



Single-dose, Systemic, Intra-Operative Administration of Dexamethasone Is Associated With A Small Reduction in Pain-Related Patient Reported Outcomes After Surgery: Analysis from the Perioperative Pain Registry, PAIN OUT

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Intra-operative dexamethasone was associated with improvement in a multi-dimensional pain score in orthopaedic/trauma & OBGYN surgical patients.

BACKGROUND AND AIM

Dexamethasone (DEX) is a potent glucocorticoid steroid, commonly used for managing post-operative nausea and vomiting (PONV). Intra-operative DEX reduces postoperative pain and opioid requirements, acting as a co-analgesic, within a multi-modal treatment regimen. However, compared with PONV, the effects of DEX on pain are less studied [1,2].

The **AIM** of this investigation was to assess a large cohort of patients cared for in the clinical routine to: [i] identify the surgical disciplines in which patients received systemic, intra-operative DEX and [ii] evaluate the association between DEX and pain-related Patient Reported Outcomes (PROs).

METHODS

PAIN OUT, is an international perioperative pain registry, offering hospital-based clinicians with web-based tools for standardized evaluation of PROs and management on the first post-operative day.

The **primary endpoint** was the association between receiving intra-operative, systemic DEX and **the Pain Composite Score (PCS)** in the complete cohort and by surgical discipline.

PCS_{TOTAL} is a **multidimensional composite score**, evaluating 12 continuous PROs in the PAIN OUT patient outcomes questionnaire addressing pain intensity, pain interference, and side effects. **Secondary endpoints** were a corresponding analyses for **three sub-scores** of the PCS addressing **pain intensity, pain-related interference and side effects**.

To account for the multi-center structure of the data, we applied **mixed regression models** with a random intercept for every participating ward. **PCS_{TOTAL}** and the **sub-scores** served as dependent variables. Intraoperative DEX served as the main independent variable. All models were controlled for age, sex, pre-existing chronic pain and type of anesthesia (general [GA], regional [RA], combined GA&RA).

The **PCS** was standardized before modelling. Thus, the adjusted mean differences can be interpreted as standard deviations (≥ 0.1 small, ≥ 0.3 medium, ≥ 0.5 large **effect size**). P-values < 0.05 were considered as significant.

RESULTS The study sample consisted of 29,082 patients from 181 wards in 19 countries, recruited between January 2018 – January 2020.

Of the cohort, 21.2% of patients received intra-operative DEX (n = 6,165/29,082). DEX was most commonly given in OBGYN (36.1%) > orthopaedic/trauma surgery (19.7%) > general surgery (18.0%). It was administered less frequently in cardiac/thoracic/vascular (10.5%) and urologic surgery (8.5%).

When administered, 99% of patients received a single intra-venous dose of DEX. Its median dose was 8 mg (Q₁: 5mg, Q₃: 8 mg).

Primary endpoint: In the complete cohort, DEX was significantly associated with lower values of the **PCS_{TOTAL}** (**Figure 1**), a **small effect size** (**top Figure 2**). By surgical discipline, DEX was associated with lower values in orthopaedic/trauma & OBGYN surgery (**Figure 1**), both were **small effect sizes** (**top Figure 2**).

Secondary endpoints: In the total sample, DEX administration was significantly associated with a reduction in the **intensity & interference sub-scores** (**both small effect size**) but not for the side effects. By surgical discipline, DEX administration was associated with lower **pain intensity & interference sub-scores** in patients who underwent orthopaedic/trauma surgery (**small effect size**) but not side effects (**Figure 2**).

CONCLUSION Findings from a large sample of patients undergoing mixed surgical procedures in the clinical routine, indicate that a single systemic dose of 8 mg dexamethasone (DEX) was given to a fifth of patients, most commonly in OBGYN followed by ORTHO and GENERAL surgery. The treatment was associated with a small effect size reduction in a multi-dimensional pain score. Effects of DEX were most prevalent in ORTHO and OBGYN patients, related to pain but not to side effects. DEX may have beneficial role in reducing post-operative pain in some patient populations, as part of a multi-modal treatment regimen.

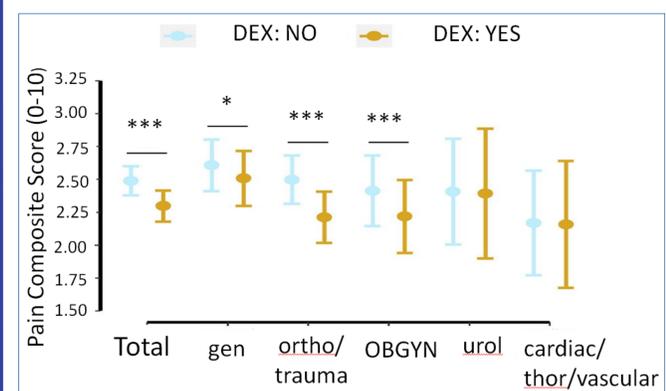


Figure 1 shows the estimated marginal means (dots) and 95% confidence intervals (capped lines) for the Pain Composite Score for the total sample and separate surgical disciplines. Unadjusted p-values: * $p < 0.05$, *** $p < 0.001$

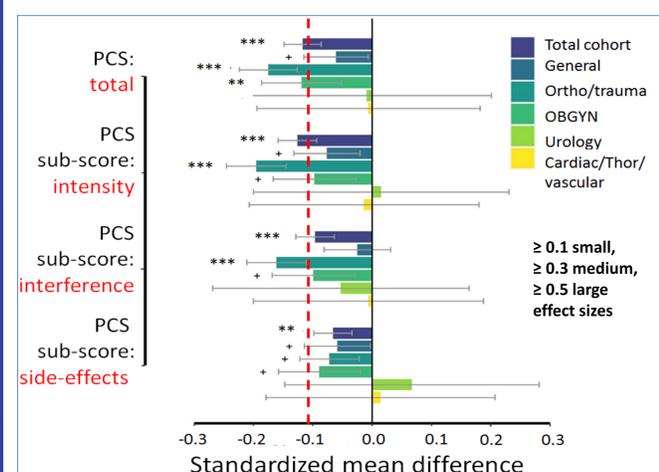


Figure 2 shows effect sizes for the primary and secondary endpoints for the whole sample & by discipline. Standardized estimated marginal mean differences (bars) and 95% CI between patients with vs. without DEX for the Pain Composite Score (PCS) and sub-scores (intensity, interference and side effects). Negative values indicate lower values, i.e. better outcomes. The red dotted line indicates the threshold for a small effect size. Significant differences are marked with asterisks (Bonferroni-Holm adjusted p-values: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$). The plus signs indicates unadjusted p-values < 0.05 that did not survive the adjustment for multiple testing.

References

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The authors declare that they have no conflict of interest related to this study.

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