



Review Article

Alternative medicine and anesthesia: Implications and considerations in daily practice

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Abstract

Nowadays, herbal medicines are widely used by most of the people, including the pre-surgical population. These medicines may pose numerous challenges during perioperative care. The objective of the current literature review is to dwell upon the impact of the use of herbal medicines during the perioperative period, and to review the strategies for managing their perioperative use. The data was generated from various articles of different journals, text books, web source, including, Entrez Pubmed, Medscape, WebMD, and so on. Selected only those herbal medicines for which information on, safety, usage, and precautions during the perioperative period was available. Thereafter, the information about safety, pharmacokinetics, and pharmacodynamics from selected literature was gathered and analyzed. The whole review focused on the fact that these commonly used alternative medicines could sometimes pose as a concern during the perioperative period, in various ways. These complications could be due to their direct action, pharmacodynamic effect, or pharmacokinetic effect. In view of the serious impacts of herbal medicine usage in perioperative care, the anesthesiologist should take a detailed history, especially stressing on the use of herbal medicine during the preoperative anesthetic assessment. The anesthesiologist should also be aware of the potential perioperative effects of those drugs. Accordingly, steps should to be taken to prevent, recognize, and treat the complications that may arise due to their use or discontinuation.

Key words: Anesthesia, Ayurveda, *Echinacea*, ephedra, garlic, ginger, herbal medicines

Introduction

Since ancient times, the practice of Ayurveda has reigned supreme in Indian society. In the modern era, advancements in allopathy have further widened the therapeutic scopes in various diseases. Nowadays, an increasing number of patients are presenting to the hospital for various surgical procedures. A majority of these patients have invariably used Ayurvedic and herbal medicines for their current surgical problem or would have taken similar medicines for other comorbid diseases. The clinical scenario becomes challenging when these patients hide their current treatment regimens, especially their treatment with herbal medicines. The common belief behind these medication profiles, among the general public, is the total harmless nature of these therapeutic agents.

The practice of complementary and alternative medicine has gained tremendous popularity due to their claimed beneficial effects in cardiac, respiratory, and chronic diseases, as also other disorders.^[1] The most threatening aspect related to these practices pertains to the self-administration of herbal medicines even by the highly educated and intellectual strata of society.^[2] The rising consumption pattern among the general public is based on false misconceptions that such products are safe for use as they are completely natural. The marketing of these products through media is another factor for their popularity and widespread use. Ironically, a majority of these drugs never undergo any stringent testing and moreover there is hardly any description or proper documentation of the various ingredients contained in these products.^[3] As such, a majority of the users are totally unaware of the side effects associated with these medicines. Also there are significant potential risks of drug interaction because of these medicines, as they can prove to be catastrophic and devastating in various clinical settings.^[4]

Challenges for the Anesthesiologist

The most significant concern for the anesthesiologist during the perioperative period is the altered baseline physiological

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functions due to the practice of polypharmacy by this surgical subset of patients, and the associated co-morbidities that can greatly increase the mortality and morbidity.^[5] The clinical consequences and complications can affect any organ system and may lead to myocardial infarction, stroke, bleeding, higher anesthetic consumption, delayed recovery from anesthesia, respiratory complications, renal disturbances, nullification of the therapeutic effect of other medications, and even transplant rejection. Drug interactions of these medicines in the surgical population are of utmost importance and warrant complete knowledge on the part of the anesthesiologists, of the pharmacokinetic and pharmacodynamic properties of these medicines.^[6] However, the difficulties become manifold when these patients do not reveal the use of any such medication, either deliberately or out of ignorance during the preanesthetic evaluation. As such, appropriate plans to deal with such possible hazards cannot be formulated beforehand and may lead to devastating clinical consequences later on.^[1] The lack of information further makes it virtually impossible for physicians to assess the possible concentration of the drug, its active ingredients, dose requirement during surgical procedures, metabolism, and metabolite formation of these agents, as also their possible excretory pathway from the body.

