Primary outcome

Postoperative pain level comparison among groups.

At the timepoint of 4 h after surgery, the mean pain level did not differ significantly among the three study groups (P = 0.068). The mean NRS score at rest was 1.21, 95% CI (0.2, 2.22) in the control group, 0.48, 95% CI (0.03, 1.00) in the ITM 0.1 mg group and 0.17, 95% CI (0.18, 0.53) in the ITM 0.2 mg group.

At the timepoint of 7h after surgery, the mean pain NRS score was statistically significantly different among the three study groups: 2.62, 95% CI (1.58, 3.63) in the control group versus 1.0, 95% CI (0.12,1.81) in the ITM 0.1 mg group versus 0.17, 95% CI (0.12, 0.46) in the ITM 0.2 mg group, $p < 0.001$. The lowest pain level manifested in the ITM 0.2 mg group.

At the timepoint of 12 h after surgery, the mean pain NRS score was statistically significantly different among the three study groups: 3.08, 95% CI (1.92, 4.24) in the control group versus 0.65, 95% CI (0.01, 1.32) in the ITM 0.1 mg group versus 0.37, 95% CI (0.07, 0.83) in the ITM 0.2 mg group, $p < 0.001$. The pain level was lowest in the ITM 0.2 mg group.

At the timepoint of 24 h after surgery, the mean pain NRS score was statistically significantly different among the three study groups: 2.50, 95% CI (1.35, 3.65) in the control group versus 1.20, 95% CI (0.38, 2.03) in the ITM 0.1 mg group versus 0.41, 95% CI (0.07, 0.9) in the ITM 0.2 mg group, $p = 0.001$. The pain level was lowest in the ITM 0.2 mg group (Table 2, Fig. 2).

Table 2. Pain level after THA at different timepoints

Time after surgery, hours	**Control group, NRS points (95% CI)**	**ITM 0.1 mg, NRS points (95% CI)**	**ITM 0.2 mg, NRS points (95% CI)**	**p-value**

4 h	1.21 (0.2,2.22)	0.48 (0.03,1.00)	0.17 (0.18,0.53)	0.068
7 h	2.62 (1.57,3.63)	1.00 (0.12,1.81)	0.17 (0.12,0.46)	< 0.001
12 h	3.08 (1.92,4.24)	0.65 (0.01,1.32)	0.37 (0.07,0.83)	< 0.001
24 h	2.50 (1.35,3.65)	1.20 (0.38,2.03)	0.41 (0.07,0.9)	0.001

