CIRUGÍA ESPAÑOLA

www.elsevier.es/cirugia

Review

Perioperative pharmacological treatment recommendations

Matilde Cháfer Rudilla,[a,] J. Pablo Domínguez Rodríguez,[b] Ana Reyes Santana,[a] Marta Gorchs Molist,[a] María de los Ángeles Ocaña Gómez,[a] José Antonio Martín Conde,[a] and Javier Merino Alonso[a]*

[a]*Servicio de Farmacia Hospitalaria, Hospital Universitario Nuestra Señora de Candelaria de Tenerife, Santa Cruz de Tenerife, Spain*
[b]*Servicio de Cardiología, Hospital San Juan de Dios, Santa Cruz de Tenerife, Spain*

ARTICLE INFO

Article history:
Received February 9, 2009
Accepted April 29, 2009
Online August 3, 2009

Keywords:
Perioperative care
Prevention and control
Practice guidelines
Antibiotic prophylaxis
Venous thrombosis
Pain
Postoperative nausea and vomiting

ABSTRACT

Despite the advances in surgical techniques and anaesthesia, there are still a significant number of postoperative complications in surgery, the most common being, surgical wound infections, sepsis, respiratory and cardiovascular complications, and thromboembolic events. All of these complications increase hospital stay, health costs and mortality. Different pharmacological perioperative strategies have been employed to reduce their incidence, but these have varied widely between hospitals, and even among professionals in the same hospital. In this article we review the recommendations of clinical practice guidelines on the medication routinely used in this situation, such as antibiotics, antithrombotics, analgesics and antiemetics.

Recomendaciones sobre el tratamiento farmacológico perioperatorio

Palabras clave:
Cuidados perioperatorios
Profilaxis
Guías de práctica clínica
Profilaxis antibiótica
Trombosis venosa
Dolor
Náuseas y vómitos postoperatorios

RESUMEN

A pesar de los avances en las técnicas quirúrgicas y en la anestesia, todavía se produce un número significativo de complicaciones en el postoperatorio de la cirugía mayor. Las más frecuentes son las infecciones de la herida quirúrgica, la sepsis, las complicaciones cardiovasculares y respiratorias y los fenómenos tromboembólicos. La aparición de estas complicaciones aumenta la estancia hospitalaria, los costes sanitarios y la mortalidad. Para reducir su incidencia, se han introducido diferentes estrategias farmacológicas perioperatorias que, sin embargo, han estado sometidas a una gran variabilidad de unos hospitales a otros e incluso entre los profesionales de un mismo centro. En el presente artículo se revisan las recomendaciones de las guías de práctica clínica más establecidas sobre la medicación habitualmente empleada en esta situación, como los antibióticos, antitrombóticos, analgésicos y antieméticos.

*Corresponding author.
E-mail address: mcharud@telefonica.net (M. Cháfer Rudilla).

Introduction

Despite the advances in surgical techniques and anaesthesia, a significant number of complications still arise in postoperative stages after major surgery.[1,2] The most frequent are infections of surgical wound, sepsis, respiratory and cardiovascular complications, and thromboembolic phenomena. These complications extend hospital stay and increase health costs and mortality.[3,4] Different therapeutic strategies have been introduced in order to reduce their incidence, among which perioperative pharmacological therapy should be highlighted.

However, the use of drugs in this situation has been subject to large variability from some hospitals to others, and even between health professionals at the same health center.[5] This has resulted in significant differences in prevention outcomes of postoperative complications at different hospitals. Some studies have demonstrated that, with certain frequency, administration and dosage guidelines at perioperative stage are not in agreement with recommendations from clinical practice guidelines.[6] On the other hand, indiscriminate use of medication at perioperative stage leads to unnecessary economic expenditure and, in some cases, it can cause adverse pharmacologic reactions in the patients undergoing treatment.

Because of this, the introduction of control programs in hospitals is necessary for the appropriate use of perioperative medication. The first step to start these programs is based on thorough knowledge of the clinical practice guidelines for perioperative pharmacological therapy. This article reviews recommendations on medication most frequently used in this situation, such as antibiotics, antithrombotics, analgesics, and antiemetics.

Antibiotic prophylaxis

Surgical site infection (SSI) is the second most frequent cause of nosocomial infection,[7,8] with a resulting increase in morbidity and mortality and derived health costs.[7,9] Its incidence varies from 2% to 20% of the interventions and depends on the type of surgery.[10]

Most SSIs are caused by microorganisms from the skin flora, digestive mucosa, and genitourinary system, but they may also come from health staff or the environment. There are multiple causes, being worthy to mention bacterial inoculum and their virulence, clinical situation of patient and incorrect use of preventive measures. A significant number of these infections could be prevented by compliance with antibiotic prophylaxis (AP) guidelines. It is essential to set AP protocols for surgery in hospitals, as well as to implement responsive multidisciplinary systems for epidemiologic surveillance, with periodic evaluations and that are in fluent communication with all those involved in the process to develop improvement procedures.

