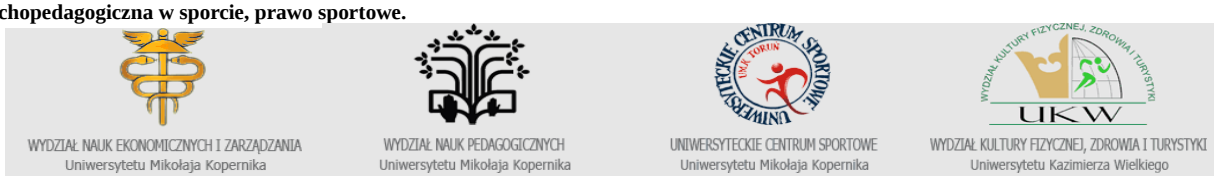
W związku z zapotrzebowaniem na szukanie odpowiedzi dotyczącej jakości w sporcie oraz podnoszeniu efektywności wyników klubów sportowych Wydział Nauk Ekonomicznych i Zarządzania, Wydział Nauk Pedagogicznych, Uniwersyteckie Centrum Sportowe Uniwersytetu Mikołaja Kopernika, oraz Wydział Kultury Fizycznej, Zdrowia i Turystyki Uniwersytetu Kazimierza Wielkiego stworzyły projekt konferencji naukowej pt. __Jakość w sporcie.

Bloki tematyczne: zarządzanie jakością w sporcie, sport jako forma autokreacji, oraz psychorehabilitacja i pomoc psychopedagogiczna w sporcie, prawo sportowe.



DO PREOPERATIVE PSYCHOLOGICAL CONDITION AND M1-OPIOID RECEPTOR GENE POLYMORPHISM 118A>G AFFECT OPIOID ANALGESIA EFFICACY AFTER MAJOR UROLOGICAL SURGERIES?

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The problem of adequate postoperative pain control remains topical both in our country and abroad [1]. According to the working group PROSPECT (www.postoppain.org), 70% of patients experience pain after the surgery ranging from mild to severe. An essential role in the formation of pain sensation belongs to psychological factors. Due to the emotional component, pain is perceived as subjective parameter, and its severity may be affected by changes in affective background, in particular, by depressive and anxiety disorders. According to Larson S.L. et al. (2004), patients with more severe manifestations of depression are significantly more likely to report about pain sensations [2]. Nowadays, it is suggested to analyze pain within the scope of biopsychosocial model [3], taking into account psychological status of patients, social and environmental factors.

At the same time, individual pain sensitivity is affected by genetic factors. Among the genes involved in the nociceptive processes, the μ_1-opioid receptor gene (OPRM1) is a primary candidate for genetic influence on the opioid efficacy. OPRM1 gene codes for the μ_1-opioid receptor, which is the main target of both endogenous and clinically relevant opioids. It has been recognized, that OPRM1 gene single nucleotide polimorphism (SNP) 118A>G (rs1799971) modulates pain perception, as well as may influence on patients emotional reactions [4]. Therefore, it is topical to conduct studies aimed at assessing the relationship between patients preoperative psychological status, OPRM1 gene SNP 118G>A and pain intensity after the surgery.

The aim of this study is to evaluate the interrelation between patients preoperative psychological condition, variations of the OPRM1 gene and pain intensity after the surgery.

MATERIALS AND METHODS

A prospective observational cohort study has been conducted on 100 consecutive patients who underwent surgery at the Department of Emergency Medicine and Anesthesiology during the period from February to July 2013 (table 1). Criteria for patients inclusion in the study were as follows: scheduled urological intervention with lumbotomic access (nephrectomy, pyelolithotomy, ureterolithotomy in the upper third), consent to cooperate, understanding the meaning of the proposed questionnaire. All surgeries were performed under the endotracheal anesthesia (sevoflurane + fentanyl).

For pain management in the postoperative period, intramuscular trimeperidine (μ-agonist) and NSAIDs on doctor's prescription were used. All patients underwent preoperative assessment of anxiety and depression level using the Hospital Anxiety and Depression (HADS) recommended for screening of

psychological distress in patients from intensive care units [5]. Retrospectively, patients were divided into 3 groups: group 1 – the norm (0-7 HADS score), group 2 – subclinical anxiety/depression (8-10 HADS score), group 3 – clinical anxiety/depression (≥ 11 HADS score). Pain intensity after the surgery was assessed using a questionnaire in which patients were asked to answer 5 questions related to pain within the first 24 hours after the surgery: maximal pain was assessed from 0 to 10 points (1), duration of maximal pain within the first 24 hours from 0 to 100% (2), to what extent the pain prevented from moving in bed (3), breathing deeply (4), sleeping (5) – from 0 to 10 points.