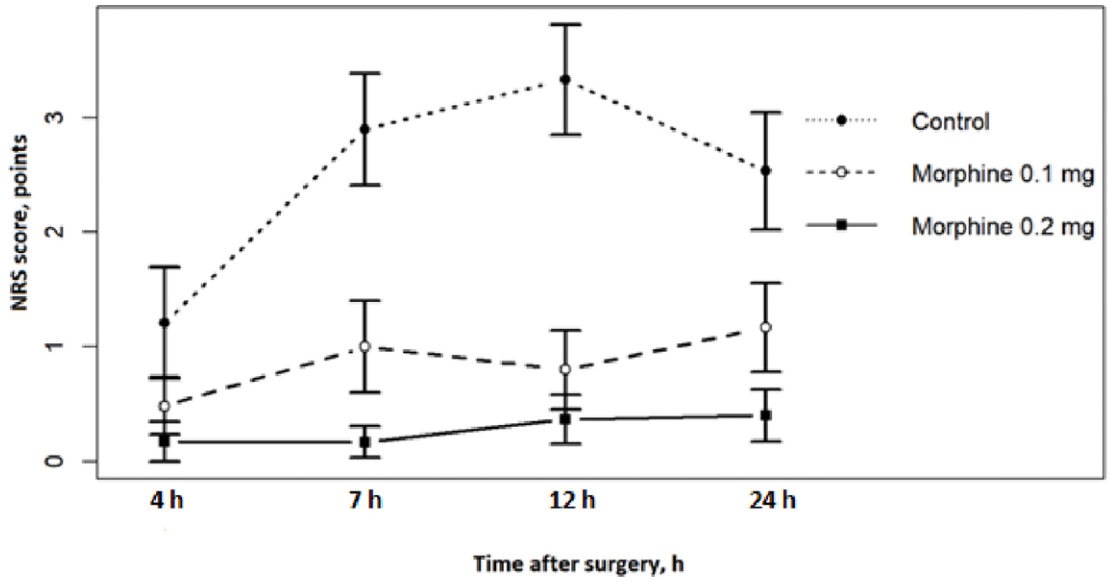

Fig. 2. Pain dynamics after total hip arthroplasty

Pain dynamics in each group

Comparing the pain level changes in the control group at the timepoints of 4 h, 7 h, 12 h and 24 h after surgery, statistically significant differences were found between the NRS scores: in 4 h and 7 h – 1.21 vs 2.90, p = 0.0039; 4 h and 12 h – 1.21 vs 3.33, p = 0.0017; 4 h and 24 h – 1.21 vs 2.53, p = 0.34. The pain levels at the timepoints of 12 h and 24 h after surgery had no statistically significant differences: 3.33 vs 2.53, p = 0.21. The pain level in the control group was significantly higher in 7 h, 12 h and 24 h after surgery than in 4 h.

Comparing the pain level changes in the ITM 0.1 mg group at the timepoints of 4 h, 7 h, 12 h and 24 h after surgery, no statistically significant differences were found: in 4 h and 7 h – 0.48 vs 1.00, p = 0.16; 4 h and 12 h – 0.48 vs 0.80, p = 0.28; 4 h and 24 h – 0.48 vs 1.17,

p = 0.21; 12 h and 24 h – 0.80 vs 1.17, p = 0.74. The pain level in the ITM 0.1 mg group had no significant changes within 24 h after surgery.

Comparing the pain level changes in the ITM 0.2 mg group at the timepoints of 4 h, 7 h, 12 h and 24 h after surgery, no statistically significant differences were found: in 4 h and 7 h – 0.17 vs 0.17, p = 0.62; 4 h and 12 h – 0.17 vs 0.37, p = 0.20; 4 h and 24 h – 0.17 vs 0.40, p = 0.35; 12 h and 24 h – 0.37 vs 0.40, p = 0.74. The pain level in the ITM 0.2 mg group had no significant changes within 24 h after surgery.

Secondary outcomes

Peripheral capillary blood oxygen saturation

Data of the mean SpO2 level within the first 24 hours post-surgery are shown in Figure 3.

The mean SpO2 (%) levels in the control, ITM 0.1 mg and ITM 0.2 mg groups were as follows: 96.68 (SD = 2.2, 95% CI [95.86, 97.51]) vs 95.73 (SD = 2.21, 95% CI [94.91, 96.56]) vs 96.07 (SD= 2.18, 95% CI [95.25, 96.88]), p = 0.294. The mean SpO2 measurements obtained did not differ statistically significantly among all three groups (Fig. 3).

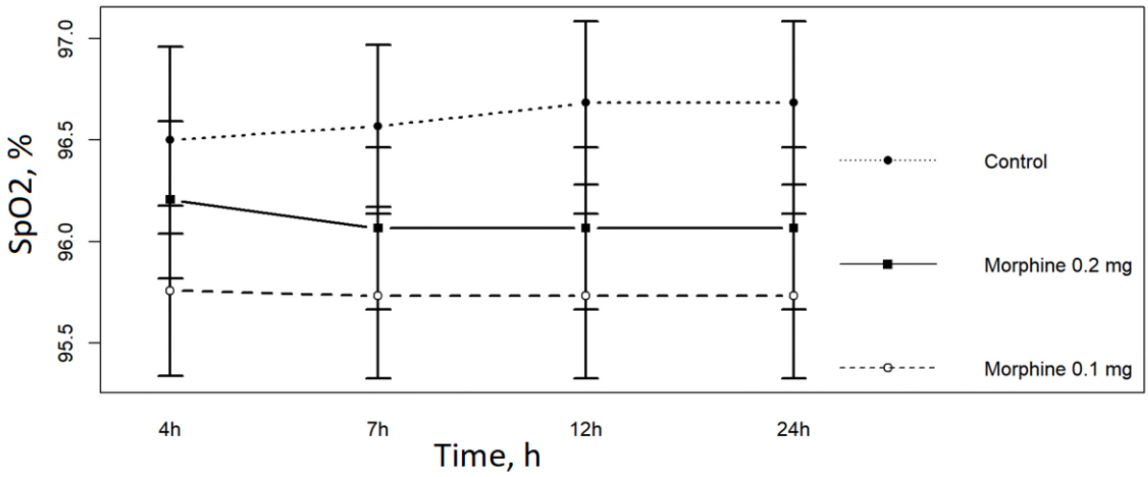

Fig. 3. Mean oxygen saturation levels (SpO2, %) within the first 24 hours post-op

Respiratory rate

The mean respiratory rate observed within 24 hours after surgery did not differ significantly among the study groups ($p = 0.114$). The mean respiratory rate in the control group was 16.11 (SD= 1.66) x/min within an interval of 13 to 20 x/min, 95% CI (15.46, 16.57). The mean respiratory rate in the ITM 0.1 mg group was 15.23 (SD = 2.13) x/min within an interval of 10.5 to 19 x/min, 95% CI (14.44, 16.03). The mean respiratory rate in the ITM 0.2 mg group was 15.22 (SD = 2.27) within an interval of 11.5 to 20x/min, 95% CI (14.26,16.06) (Fig. 4).