Various AP guidelines have been published regarding surgical wound treatment; whose recommendations are included below.[11-15]

Indications: AP is indicated to eliminate residual inoculum from the most common pathogen agents from each intervention that may have remained after exhaustive perioperative aseptic measures. Generally speaking, it is indicated for clean surgery with prosthetic material, clean-contaminated surgery, and contaminated surgery (although in this case it would not be true prophylaxis, but antibiotic treatment). It is important to bear in mind the infection risks and factors inherent in each particular patient. In the future, introduction of mildly invasive techniques may force to revise AP indications.

Choice of antibiotic: SSI, except when implanting prosthetic material, is generally caused by a small number of common pathogen agents, that are the target of the antibiotics used in prophylaxis. Consequently, the medication used should be updated continually depending on bacterial sensitivity patterns.

The antibiotic of choice should be the right one against those bacteria that are most likely to contaminate the surgical wound, and it should depend on the area where the incision will be practiced. Moreover, it should be safe for the patient, with the less impact as possible over normal bacterial flora and at an economically accessible cost. On the other hand, the use of broad spectrum antibiotics should be avoided, in order to prevent bacterial resistance (indiscriminate use of 3rd and 4th generation cephalosporin may cause diarrhoea by *Clostridium difficile*, increase of enterobacteria with extended spectrum betalactamase and appearance of Methicillin-resistant *Staphylococcus aureus* [MRSA]). With all these factors in mind, antibiotics of choice are the older ones and with a narrower anti-bacterial spectrum; the Beta-lactam antibiotics are first line agents for most surgical procedures. The most usually recommended antibiotics depending on type of surgery are shown in Table 1.

Patients that are *Staphylococcus aureus* or MRSA carriers have an especially high risk of infection, mostly in high risk procedures, and it is recommended that they are subjected to prior prophylaxis with an adequate antibiotic for local sensitivity.

Optimal dose: dose to be administered should max out in order to reach values above minimal inhibitory concentration during a time longer than the necessary for the intervention to take place. Doses and administration guidelines for antibiotics most commonly used in prophylaxis are shown in Table 2.

Starting on AP: the antibiotic should be administered at a favourable moment to reach an effective serum and tissue concentration to eliminate microorganisms introduced during intervention, that is, it should be around the onset of surgical incision. It is currently recommended to start administration 30 minutes before intervention and no more than 3 hours after starting intervention. In the case of vancomycin, administration should be started 120 minutes before incision to prevent reactions associated with this drug administration.

AP duration: it has been proven that for most surgical interventions one single antibiotic dose is enough as long as its half-life is adequate to be active during the length of time covered by the intervention. Additional doses should