SNP OPRM1 118A>G was analysed using real-time polymerase chain reaction (Thermocycler "Rotor Gene", Corbett, Australia, software tools: Rotor-Gene Q 6plex Priority Package Plus). After genotyping the patients were divided into 2 groups: AA and AG+GG. The differences in the level of preoperative anxiety and depression, pain scores were evaluated between groups.

Table 1. Clinical characteristics of patients

Age, years of	59 (52-66)*
Sex, male/female	47/53
ASA	II-III
Duration of surgery, min	75 (60-90)*
Duration of anesthesia, min	100 (85-122,5)*
Total fentanyl dose during surgery, mg	0,6 (0,5-0,8)*
Nephrectomy, nephroureterectomy	36
Pyelolithotomy	45
Ureterolithotomy in the upper third	9
Partial nephrectomy	6
Others	4

* Me, (Q_I-Q_{III})

Results were processed using Statistica 10.0. Data are presented as median (Me) and values of 1 and 3 quartiles (Q_I-Q_{III}). To assess differences between groups, nonparametric single-factor analysis of variance (ANOVA Kruskal-Wallis) and Mann-Whitney test were used. Differences were considered statistically significant at $p<0.05$.

RESULTS AND DISCUSSION

Assessment of the relationship between the level of preoperative anxiety and pain intensity after the surgery has demonstrated the following results (table 2). Out of 100 patients, 24% experienced clinical anxiety, 18% – subclinical anxiety, 58% had no significant symptoms of

anxiety. Significant differences in the following parameters were observed between the groups: maximal pain syndrome, its duration within the first 24 hours after the surgery and the extent of pain interference with moving in bed, deep breathing and sleeping.

Table 2. Pain intensity parameters within the first 24 hours after the surgery in patient groups depending on the level of preoperative anxiety [Me, (Q_I-Q_{III})]

Parameter	Group 1 (n=58)	Group 2 (n=18)	Group 3 (n=24)	ANOVA Kruskal-Wallis
1	5 (4-8)	8 (5-9)	9 (7-10)	p < 0.001
2	30 (20-40)	50 (40-70)	60 (30-80)	p < 0.001
3	6 (3-8)	7.5 (6-9)	8.5 (8-10)	p < 0.001
4	4 (2-8)	8 (6-8)	8 (7-9)	p < 0.001
5	3 (1-6)	6 (4-8)	8 (5-10)	p < 0.001

The relationship between the level of preoperative depression and pain intensity after the surgery was also demonstrated in our study. It has been established, that 17% of patients had clinical depression, 16% of patients – subclinical depression, 67% of patients had no symptoms of depression. Significant differences in the all of studied parameters have been revealed in the group of patients depending on the level of depressive disorders (table 3).

Table 3. Pain intensity parameters within the first 24 hours after the surgery in patients groups depending on the level of preoperative depression [Me, (Q_I-Q_{III})]

Parameter	Group 1 (n=67)	Group 2 (n=16)	Group 3 (n=17)	ANOVA Kruskal-Wallis
1	6 (5-8)	7 (5-9)	10 (9-10)	p < 0.001
2	30 (20-50)	45 (30-50)	70 (50-80)	p < 0.001
3	6 (3-8)	8 (6-9.5)	9 (8-10)	p < 0.001
4	5 (2-8)	8 (5-8)	8 (7-9)	p < 0.001
5	3 (1-6)	6.5 (4-7.5)	9 (7-10)	p < 0.001

According to our study, OPRM1 118A>G genotype frequencies were as follows: AA - 66%, AG – 24%, GG – 10%. It has been determined, that the OPRM1 genotype data significantly deviates from the Hardy-Weinberg equilibrium (p<0,005), that may reflect selection toward certain allele combination [6].

We found no statistical differences in pain intensity and any other pain characteristics at the first postoperative day between genotype groups. But, the relationship between SNP OPRM1 118A>G and patients preoperative psychological status has been identified (table 3). The preoperative anxiety and depression scores in the group of AG+GG carriers were 45.4-72.7% higher than in AA genotype carriers.

