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Review Article

The effects of propofol on TNF-α and IL-6 in patients with endometrial and cervical cancer

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Summary

Genital carcinomas in women, such as endometrial and cervical carcinoma, remain one of the main reasons for death in women worldwide due to malignant tumours, and while the treatment options are relatively established today, the progression rate of the disease is still at high levels. Cytokines have been found to have a significant impact on the development and progression of these diseases, with pro-inflammatory factors such as interleukin-6 (IL-6) and tumour necrosis factor-alpha (TNF-α) influencing the tumour's growth, angiogenesis, and metastasis. The anaesthetics used during surgical treatment for these tumours have proven effects on the serum levels and local expression of cytokines in experimental settings. However, the results for propofol, which is the commonest choice for inducing anaesthesia, remain unclear in clinical settings, though the anti-cancer properties of propofol have been reported in specific carcinoma cell lines.

Key words: Cervical cancer, endometrial cancer, IL-6, propofol, TNF-α

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Introduction

Cervical cancer remains one of the top 5 most common cancers in women in both incidence and mortality worldwide. Important factors in the development of this cancer include HPV infections, smoking and long-term use of oral contraceptives. Despite being so common, there has been a decline in cervical cancer incidence rates in many countries in recent years. The decline is presumed to be due to the rise in human development levels, associated with improving genital hygiene and a decrease in sexually transmitted diseases (Bray et al. 2024).

One of the other most common malignant tumours in women is the endometrial carcinoma. It is one of the few cancers which have led to an increased mortality rate in recent years, 1.5% per year from 2013 through 2022 (Siegel et al. 2025). A higher prevalence of obesity is considered an important factor in the development of endometrial cancer (Dimitrov et al. 2016).

Many tumour-promoting factors have been associated with cancer progression. Interleukin-6 (IL-6) is one of the factors that has been found to play a significant role in malignant transformation, metastasis, angiogenesis, and tumour proliferation (Bharti et al. 2016).

IL-6 is a cytokine with multiple functions, such as regulating the normal cell inflammatory processes, the host immune defence mechanisms and modulation of cellular growth. Over the years, studies have shown that IL-6 overexpression is present in almost every tumour studied (Guo et al. 2012). This cytokine has been shown to have a significantly higher expression in cervical cancer tissues specifically, and is associated with cervical cancer progression and metastasis (Song et al. 2016). A study from 2022 reported that high IL-6 levels were related to a poorer prognosis in cases of cervical cancer and a lower survival rate (Cai et al. 2022). IL-6 is one of the major pro-inflammatory cytokines whose expression level increases in the adipose tissue of obese mice and patients (Cao 2014), which could explain the link between obesity and endometrial carcinoma, as it is more frequent in obese women. Several studies have linked this cytokine to endometrial cancer cell migration (Che et al. 2014; So et al. 2015; Che et al. 2019).

TNF-α is a cytokine with pro-inflammatory properties, associated with angiogenesis, which is associated with the progression of malignant tumours, including endometrial carcinoma and cervical carcinoma (Chopra et al. 1998; Ray et al. 2022). TNF-α serum levels were found to be elevated in all stages of cervical cancer, directly corresponding to the stages of cancer progression. Other cytokines that were found to be elevated at different stages include IL-2, IL-6, IL-7, IL-8, and IL-10, among others. All of these biomarkers possess angiogenic properties, which could lead to tumour growth, recidivism, and metastasis (Chopra et al. 1998).

The definitive treatment of cervical and endometrial carcinoma often includes operative interventions, mostly commonly performed under general anaesthesia (Beckmann et al. 2021; Tomov et al. 2022).

Propofol is the most commonly used induction agent for induction to general anaesthesia nowadays, and multiple studies have shown that it has a prominent effect on serum levels of cytokines (Xu et al. 2020).

Discussion

Surgical trauma is always associated with disturbances of the homeostasis of the patient by inducing stress, as there is an activation of the innate immune system by initiating the response of neutrophils and monocytes, which produce cytokines. There is an increased production of pro-inflammatory cytokines, such as IL-6 and TNF-α, in the perioperative and postoperative periods, and this increase is linked to cancer progression in several trials (Dąbrowska and Slotwinski 2014).

Even though the choice of anaesthetics in cancer patients is discussed in many clinical trials and studies, there is still not enough data to support that choice in cases of cervical cancer and endometrial cancer. Most experiments are done in vitro on cancer cell lines, but fewer studies are conducted in vivo.

The effects of propofol on the serum levels of cytokines such as IL-6 and TNF-a in patients with cervical and endometrial carcinoma are of notable importance, given the fact that it remains one of the most commonly used general anaesthetics in anaesthesia practice and the intensive care units.

Propofol is a gamma-aminobutyric acid (GABA) receptor agonist which has been used in Europe since 1986. It has several properties that make it the most

commonly utilised in routine clinical anaesthetic practice, such as its short context-sensitive time, rapid half-life, and low incidence of postoperative nausea and vomiting. It is important to note the unfavourable effects of the drug, such as hypoventilation, bradycardia and hypotension. The mechanism by which propofol exhibits its main effect of loss of consciousness has long been attributed to the GABA receptor activity, but recent investigations suggest additional molecular targets by which the state of unconsciousness is achieved (Sahinovic et al. 2018; Tang and Eckenhoff 2018). Recent studies suggest that propofol has anti-tumour or carcinogenic activity in different types of cancer. One of them, conducted in vivo and in vitro, found that propofol had an inhibitory effect on cell proliferation, migration and invasion but promoted apoptosis in endometrial cancer cells by regulation of the Sox4 gene. For this study, the cancer cells were transfected into Ishikawa cells, and the results showed a significant downregulation of Sox4, leading to an inhibition of endometrial cancer cell proliferation (Du et al. 2018).