Preoperative Evaluation

During preoperative evaluation, a complete knowledge about the current medication helps in formulating a well-planned anesthetic and surgical procedure, to counter the possible adverse outcomes as a result of these herbal products. An altered coagulation profile can potentially be caused by garlic, ginseng, and ginkgo, and can result in more than the anticipated blood loss during a surgical procedure.^[7] The effect of general anesthesia can be potentiated by kava and valerian, which are known to possess sedative properties.^[8] The hepatic microsomal enzyme cytochrome P450 3A4 is stimulated by St. John's wort and has been observed to alter the metabolism of an immunosuppressant and oncological chemotherapy.^[9] The worst fears in our country at present are the overuse of Chinese herbal medicines that have flooded the drug market. These products are not standardized and are a mixture of various herbs, which can prove to be extremely detrimental to surgical patients.^[10]

The consumption of these medications is not limited to adults alone. Even the pediatric population is administered herbal, homeopathic, and Ayurvedic medicines for various ailments.^[11] The most common among these medications include Echinacea, Aloe, sweet oil, *Arnica*, and so on. The consequences of these medications on the interaction with allopathic medicines can be very devastating, comparable to similar interactions in the adult population.

It has been observed by various studies that a majority of anesthesiologists are not aware of the mechanism of action and side effects of these Ayurvedic and herbal medicines.^[12] Data from other studies have shown that complementary and alternative medicines were used by 57.4% of the population. Among these, the most commonly used medicines include herbal medicines (6.8%), megavitamins (6.8%), homeopathic medicines (1.4%), and 1.2% use folk remedies.^[13] Even the

pregnant population has been a regular user of herbal medicines, as 7.1% of parturients, who were in their mid-pregnancy stage, have reported use of herbal products, and only 14.6% of these parturients were actually aware of the intended pharmacological use of these drugs.^[14] The drug interactions can be of immense significance in these parturients, especially those who prefer painless labor. The increased bleeding tendencies in these patients make them highly vulnerable to the potential complication of neuraxial anesthesia along with possible fluctuations in maternal hemodynamics.^[15,16] The maternal ingestion of ginger for a prolonged duration can possibly cause inhibition of fetal binding of testosterone, as ginger is a potent thromboxane synthetase inhibitor.^[17]

Application of Guidelines and Protocols

Although guidelines and protocols have been established by the American Society of Anesthesiologists (ASA) with regard to the possible drug interactions in patients on herbal and alternative medicines, somehow these are either not properly followed or are sometimes difficult to adhere to, such as in emergency surgical situations. Their combination with conventionally prescribed medicine can prove to be fatal, as has been observed by various studies.^[18] The use of multiple medications as a part of balanced anesthesia over a short duration of time can have multiple interactions with these herbal and Ayurvedic drugs. Genuine efforts must be made by the attending anesthesiologist to elicit any history of herbal medication possibly by a survey questionnaire; similar attempts have been made earlier also.^[8] Augmentation of the bleeding tendencies with use of ginkgo and garlic, exaggeration of hypertension with ginseng, and excessive sedation with St. John's wort, are few of the common side effects encountered daily in the routine practice of anesthesia.^[8,19] Garlic is also known for increasing bleeding tendencies due to inhibition of platelet aggregation, which mandates extra cautiousness during administration of epidural anesthesia, as there are increased chances of the development of an epidural hematoma.^[20,21] *Ginkgo biloba* is commonly used by the people as it is considered to possess memory-improving qualities. It has also been reported to possess anti-inflammatory properties as well as it inhibits platelet activity. Thus, its use is also fraught with increased danger of perioperative bleeding.^[22,23] Therefore, it is mandatory to stop these drugs in patients taking non-steroidal anti-inflammatory drugs before any proposed surgical procedure.^[24] The mechanisms by which St. John's Wort and valerian augment the anesthetic effect include modulation of the Gamma Amino Butyric Acid (GABA) neurotransmitter. The properties of ginseng are utilized during the treatment of type-II diabetes mellitus patients as it lowers the blood sugar levels.^[25] The risk of wound infection is possibly increased with the use of *Echinacea*, as it has immunosuppressant properties. Although, homeopathic *Arnica* is believed to control bruising and promote healing after local tissue trauma, various studies have come out with contrasting observations.^[26]