Table 4. The level of preoperative anxiety and depression in OPRM1 118A>G genotype groups

Scale	AA (n=66)	AG+GG (n=34)	p value
$HADS_{anxiety}$	6,5 (3-8)	10 (6-14)	<0,001
$HADS_{depression}$	5,5 (4-7)	8 (5-12)	0,015

The present results suggest, that the level of preoperative anxiety and depression influence on the pain intensity after the surgery. It has been displayed, that the signs of psychological distress affect not only the intensity of acute pain after nephrectomy, but the formation of chronic pain syndrome as well [7]. Understanding of psychological distress mechanisms in patients can open up new opportunities not only regarding the effective pain management, but also the successful therapy in general. A number of studies show, that depressive disorders promote transient inhibition of the immune system and prolong the terms of hospitalization [8].

The revealed relationship between SNP OPRM1 118A>G and preoperative anxiety and depression confirms the fact, that endogenous opioid system can be involved in the formation of the patients psychological state. In fact, it has been reported, that SNP OPRM1 118A>G may cause emotional reactions to environmental stressors [4].

Despite the fact that basic biochemical mechanisms of nociception has been studied well enough, finding reliable predictors of postoperative pain sensation remains a topical issue. It is known, that in addition to the sensory component, pain includes the affective component too and is a subjective feeling affected by psychological, social, cultural factors and patient's personal experience. Mechanisms of psychological status influence on the level of postoperative pain are still not clear and are the subject of debate. It may be associated with participation of those brain structures, receptors and neurotransmitters in the pain modulation processes which are responsible for emotional instability, depressive and anxiety disorders, pathological response to stress factors. The present study has revealed the potential role of SNP OPRM1 118A>G in the molecular mechanisms of affective disorders and, consequently, modulation of pain perception. Our data also

suggest presumable predictive value of patients preoperative psychological assessment relative to the postoperative pain intensity. Nevertheless, a further search for relationship between psychological, genetic factors and pain intensity after the surgery is of significant scientific and practical importance.

CONCLUSIONS

1. The level of preoperative anxiety affects the severity of pain during the first day after the surgery – maximum pain level was 9 (7-10) points in the group of patients with clinical anxiety.

2. Severity of depression before the surgery is also associated with the intensity of postoperative pain – in the group of patients with clinical depression maximum pain level within the first postoperative day was 9 (9-10) points.

3. The relation between the SNP OPRM1 118A>G and patients preoperative psychological status has been identified – the level of preoperative anxiety and depression in the group of AG+GG carriers was 45.4-72.7% higher than in AA genotype carriers ($p<0.001$; $p<0.05$).

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Background. Effective postoperative analgesia remains an essential problem in modern anesthesiology. The search of factors affecting the pain intensity after the surgery is of significant practical importance. It is known, that personal experience, psychological and social state may be related to the level of postoperative pain syndrome. At the same time, genetic factors regulating opioid pharmacodynamics contribute to the large interpatient variability in postoperative opioid requirements. Thus, OPRM1 gene polymorphism 118A>G is a primary candidate for genetic influence on the efficacy of opioids, as well as patients emotional reactions.

The aim of this study is to evaluate the interrelation between patients preoperative psychological condition, variations of the OPRM1 gene and pain intensity after the surgery.

Materials and Methods. The observational study has been conducted, which included 100 consecutive patients undergoing major urological surgeries with lumbotomic access. Postoperative

pain management included intramascular administration of trimeperidine and NSAIDs on doctor's prescription. The level of preoperative anxiety and depression was assessed using the HADS scale (Hospital Anxiety and Depression Scale). Pain after the surgery was assessed within the first 24 hours after the surgery. SNP OPRM1 118A>G was analysed using real-time PCR. Differences in patient groups were considered statistically significant at $p<0.05$.

Results. Clinical anxiety was revealed in 24% patients, clinical depression - in 18%. In the group of patients with clinical anxiety the maximal level of pain on the first day after the surgery was 9 (7-10) points, 8 (5-9) points in the group of subclinical anxiety, and 5 (4-8) points in the group with no anxiety symptoms ($p < 0.001$). Significant differences in the following parameters were also observed between groups: duration of maximal pain syndrome within the first postoperative day and the extent of pain interference with moving in bed, deep breathing and sleeping. Moreover, significant differences in the all of studied parameters have been revealed in the group of patients depending on the level of depressive disorders. The relationship between SNP OPRM1 118A>G and patients preoperative psychological status has been identified: the preoperative anxiety and depression scores in the group of AG+GG carriers were 45.4-72.7% higher than in AA genotype carriers.

Conclusions. Preoperative psychological state affects the pain intensity after the surgery. The potential role of SNP OPRM1 118A>G in the molecular mechanisms of affective disorders and modulation of pain perception has been revealed. In order to improve the effectiveness of postoperative pain management, it is advisable to continue the search of interrelationship between these parameters.

Keywords: *surgery, pain, anxiety, depression, genetic polymorphism*

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