The inhibitory effect of propofol has been studied in many types of cancer, and overall, the results indicate that it promotes immune suppression. Patients experience a better outcome with the use of total intravenous anaesthesia (TIVA) with the drug, compared to the use of inhalational anaesthetics such as sevoflurane and desflurane. The specific regulatory mechanisms, however, need to be studied further to determine the exact way in which propofol affects different kinds of malignant tumours (Gao et al. 2020). In 2021, a study examined the effect of propofol on two lines of cervical cancer cells in vitro and reported that after48-hour exposure to the drug, the cells' viability was significantly suppressed, the invasion and migration of the cells was evidently restrained, and there was a promotion of apoptosis in the lines of cervical cancer cells, ultimately leading to the conclusion that the intravenous anesthetic relieved the malignancy of these cell lines (Sun et al. 2021).

Interleukin-6

The regulation of the immune response is another mechanism by which propofol exhibits an anti-cancer effect, inhibiting cell proliferation and promoting cell apoptosis in cervical cancer (Zhang et al. 2016). IL-6 is one of the cytokines affected by the use of propofol. While comparing the dynamic changes in IL-6 levels in mouse model groups given propofol or sevoflurane, Li et al. discovered that the intravenous anaesthetic group had significantly lower IL-6 levels (Li et al. 2020). Cytokines are of great importance to the normal endometrium functions and for carcinogenesis in endometrial cells. Anti-inflammatory cytokines allow for the tumour cells to effectively avoid the immune system of the host, while pro-inflammatory cytokines such as IL-6 contribute to tumour growth and lower the rate of apoptosis in endometrial carcinoma (Azadehrah et al. 2022). With that being said, the effects that propofol exhibited in multiple studies over the years, confirming the drug's suppressive effects on IL-6, could be considered of notable importance in the prognosis and development of endometrial cancer.

While most in vitro experiments point to a certain effect of propofol on cytokines, the in vivo results are inconclusive. A 2022 meta-analysis, which included 1611 patients, comparing TIVA with propofol and anaesthesia with sevoflurane,

stated that there were increased levels of inflammatory biomarkers, including IL-6, IL-10, and TNF-α, following surgery in both groups. There was virtually no difference in effect on the biomarkers between the two groups. This study suggests that the dynamics of the biomarkers depend on factors other than the used anaesthetic, such as surgical trauma (O'Bryan et al. 2022).

TNF-a

While the link between TNF-α and cervical and endometrial cancer has been reported throughout the years, there are still not enough studies on the relationship between propofol and the cytokine dynamics in patients with these kinds of malignant tumours.

Several experiments on laboratory mice and rats have proved that propofol has an inhibitory effect on the inflammatory response in vivo and in vitro (Taniguchi et al. 2003; Takemoto 2005; Hsing et al. 2011).

While propofol has been found to inhibit the TNF-α production in experimental mouse neuroblastoma cell lines by a modulation of nuclear transcription factor κB (NF-κB) (Hu et al. 2020), clinical trials on the effect of the drug on serum levels of the cytokine during colorectal and breast cancer surgery reported similar pro- and anti-inflammatory activation with the use of Propofol for TIVA and Sevoflurane for balanced anesthesia (Kvarnström et al. 2012; Lim et al. 2018).

Conclusion

The link between cytokines and cancer progression has been documented over the years. IL-6 and TNF-α are two of the pro-inflammatory cytokines that contribute to cancer progression. Elevated levels of these biomarkers have been reported in cases of cervical and endometrial cancer and have been found to lead to worse outcomes in patients with these malignant tumours. With the definitive treatment for uterine carcinomas involving operative interventions, general anaesthesia must be provided to the patients, and the drugs used during that time influence the serum levels of IL-6 and TNF-α. Propofol, being the most common choice for the induction of general anaesthesia, has a certain effect on the dynamics of serum cytokine levels. While most in vitro and in vivo studies report an inhibitory effect of this drug on IL-6 and its anti-cancer properties, others report contrary results in patients examined during operative interventions. The clinical trials performed on patients with cervical carcinoma and endometrial carcinoma undergoing operative interventions are not enough to conclude definitive statements on the benefits of propofol in cases of endometrial and cervical carcinoma. The results regarding TNF-a remain inconclusive in these patients as well, with a few studies suggesting no difference in the effects of propofol and inhalational anaesthetics used for general anaesthesia.

Additional information

Conflict of interest

The authors have declared that no competing interests exist.

Ethical statements

The authors declared that no clinical trials were used in the present study.

The authors declared that no experiments on humans or human tissues were performed for the present study.

The authors declared that no informed consent was obtained from the humans, donors or donors' representatives participating in the study.

The authors declared that no experiments on animals were performed for the present study.

The authors declared that no commercially available immortalised human and animal cell lines were used in the present study.

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Author contributions

Writing – original draft: MG. Writing – review and editing: KT.

Data availability

All of the data that support the findings of this study are available in the main text.

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