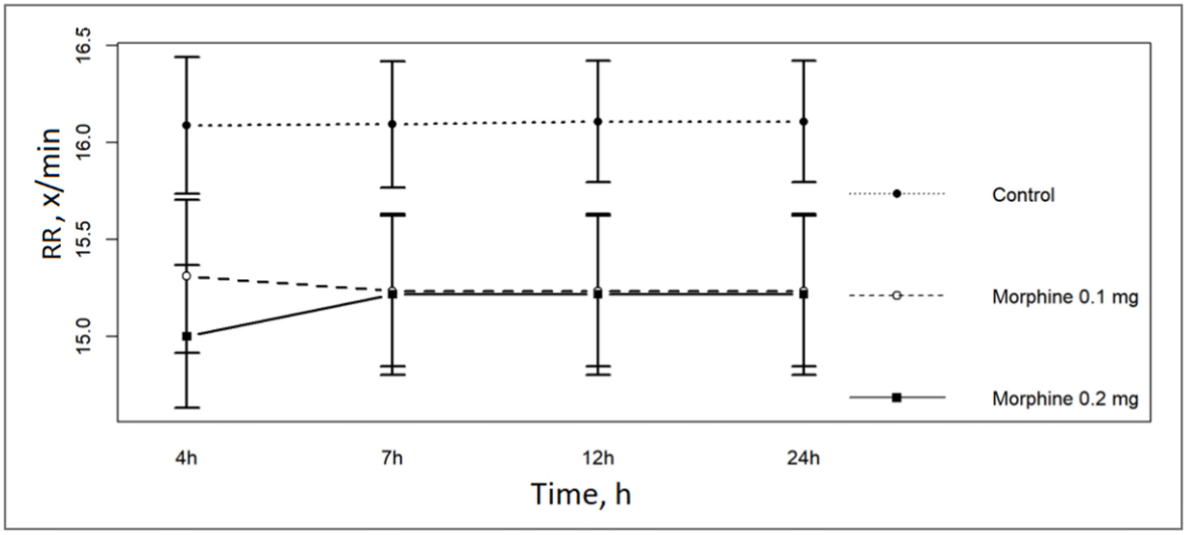

Fig. 4. Mean respiratory rate (RR) within the first 24 hours post-op.

Rescue medication (morphine SC) consumption

Of all study population, 32 subjects or 35.6% required additional analgesia with rescue medication (morphine SC) after THA, while 58 subjects or 64.44% did not need add-on analgesia. It can be inferred from the obtained results that the consumption of morphine in the postoperative period was highest in the control group, where 23 subjects or 76.7% needed it, and was comparatively lower in Groups II and III – five subjects or 16.6% in the ITM 0.1 mg group and four subjects or 13.3% in the ITM 0.2 m group asked for additional analgesic.

The average dose of additional morphine SC in the control group was 8.7 mg per capita, while in the ITM 0.1 mg group it was 2 mg per capita and in ITM 0.2 mg group – 1.3 mg per capita. There was a significant difference in the amount of morphine consumed post-operation between the control group and both ITM groups (P < 0.001) (Fig. 5).