Table 1 – Antibiotic prophylaxis according to type of surgery

AP indication according to type of surgery	Probable microorganisms	Recommended antibiotic	Alternative when allergy to Betalactams
Clean surgery[a]	Skin microorganisms	Cefazolin/2G Cephalosporins/Amoxicillin plus clavulanic acid	Vancomycin
Esophageal and gastroduodenal surgery	*Streptococcus viridans, Streptococcus faecalis, Escherichia coli, Klebsiella,*	Cefazolin, amoxicillin plus clavulanic acid, 2G Cephalosporins	Vancomycin/linezolid plus aminoglycoside[b]
	Bacteroides, Candida, oral anaerobes		Metronidazole plus aminoglycoside
			Pseudomonas suspected: piperacillin plus tazobactam
Bariatric surgery (adjust according to BMI)	Enterobactereae, Gram positive cocci	Amoxicillin plus clavulanic acid/2G Cephalosporins	Metronidazole plus aminoglycoside
Percutaneous endoscopic gastrostomy		Amoxicillin plus clavulanic acid	
Hepatobiliary surgery (no high risk)	Enterobactereae, Gram positive cocci	2 G. Cephalosporins/ Amoxicillin plus clavulanic acid	Metronidazole plus aminoglycoside
Laparoscopic cholecystectomy (no high risk)	Enterobactereae, Gram positive cocci	1 to 2 G. Cephalosporins/ Amoxicillin plus clavulanic acid	Metronidazole plus aminoglycoside
High risk ERCP (biliary obstruction)	*Enterococcus faecalis, Pseudomonas, Enterobacter*	Amoxicillin plus clavulanic acid	
		Pseudomonas suspected: ceftazidime	
		Suspect of enterococcus or *Pseudomonas*: piperacillin plus tazobactam	
Small intestine surgery	Anaerobes and enterobacteria	Amoxicillin plus clavulanic acid	Metronidazole plus aminoglycoside
		If terminal ileum surgery: Safe prophylaxis as for colorectal surgery	
Appendicular surgery	Anaerobes (*bacteroides*) and Gram negative	Metronidazole plus gentamicin/ Amoxicillin plus clavulanic acid.	Metronidazole plus aminoglycoside
		Metronidazole plus cefazolin/ Metronidazole plus cefotaxime	
Colorectal surgery	Anaerobes and Gram negative	Amoxicillin plus clavulanic acid/ Metronidazole plus aminoglycoside/	Metronidazole plus aminoglycoside
		Metronidazole plus 2G Cephalosporin.	
		± oral: Neomycin/Kanamycin plus eritromicin/ Metronidazole[c].	
Vascular surgery	Gram positive cocci, enterobacteria	2G Cephalosporins/Amoxicillin plus clavulanic acid	
Amputations of lower extremities	Staphylococcus aureus, enterobacterias, *Clostridium* (gangrene)	2G Cephalosporins/Amoxicillin plus clavulanic acid	
Exploratory laparotomy for abdominal traumatism	Enterobacteria, enterococci	Amoxicillin plus clavulanic acid	Metronidazole plus aminoglycoside

AP indicates antibiotic prophylaxis; BMI, body mass index; ERCP, endoscopic retrograde cholangiopancreatography; G, generation.
[a]Assess prophylaxis change if prevalence of *Staphylococcus aureus* resistant to methicillin o *Staphylococcus epidermidis* resistente a Betalactams.
[b]Gentamicin or tobramycin.
[c]Administer 19–18 and 9 hours before intervention.

Table 2 – Most usual antibiotics for perioperative prophylaxis with administration guidelines

Antibiotic	Standard dose	Administration route	Duration of infusion, min	Interval between doses, h
Amoxicillin plus clavulanic acid	1–2 g	IV	Bolus: 3–5 Infusion: 15–60	6
Aztreonam	1–2 g	IV	Bolus: 3–5 Infusion: 20–60	3–5
Cefazolin	1–2 g	IV	Bolus: 3–5 Infusion: 15–60	2–5
Cefuroxime	1.5 g	IV	Bolus: 3–5 Infusion: 15–60	3–4
Cefamandole	1 g	IV	Bolus: 3–5 Infusion: 15–60	3–4
Cefoxitin	1–2 g	IV	Bolus: 3–5 Infusion: 15–60	2–3
Clindamycin	600–900 mg	IV	10–60	3–6
Erythromycin	1 g 19, 18, and 9 h before	Oral	–	–
Gentamicin	1.5 mg/kg	IV	30–60	3–6
Neomycin	1 g 19, 18, and 9 h before	Oral	–	–
Metronidazole	0.5–1.0 g	IV	30–60	6–8
Vancomycin	1 g	IV	60	6–12

be administered if surgical intervention extends beyond 2 antibiotic half-lives from initial dose, or if blood loss is more than 1500 mL after fluid administration. Prolonging prophylaxis beyond 24 hours has not been shown to be useful in most surgical procedures.

Administration route: the antibiotic is usually administered by IV route. Oral administration is habitually used, associated or not with IV route, for AP in colon surgery. Topical antibiotics have shown to be effective to prevent SSI in contaminated surgery, in prosthetic articulatory replacements, and in cataracts surgery or for penetrating ocular lesions.

Thromboembolic prophylaxis

Various reasons justify prophylaxis for vein thrombosis at perioperative stage. On the one hand, most patients undergoing major surgery have one or more classical risk factors for venous thromboembolism (VTE), such as immobility, varicose veins, obesity, neoplasia, smoking, advanced age, or treatment with oestrogens.[16] Besides, additional factors may add up during surgery, such as general anaesthesia (of higher risk than spinal or epidural), dehydration, and blood transfusions. Similarly, certain types of surgery, such as major orthopaedic interventions, are associated with increased risk of venous thromboembolism. On the other hand, thromboembolic complications are frequently asymptomatic and it is difficult to predict which patient will present with them. Without thromboprophylaxis, incidence of deep vein thrombosis is 15% to 40% in patients undergoing surgery and it rises to 60% for those undergoing major orthopaedic surgery.[17,18]