As per the new guidelines, ASA has recommended discontinuation of all herbal medicines two weeks prior to surgical intervention.^[27] However, these recommendations cannot be applied uniformly to all types of herbal medicines, as they invariably have different half lives, some have very short half lives, while others have fairly prolonged half lives,

along with different pharmacokinetic attributes. Depending on the generation of active metabolite, it has been suggested that sometimes it is far better to apply individual discretion during stoppage of these medicines rather than going by fixed recommendations. It can unduly prolong the waiting period for surgery for drugs of short duration half lives, or can still pose challenges with those drugs whose half life is more than two weeks. As evidence, kava and ephedra have to be stopped 24 hours prior, ginkgo 36 hours prior, and St. John's wort more than a week prior to surgery.^[8] Moreover, patients present to hospitals only a few days before the recommended surgical procedure and as such it becomes difficult to implement the required set of protocols.

In India, the marketing companies have been spreading a massive campaign in popularizing traditional Chinese herbal medicines and other herbal products, with emphasis on promoting the health benefits of these medicines.^[28] Claims have also been made about treating almost every type of illness with these herbal products, including serious illnesses, as compared to western medicines.^[29] Various observational studies have shown concerns from time to time with regard to potential perioperative complications due to a possible drug interaction.^[8,19] Among the consequences of these possible drug interactions the most important are, impaired coagulation, electrolyte disturbances, cardiovascular effects, and prolongation of anesthesia duration, which are of high concern to the operating surgeon and the attending anesthesiologist.^[30] These side effects and interactions are a result of various possible mechanisms during the perioperative period. This can range from direct effects such as intrinsic pharmacological effects, pharmacodynamic interaction causing alteration of the effect of conventional drugs at the effector site, and pharmacokinetic interaction leading to alteration of the absorption, distribution, metabolism, and elimination of conventional drugs.

Common Drugs Profile from Anesthesia Perspective

Various researches and trials have been conducted in the past and many are going on at present, which concern the drug interaction of Ayurvedic and herbal drugs with allopathic medicines. Based on the evidence of these activities, many new properties of these drugs have come to the fore, which can be of significant concern to the anesthesiologist.

Echinacea purpurea

At the molecular level, Echinacea has got a lipophilic fraction, which is more active than the hydrophilic fraction. The higher activity of the lipophilic fraction is attributed to the presence of alkylamide polyactylenes and essential oils. It is considered a very useful prophylactic and therapeutic agent in the treatment of viral, bacterial, and fungal infection of the upper respiratory tract. The immunostimulatory properties of Echinacea have also been studied. However, evidence is lacking about a possible interaction of simultaneous concomitant use of Echinacea and immunosuppressive drugs.^[31-33] Therefore, a general consensus exists about the avoidance of Echinacea in patients who are being administered immunosuppressive drugs, especially in patients undergoing organ transplant procedures. A contrasting feature to this fact is the immunosuppression with long-term

use of Echinacea, for greater than eight weeks, which increases the risks of poor wound healing and opportunistic infections. Moreover, it has also been incriminated in causing allergic and anaphylactic reactions.^[34] Therefore, cautious use is warranted in patients with asthma and atopic or allergic rhinitis. Furthermore, there are also concerns about its potential hepatotoxicity, but nothing conclusive has been established as yet. Still, the use of this product has to be done carefully in patients with pre-existing hepatic dysfunction as well as in surgeries where hepatic functions and hepatic blood flow is more likely to be compromised.