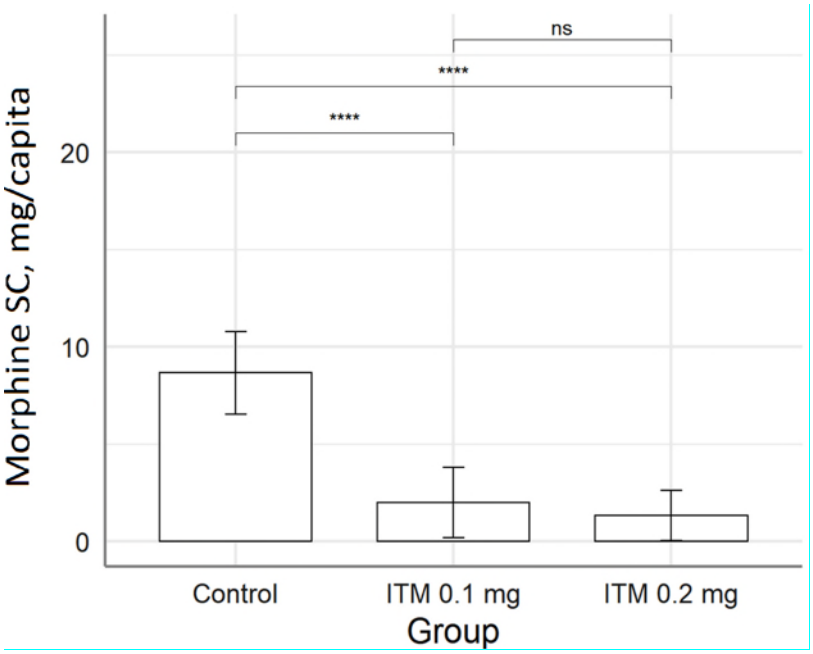

Fig. 5. Average supplemental morphine consumption per subject

Oxygen supplementation

Eleven patients or 36.7% in the control group required supplemental oxygen within the first 24 hours post-operation. The need for oxygen therapy was relatively lower in Groups II and III, where six subjects or 20% in the ITM 0.1 mg group and four subjects or 13.3% in the ITM 0.2 mg group needed oxygen therapy. No statistically significantly different data were obtained regarding the need for oxygen therapy in the postoperative period for all three study groups (P = 0.089).

PONV incidence

Nausea and/or vomiting after the surgical procedure were mostly observed in the ITM 0.1 mg group – in seven subjects or 23.3% – and, to a relatively lesser extent, in the control

group and in the ITM 0.2 mg group – in three subjects or 10% in each group. The data obtained did not show statistically significant differences among the three study groups (P = 0.279) (Fig. 6).

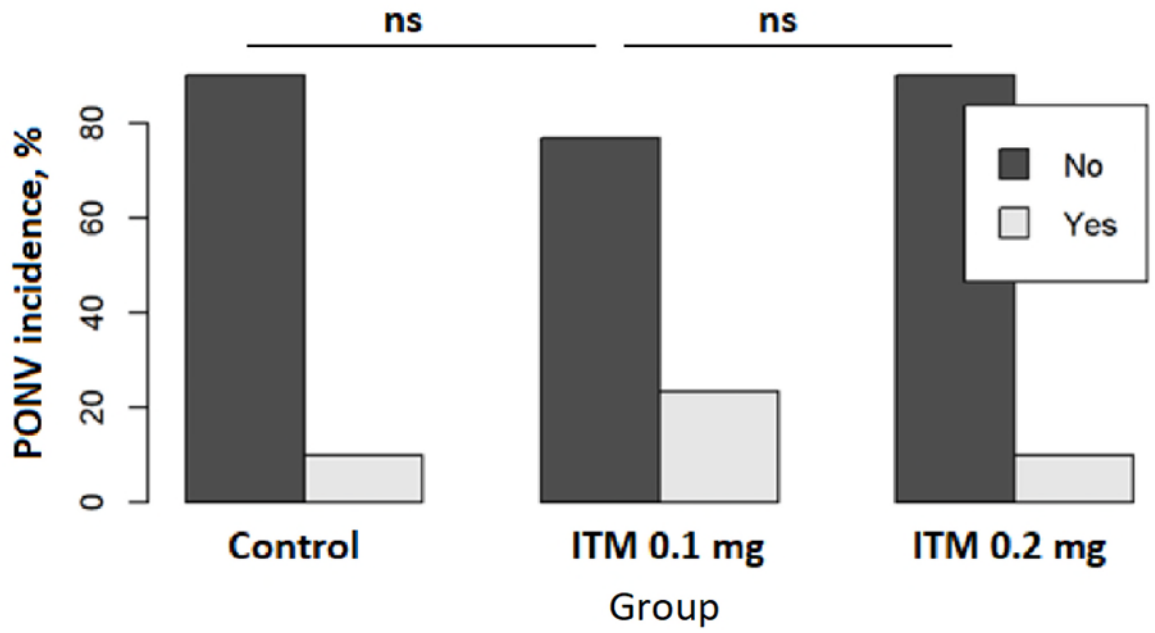

Fig.6. Nausea and vomiting in the postoperative period

Pruritus

Pruritus in the postoperative period was observed only in the ITM 0.2 mg group – in seven subjects or 23.3%. The obtained results were statistically significantly different among all three study groups ($p < 0.001$).

No other adverse events were observed in respondents.