Thromboembolic complications at postoperative stage suppose morbidity and considerable resource consumption, the possibility of chronic consequences with ensuing clinic and economic consequences, and risk of death due to severe pulmonary embolism. A patient suffering VTE, apart form extending his/her stay at hospital, requires anticoagulant therapy, with the added risk of haemorrhage. In addition, a significant number of patients that presented with deep vein thrombosis have recurrent thrombosis in the future, while others present with stenosis or obstruction to the affected veins, or vein valve insufficiency, late complications that are not frequently taken into account.[19]

Various studies have shown that thromboprophylaxis reduces incidence of vein thrombosis and pulmonary embolism, as well as mortality derived from these complications,[20,21] therefore improving prognosis for patients and reducing health costs significantly.[22] Although the use of antithrombotic drugs favours haemorrhaging, many studies have shown that, with appropriate thromboprophylaxis guidelines, risk-benefit and cost-effectiveness ratio are clearly favourable.[23,24]

Thromboprophylaxis guidelines for each patient should be based on predisposing factors, disease presented, and intervention to be performed. Individualization is, however, difficult, and thromboprophylaxis is usually decided for groups of patients, according to surgical specialty, type of surgery (minor or major), patient age (<40 years, 40 to 60 years, and >60 years), and presence of thromboembolism risk factors.[25,26]

It has repeatedly been proven that early mobilization and thromboprophylaxis may reduce perioperative thromboembolic complications in more than 70%; clinical practice guidelines recommend both for all major surgery procedures.[27] Non-fractionated heparin in low doses as well as low-molecular weight heparin (LMWH) have similar efficacy, but LMWH has the advantage of allowing administration once a day and present with less risk of thrombocytopaenia.

Guidelines recommend prophylaxis by mechanical means (intermittent pneumatic compression, graduated compression

stockings, or foot venous pump) for patients with high risk of haemorrhaging. It is also advisable to associate mechanical measures to pharmacological prophylaxis in patients with high risk of venous thromboembolism. The use of aspirin alone is not recommended as prophylaxis for vein thrombosis. The guidelines recommend to follow manufacturer dosing indications for each drug and reduce dosing in case of significant renal insufficiency, in the elderly and in patients with high risk of haemorrhage.

In major orthopaedic surgery LMWH may be started before or after intervention, but it is recommended to start on fondaparinux 6 to 8 hours after surgery or the day after it. It is also recommended not to use VTE sieving methods systematically in asymptomatic patients. Due to its particular risk, it is recommended to perform thromboprophylaxis with LMWH, vitamin K antagonists (international normalized ratio [INR], 2.0-3.0) or fondaparinux (first choice for hip fracture) for at least 10 days and up to 35 days after intervention. Guidelines for thromboprophylaxis recommended for each type of surgery are shown in Table 3.

Pain management

It is considered perioperative pain that which was present in a surgical patient caused by a previous disease, the surgical procedure, or by a combination of both. Up to 75% of the patients undergoing surgery experience significant pain,[28] which represents an important social, clinical and economic impact.[29,30]

Deficient perioperative control is related to cardiovascular, thromboembolic, pulmonary, gastrointestinal, infectious, and neuroendocrine complications. All these complications affect quality of life for the patient, interfere with rehabilitation, extend hospital stay, cause re-admissions and may predispose to chronic pain. Because of all this, it is necessary to extend the correct usage of effective analgesic measures for all surgical patients.

Effectiveness in relieving postoperative pain is related to each patient's needs, as it depends on his/her own assessment, and such needs vary during surgical process. Up to 30% of the patients undergoing major surgery experience moderate to intense pain when receiving standard analgesia. The use of more potent drugs may, however, be associated to adverse effects that counterbalance their benefit. For this reason, postoperative analgesic treatment requires measures towards achieving equilibrium between satisfactory pain relief and minimal adverse effects.

All the guidelines for clinical practice cover a series of strategic points for postoperative pain management.[30-32] The basic measure consists in an ongoing training program that guarantees health staff competence in postoperative pain management. An update in knowledge of pain physiology, pharmacology of analgesics, basic pain assessment, and anaesthetic and non-pharmacological techniques is called for.

Since these guidelines appeared, it has been proposed to set up multidisciplinary acute pain units formed by surgeons, anaesthetists, physical therapists, nurses and pharmacists. The North American model, mainly private, has more availability of medical and nursing staff. Contrastively, the European model is based mainly on nursing staff and the unit functions as an integrating element in pain management.

The approach, however, starts with providing the patient with adequate information orally as well as in written form. Following that, a preoperative evaluation should be performed, including a physical pain-targeted exploration by using a visual analogical scale, or otherwise a simple verbal scale. After that, the following should be considered: type of intervention, expected pain intensity, risk-benefit ratio of different analgesic modalities and patient preferences.