Ephedra vulgaris

It is considered highly useful for promoting weight loss, increasing energy and for treating most of the respiratory infections. The therapeutic actions of this product are mainly due to its various active alkaloid ingredients like ephedrine, pseudoephedrine, norepinephrine, and methylephedrine. Among these metabolites, ephedrine, a non-catecholamine sympathomimetic agent, is the most active compound, which acts on α_1 , β_1 , and β_2 adrenergic receptors, and exerts its actions by release of endogenous norepinephrine. In larger doses, these sympathomimetic effects can prove to be hazardous for the cardiovascular and central nervous systems, as they cause intense vasoconstriction in the cerebral and coronary vasoconstrictions. As such, anesthesia concerns grow exponentially, as these agents can greatly sensitize the myocardium, to develop arrhythmogenic potential on administration of exogenous catecholamines. Furthermore, prolonged use of this product can lead to a catecholamine-depleted state, and thus, predispose the patients to a high risk of hemodynamic instability, during anesthesia and surgery. The simultaneous use of Monoamine-oxidase Inhibitor (MAO-I) can cause intensive drug interaction, as it can lead to life-threatening complications like, malignant hyperthermia, hypotension, and coma. There have been reports of the formation of renal stones on its prolonged use. Considering the evidence-based pharmacological profile, ephedra must be discontinued at least 24 hours prior to the surgical procedure.^[35]

Garlic - Allium sativum

Garlic is considered to be a natural antibiotic. It has also been observed to exert anti-tussive, expectorant, and diuretic activities and is a cholesterol lowering agent. The lipid and cholesterol lowering effects significantly reduce the risk of atherosclerosis and subsequently lower the blood pressure and incidence of thrombus formation.^[36] These effects are largely attributed to an active metabolite allicin, which contains sulfur and gives garlic its characteristic smell. A decrease in pulmonary and systemic resistance has been observed in the laboratory animals with allicin. The platelet aggregation is inhibited in a dose-dependent manner. Another active compound of garlic, ajoene, is responsible for the irreversible inhibition of platelets, by potentiating the effects of platelet inhibitors.^[37,38] It is believed to possess immunomodulator and anticancer properties.^[39] It is associated with few side effects like bad breath, bad odor from skin, gastrointestinal upsets, and skin rashes. On the basis of insufficient data about the pharmacokinetics of its constituents and its effect on platelet function, it should be stopped at least seven days prior to surgery, especially when there is a possibility of epidural hematoma formation and postoperative bleeding.

Ginkgo biloba

It is derived from the leaves of *Ginkgo biloba* and exerts its pharmacological action through terpenoids and flavonoids. It is commonly used in the treatment of cognitive disorders and memory-related dysfunction, as it is believed to stabilize the cognitive functions, especially in cases of Alzheimer disease with multi-infarct dementia. The other possible uses of this product include peripheral vascular disease, vertigo, age-related muscular degeneration, and so on. The main mechanism of its action seems to be due to its effect on vasoregulation, modulation of neurotransmitter, and its receptor activity, as well as, inhibition of the platelet-activating factor. Contrary to the claims, there have been instances when bleeding complications have been observed, especially spontaneous intracranial bleeding, hyphema, and postoperative bleeding in laparoscopic cholecystectomy, in patients who are Ginkgo users.^[40-45] The data and pharmacological profile of the drug mandates its discontinuation 36 hours prior to surgery, to decrease the risk of bleeding.

Ginseng - Panax ginseng

It is considered to be a stress relieving product besides restoring homeostasis and is popularly called adaptogen.^[46] The pharmacological action of this product is mainly due to ginsenosides, which belong to a group of compounds called steroidal saponine. As such, the mechanism of action very much resembles that of steroidal hormones. The blood glucose lowering effect of ginseng makes it a useful agent to be used in non-diabetic and type II diabetes for reduction of postprandial blood sugar levels. Thus, precaution should be exercised in fasting patients, who are posted for surgery and currently taking ginseng, as there exists a possible risk of severe hypoglycemia. It can influence the coagulation pathway as well as inhibit platelet aggregation.^[47,48] These effects are evident in the prolongation of both coagulation time of the thrombin and activated partial thromboplastin time. The evidence-based literature recommends its stoppage, at least seven days prior to surgery.