Patient preoperative preparation should include adjusting habitual medication to prevent sudden drug removal that might cause withdrawal symptom, with special emphasis on analgesic treatment.

Pain management should be programmed preoperatively, for example, by selecting candidates for continuous percutaneous analgesia (CPA), and it should be initiated during the intervention.

As long as it is possible, a multimodal approach should be used by employing different analgesic patterns, occasionally administered in distinct anatomical areas and with varied action mechanisms. This allows using lower pharmacological doses and thus reduces adverse effects. Treatment is to be chosen depending on postoperative stage and patient response; also, follow-up is to be carried out, and effectiveness and adverse effects should be recorded in the case history. All these aspects should be periodically evaluated in order to reach and maintain quality standards.

In the European minimum standards for management of postoperative pain[33] it is recommended to use an analgesic scale similar to that of the World Health Organization for chronic pain. For minor surgery the following are recommended: paracetamol, non-steroid anti-inflammatory (NSAI) or weak opiate, infiltrating wound with local anaesthetics or peripheral nerve blocking; for a "moderate" surgery paracetamol or NSAI are indicated, together with wound infiltration with local anaesthetics or peripheral nerve blocking plus CPA. For major surgery, the indication is paracetamol/NSAI plus epidural anaesthesia, plus opiate or combination or CPA. Table 4 shows the analgesics most commonly used in management of perioperative pain.

Treatment of postoperative nausea and vomit

Postoperative nausea and vomit (PONV) affects 20% to 30% of general surgery patients, but it can reach up to 80% of those with high risk.[34,35] PONV extends patient waking hours, increases medical and nursing care as well as potential hospital admission with the economic expenses this involves.

Risk factors associated with PONV: various models have been developed to assess individual PONV risk and identify those patients that could benefit from prophylaxis.[36,37] The only risk factors that have been proven enough regarding the patients are: female sex, not smoking and kinetosis; regarding those related to anaesthesia: use of volatile anesthetics, nitric oxide, and use of opiates. There is great controversy with

Table 3 – Thromboprophylaxis indicated according to type of surgery

Intervention	Recommendation	Duration
General Surgery		
Low risk or minor surgery	Early mobilization	Until discharge
Moderate risk or major benign surgery	LMWH, HNFLD/ 12 h or fondaparinux	Until discharge
High risk or major surgery	LMWH, HNFLD/8 h or fondaparinux	Until dischargea
Multiple risk factors	(LMWH, HNFLD/8 h or fondaparinux) plus MM	Until dischargea
Vascular surgery		
Low risk	Early mobilization	Until discharge
Major surgery with risk factors	LMWH, HNFLD or fondaparinux	Until discharge
Gynaecological surgery		
Low risk or minor benign surgery	Early mobilization	Until discharge
Low risk or laparoscopic surgery	Early mobilization	Until discharge
Laparoscopic with risk factors	LMWH, HNFLD or MM	Until discharge
Major benign surgery with no risk factors	LMWH, HNFLD or CMI	Until discharge
Major surgery for cancer or risk factors	LMWH, HNFLD/8 h or CMI	Until discharge[a]
	Alternative: LMWH or (HNFLD plus MM) or fondaparinux	Until discharge
Urologic surgery		
Transurethral surgery or of low risk	Early mobilization	Until discharge
Open surgery	HNFLD or MM, or LMWH or fondaparinux or (drugs plus MM)	Until discharge
Laparoscopic surgery[b]		
No risk factors	Early mobilization	Until discharge
No risk factors	LMWH, HNFLD, Fondaparinux or MM	Until discharge
Bariatric surgery		
	LMWH, HNFLD/8 h or fondaparinux or drugs plus IMC	Until discharge
Aortocoronary *bypass*		
	LMWH (preferably) or HNFLD or MM	Until discharge
Orthopaedic surgery		
Knee arthroscopy with no risk factors	Early mobilization	Until discharge
Knee arthroscopy with risk factors	LMWH	Until discharge
Elective hip arthroplasty	LMWH, fondaparinux, AVK (INR, 2.0-3.0) or IMC	Until discharge
	No aspirin, dextrano, HNFLD, or MM as only option	Until discharge
Elective knee arthroplasty	LMWH, fondaparinux, AVK (INR, 2.0-3.0) or IMC	Until discharge
	No aspirin, HNFLD or FVP as only option	Until discharge
Hip fracture surgery	Fondaparinux, LMWH, AVK (INR, 2.0-3.0) or HNFLD	10 to 35 after surgery
	If delayed, start prophylaxis with LMWH or HNFLD	Until discharge
Spinal surgery		
No risk factors	Early mobilization	Until discharge
With risk factors or anterior approach	HNFLD, postoperative LMWH or perioperative IMC	Until discharge
With multiple risk factors	(HNFLD or LMWH) plus IMC	Until discharge
Neurosurgery		
Major neurosurgery	IMC. Alternative: LMWH or HNFLD	Until discharge
With high risk	(HNFLD or LMWH) plus IMC	Until discharge

AVK indicates antagonists of vitamin K; FVP, foot venous pump; HNFLD, heparin not fractioned in low doses; IMC, intermittent mechanical compression; INR, international normalised ratio; LMWH, low-molecular weight heparin; MM, mechanical measures.
[a]If very high risk, maintain 28 days after surgery.
[b]Gastrointestinal and gynaecologic.

Table 4 – Analgesics most frequently used in surgery for acute pain

Medication	Route	Usual dose
Analgesics/antipyretics		
Paracetamol	OA/PA	1–2 g/6–8 h
Metamizole	OA/PA	2 g/6–8 h
Ketorolac	OA/PA	10–30 mg/4–6 h[a]
Anti-inflammatories		
Ketoprofene	OA/PA	100 mg/8 h
Diclofenac	OA/PA	75 mg/12 h
Weak opiates		
Tramadol	OA/PA	50–100 mg/4–6 h
Codeine	OA	30–600 mg/4–6 h
Potent opiates		
Morphine	OA/PA	5–15 mg/6 h
Fentanyl[b]	PA	50 µg/h
Remifentanilo	PA	0.5 µg/kg/h

OA indicates orally administered; PA, parenterally administered.
[a]In older than 65 years 15 mg every 6 h.
[b]Frequently in epidural anaesthesia with local anesthetics (bupivacaine and ropivacaine).

useful to assess individual risk, which stratifies in patient groups. The guidelines[38] recommend the use of prophylaxis only when PONV individual risk is high. Prophylaxis is also recommended, regardless of individual risk, when vomits pose a specific medical problem for the surgery in question, such as jaw, stomach or oesophagus interventions, and those associated with increasing intracranial pressure, or when the patient has put particular emphasis on these symptoms.

Reduction of baseline risk factors for PONV: the use of local anaesthesia or general anaesthesia with propofol, avoiding volatile anaesthetics and nitric oxide, and the use of lower doses of opiates reduce risk significantly. The guidelines, however, do not recommend using oxygen supplements systematically, as these have not been proven well enough to reduce global risk of PONV.

Administration of antiemetic prophylaxis in adults with moderate PONV risk: Antiemetic prophylaxis is currently recommended only in moderate to high risk patients, but introduction of generic drugs may modify this measure. First and 2nd line antiemetics are serotonin receptor 3 (anti-R5-HT3) (ondansetron, dolasetron, granisetron and tropisetron), corticoids (dexamethasone), phenotiacines (promethazine and prochlorperazine), feniletilamin (ephedrine), butyrophenones (haloperidol and droperidol), antihistamines (dimenhydrinate), and anticholinergics (transdermal scopolamine). Table 5 shows recommended dosing and administration guidelines.

Adults with moderate emesis risk should receive more than one drug with a different action mechanism. Anti-R5-HT_3, with higher antiemetic and antinausea effect, are a frequent cause of headache and, for this reason, droperidol can be associated because it is more effective against nausea and prevents headache; combination with dexamethasone is also effective.

The guidelines recommend using anti-R5HT_3, comparable in effectiveness and safety, as well as dexamethasone in one single dose. In doses for PONV prophylaxis doses droperidol does not have significant cardiovascular adverse effects and, besides, it is effective to prevent PONV induced by opiates in CPA. Transdermal scopolamine is useful as adjuvant antiemetic treatment, but the patch should be placed the night before surgery or 4 hours before end of anaesthesia, which makes its use difficult; it is also useful for CPA.

Droperidol and dimenidrinate are not so thoroughly studied. The guidelines do not recommend as first choice metoclopramide, cannabinoides, promethazine, prochlorperazine or ephedrine.

Administration of antiemetic prophylaxis in adults with high PONV risk: if general anaesthesia is used, at attempt should be made at reducing baseline risk factors. It is recommended to associate drugs of different classes such as droperidol with dexamethasone, anti-R5-HT_3 with dexamethasone; anti-R5-HT_3 with droperidol, or anti-R5-HT_3 with dexamethasone with droperidol.