Kava - Piper methysticum

The active ingredient of kava is kavalactone and is prepared from dried roots of pepper methylene, which possesses anxiolytic and sedative properties. The effects of this product on the central nervous system are dose-dependent, which are helpful in the suppression of epileptogenic focus and provide local anesthetic effects. These central effects definitely potentiate the action of anesthetic agents through GABA-mediated inhibitory neurotransmitters, thus mimicking sedatives and hypnotics. Kava dermopathy can be a niggling side effect of the product on prolonged use. The pharmacological properties of this drug dictate its discontinuation at least 24 hours prior to surgery.^[49,50]

St. John's wort - Hypericum perforatum

It is considered a useful medicine for the treatment of mild-to-moderate depression, but only as a short-term measure. However, its utility is doubtful for treating major depression and other mental disorders.^[51] The pharmacological actions are mainly mediated by two of its active compounds, hypericin and hyperforin, which act by inhibiting the re-uptake of serotonin, norepinephrine, and dopamine by the neurons. One of the side effects of these medicines is the central serotonin excess syndrome, which can occur with or without

the concomitant use of serotonin re-uptake inhibition. It is a potent microsomal enzyme inducer and causes induction of the cytochrome isoform P₄₅₀3A4 and P₄₅₀2C9. Drugs utilizing this enzyme substrate, P₄₅₀3A4, include alfentanil, midazolam, lignocaine, calcium channel blockers, and serotonin receptor antagonist, and as such, their clinical effects are reduced. The anticoagulant effect of warfarin and actions of NSAIDs are reduced due to induction of P₄₅₀2C9. This literary evidence strongly recommends the discontinuation of the drug at least five days prior to surgery.^[51,52]

Valerian - Valeriana officinalis

The most common use of the valerian compound is in the treatment of insomnia. The sedative properties of valerian are due to its active compound, sesquiterpenes. These sedative and hypnotic effects are dose-dependent and are mediated through modulation of the GABA-mediated neurotransmitters and the receptor function. As the receptor sites are covered with centrally acting anesthetic agents, there exists a high risk of potentiating of anesthetic and adjuvant drug actions that act as GABA receptors. These mechanisms can also produce physical dependence on prolonged use. The abrupt discontinuation before any surgical procedure has the ability to produce benzodiazepine withdrawal like symptoms.^[8,53]

Ginger - Zingiber officinale

The six-ginger ale and galanolactone are the active compounds of ginger, which provide therapeutic efficacy in respiratory problems, CNS symptoms, hypoglycemia, sore throat, and so on.^[54] It is also considered to be extremely useful in parturients, who are suffering from hyper emesis.^[55] The anti-emetic effect can be utilized to prevent oncology related nausea and vomiting.^[56] The side effect profile of this product ranges from hyperglycemia to prolongation of bleeding time by thromboxane inhibition.^[57] The main concern when using this compound is that caution must be exercised during administration of neuraxial anesthesia, as there are potential possibilities of epidural hematoma formation.

Guduchi - Tinospora cordifolia

The active compounds of Guduchi include clerodane, furanoditerpene, syrengin, and cardiol, which exert cardioprotective, expectorant, anti-allergic, analgesic, and anti-inflammatory effects.^[58] It is prescribed for the treatment of DM as it has been seen to lower the blood glucose level. Few studies have quoted its renoprotective, cholesterol-lowering, and anti-oxidant actions also.^[58-61] The beneficial effects in hepatic diseases like cirrhosis and hepatitis have also been demonstrated in few of the earlier studies,^[62] however, the recommendations for discontinuation of Guduchi are not clear as per ASA guidelines.

Turmeric - Curuma longa

It is the most commonly used herbal product in almost every household of the Indian subcontinent as a dye and food component. The beneficial effects of turmeric are believed to be due to its anti-infective, analgesic, anti-inflammatory, and anti-oxidant actions.^[63] The ability to inhibit microsomal enzyme P₄₅₀ causes the prolonged duration of many drugs like fentanyl, midazolam, warfarin, theophylline, bupivacaine, ropivacaine, and lignocaine. Neurocognitive effects are utilized for the treatment of depression, and stress protection from

active metabolites of paracetamol, in toxic doses, has also been observed by few researchers.^[64] The discontinuation of this product before surgery has not been mentioned in the ASA guidelines.^[65] Few studies have observed its anti-neoplastic activity, which can possibly help in protection from various cancers such as breast, prostate, colon, pancreas, and leukemia.^[66] The hepatic protection from active metabolites of paracetamol in toxic doses has also been observed by few researchers.^[67] The discontinuation of this product before surgery has not been mentioned in ASA guidelines.