A multimodal approach is also possible, since it has been scientifically demonstrated that pharmacological prophylaxis combines well with non-pharmacological prophylaxis.[39] This approach would include preoperative anxiolysis, intense hydration, oxygen, antiemetic prophylaxis with droperidol and dexamethasone in the induction and ondansetron at the end of the intervention, general anaesthesia with proforol and remifentanil, and ketorolac. Nitric oxide and neuromuscular blocking agents should be avoided.

Treatment of patients with emesis that have not received preoperative prophylaxis or for whom preoperative prophylaxis has not been effective: if prophylaxis has failed, a drug from other group should be chosen. If it has not been tried, anti-R5HT_3 in low doses are recommended, since these are the only drugs adequately studied for this indication. As an alternate treatment, dexamethasone, droperidol or promethazine may be used. Propofol has proven to be effective at resuscitation units, but its effect in low doses is probably brief.

For patients on opiates droperidol 2.5 mg/morphine 100 mg is recommended at PCA. Ondansetron 8 mg has also proven to be effective.

REFERENCES

1. Khuri SF, Henderson WG, DePalma RG, Mosca C, Healey NA, Kumbhani DJ. Determinants of long-term survival after major surgery and the adverse effect of postoperative complications. Ann Surg. 2005;242:326–41.
2. Dimick JB, Pronovost PJ, Cowan Jr JA, Lipsett PA, Stanley JC, Upchurch Jr GR. Variation in postoperative complication rates after highrisk surgery in the United States. Surgery. 2003;134:534–40.
3. Dimick JB, Chen SL, Taheri PA, Henderson WG, Khuri SF, Campbell Jr DA. Hospital costs associated with surgical complications: A report from the private-sector National Surgical Quality Improvement Program. J Am Coll Surg. 2004;199:531–7.

Table 5 – Recommended doses and administration guidelines of antiemetics used in surgery

Medication	Dose	Administration route	Administration time
Serotonin 3 receptor antagonist			
Ondansetron	4 mg	IV	End of surgery
Dolasetron	12.5 mg	IV	End of surgery
Granisetron	0.33–1.5 mg	IV	End of surgery
Tropisetron	2 mg	IV	End of surgery
Corticoids			
Dexamethasone	4–5 mg	IV	During induction
Fenotiacines			
Prometacine	6.25–25 mg	IV	During induction
Proclorperazin	5–10 mg	Intramuscular/intravenous	End of surgery
Feniletilamin			
Ephedrine	0.5 mg/kg	Intramuscular	End of surgery
Butyrophenones			
Haloperidol	0.5–2.0 mg	Intramuscular/intravenous	
Droperidol	0.625–1.25 mg	IV	End of surgery
Antihistaminics			
Dimenhydrinate	1 mg/kg	IV	
Anticholinergic			
Scopolamine		Transdermal patch	Night before or 4 h before surgery