Conclusion

These are only a few products belonging to the Ayurvedic, herbal, and homeopathic sciences that can be of huge significance during administration of anesthesia and surgery. The list is quite long, but it is out of the purview of the present article to discuss all these products. As such, a leaf can be taken out of the present article when possibly considering the clinical significance of other drugs during anesthesia and surgical procedures, and almost similar precautions can be exercised while undertaking such interventions. The main message of this review is to be extra cautious whenever patients consuming these herbal and Ayurvedic products are presented for surgical intervention, whether emergency or elective. As such alternative medicines that are considered to be very safe may not always hold true and the risk arises only during presentation of such patients for surgery, where we dread the interaction of the alternative medicines with anesthetics. In this article an attempt has been made to mention all the properties that can show interaction with the anesthetic drugs and procedures. Yet there is a wide scope to study actions from allopathic sciences retrospectively in an Ayurvedic manner. Further studies can be carried out to expand the specialty of anesthesia in Ayurveda and enrich the knowledge base. The measures discussed can be of immense clinical benefit if they are applied in a judicious and timely manner, thus providing a smooth and safe surgical atmosphere.

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हिन्दी सारांश

वैकल्पिक चिकित्सा और संज्ञाहरण: दैनिक व्यवहार में निहितार्थ और विचार

सुखमिंदरजित सिंह बाजवा, अपराजिता पाण्डा

हर्बल औषधियों का प्रयोग जनसामान्य द्वारा बहुतायत से किया जा रहा है। आजकल ये औषधियाँ शल्य चिकित्सा देखभाल के दौरान कई चुनौतियाँ खड़ी कर सकती हैं। प्रस्तुत अध्ययन का उद्देश्य शल्य चिकित्सा अवधि के दौरान हर्बल औषधियों के प्रयोग के प्रभाव पर ध्यान केन्द्रित करने के लिए और शल्य चिकित्सा प्रबंधन के दौरान उनके उपयोग के लिए रणनीति की समीक्षा करने के लिए है। साहित्य संकलन विभिन्न शोध पत्रिकाओं, पाठ्य पुस्तकों, वेब स्रोत सहित एंटेज पब्लिश, Medscape आदि से किया गया है। यहाँ केवल उन हर्बल औषधियों को चुना गया है जिनकी जानकारी शल्य चिकित्सा अवधि के दौरान इनके सुरक्षित उपयोग हेतु उपलब्ध थी। पश्चात् इन औषधियों की फार्माकोकाइनेटिक्स और फार्माकोडायनामिक्स सम्बन्धी जानकारी का विश्लेषण किया गया। पूरी समीक्षा का तथ्य यह है कि कभी-कभी आमतौर पर प्रयोग की जानेवाली वैकल्पिक औषधियाँ शल्य चिकित्सा अवधि के दौरान चिंता का विषय बन सकती हैं। ये उपद्रव इन औषधियों की प्रत्यक्ष क्रिया अथवा फार्माकोकाइनेटिक्स या फार्माकोडायनामिक्स प्रभाव के कारण हो सकते हैं। शल्य चिकित्सा उपचार में हर्बल औषधियों के उपयोग के गहन प्रभावों को ध्यान में रखते हुए, एनेस्थिसियाँलॉजिस्ट को विशेष रूप से रोग इतिवृत्त एवं शल्य क्रिया उपचार के दौरान हर्बल औषध के उपयोग पर सावधानी बरतनी चाहिए, ताकि उनके उपयोग अथवा उनके विच्छेदन से होने वाले उपद्रवों से बखूबी निपटा जा सके।