4. Khan NA, Quan H, Bugar JM, Lemaire JB, Brant R, Ghali WA. Association of postoperative complications with hospital costs and length of stay in a tertiary care center. J Gen Intern Med. 2006;21:177–80.
5. Gorecki P, Schein M, Rucinski JC, Wise L. Antibiotic administration in patients undergoing common surgical procedures in a community teaching hospital: The chaos continues. World J Surg. 1999;23:429–32.
6. Delgado M, Martínez G, Gómez A, Medina M. Quimioprofilaxis en cirugía: problemas y soluciones en su cumplimiento. Cir Esp. 2002;71:96–101.
7. Burke JP. Infection control-a problem for patient safety. N Engl J Med. 2003;348:651–6.
8. National Nosocomial Infections Surveillance System. National Nosocomial Infections Surveillance (NNIS) System Report, data summary from January 1992 through June 2004, issued October 2004. Am J Infect Control. 2004;32:470–85.
9. Perencevich EN, Sands KE, Cosgrove SE, Guadagnoli E, Meara E, Platt R. Health and economic impact of surgical site infections diagnosed after hospital discharge. Emerg Infect Dis. 2003;9:196–203.
10. Auerbach AD. Prevention of surgical site infections. En: Shojania KG, Duncan BW, McDonald KM, Wachter RM, Markowitz AJ, editores. Making health care safer: A critical analysis of patient safety practices. Evidence report/ technology assessment no. 43. Rockville, MD: Agency for Healthcare Research and Quality; 2001. p. 221–44. [cited, Dic 8, 2003]. Available from: URL: http://www.ahrq.gov/clinic/ ptsafety/pdf/ ptsafety.pdf.
11. Bratzler DW, Houck PM, Surgical Infection Prevention Guideline. Writers Workgroup. Antimicrobial prophylaxis for surgery: An advisory statement from the National Surgical Infection Prevention Project. Am J Surg. 2005;189:395–404.
12. Antibiotic prophylaxis in surgery. Treatment guidelines. The Medical Letter. 2004;2:27–32.
13. Scottish Intercollegiate Guidelines Network (SIGN). Antibiotic prophylaxis in surgery. A national clinical guideline. En: Brown K, De Beaux A, Qureshi S, Twaddle S, editors. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2008 Jul. 71 p. (SIGN publication; no. 104) [cited, Apr 2009]. Available from: URL: www.sign.ac.uk.
14. Guirao Garriga X, Badia Pérez JM. Profilaxis antibiótica en cirugía. In: Guirao X, Arias J, editors. Guía Clínica de Infecciones Quirúrgicas. Sección de infección quirúrgica. Asociación española de Cirujanos. Madrid: Arán Ediciones; 2006.
15. Badia Pérez JM, Girvent Montllor M, Sitges Serra A. Antibioticoterapia profiláctica y terapéutica en la cirugía general. In: Jaurrieta EJ, Moreno M, Parrilla P, editors. Cirugía AEC. Manual de la Asociación Española de Cirujanos. Madrid: Edit. Médica Panamericana; 2004. p. 96–108.
16. Anderson FA, Spencer FA. Risk factors for venous thromboembolism. Circulation. 2003;107:I9–I16.
17. Geerts WH, Bergqvist D, Pineo GF, Heit JA, Samama CM, Lassen MR, et al. Prevention of venous thromboembolism. American College of Chest Physicians. Evidenced-based clinical practice guidelines (8th Edition). Chest 2008;133:6 Suppl :381S–453S.
18. Anderson FA, Wheeler HB, Goldberg RJ, Hosmer DW, Patword- han NA, Jovanovic B, et al. A population-based perspective of the hospital incidence and casefatality rates of deep vein thrombosis and pulmonary embolism: The Worcester DVT Study. Arch Intern Med. 1991;151:933–8.
19. Sullivan SD, Kahn SR, Davidson BL, Borris L, Bossuyt P, Raskob G, et al. Measuring the outcomes and pharmacoeconomic consequences of venous thromboembolism prophylaxis in major orthopaedic surgery. Pharmacoeconomics. 2003;21:477–96.
20. International Multicentre Trial. Prevention of fatal pulmonary embolism by low doses of heparin. Lancet. 1975;2:45–51.

21. Halkin H, Goldberg J, Modan M, Baruch M. Reduction of mortality in general medical in-patients by low-dose heparin prophylaxis. Ann Intern Med. 1982;96:561–5.
22. Bergqvist D, Lindgren B, Matzsch T. Cost-effectiveness of preventing postoperative deep vein thrombosis. In: Hull RD, Pineo GF, editors. Disorders of thrombosis. Philadelphia, PA: WB Saunders; 1996. p. 228–33.
23. Clagett GP, Reisch JS. Prevention of venous thromboembolism in general surgical patients: Results of meta-analysis. Ann Surg. 1988;208:227–40.
24. Jorgensen LN, Wille-Jorgensen P, Hauch O. Prophylaxis of postoperative thromboembolism with low molecular weight heparins. Br J Surg. 1993;80:689–704.
25. Samama MM. Applying risk assessment models in general surgery: effective risk stratification. Blood Coagul Fibrinolysis. 1999;10:S79–84.
26. Cohen A, Alikhan R, Arcelus J, Bergmann J, Haas S, Merli G, et al. A risk assessment model for identifying medical patients who should receive thromboprophylaxis [resumen]. J Thromb Haemost. 2003;1:OC437.
27. Geerts WH, Bergqvist D, Pineo GF, Heit JA, Samama CM, Lassen MR, et al. Prevention of venous thromboembolism; American College of Chest Physicians evidence-based guidelines (8th edition) Antithrombotic and Thrombolytic Therapy. Chest. 2008;133:381S–453S.
28. Apfelbaum JL, Chen C, Mehta SS, Gan TJ. Postoperative pain experience: Results from a national survey suggest post-operative pain continues to be undermanaged. Anesth Analg. 2003;97:534–40.
29. Perkins FM, Kehlet H. Chronic pain as an outcome of surgery. A review of predictive factors. Anesthesiology. 2000;93: 1123–33.
30. Dolor postoperatorio en España. Primer documento consenso. AEC, GEDOS, SEDAR y SED. Madrid: Ed Imago Conceps and Image Development; 2005.
31. Rosenquist RW, Rosenberg J. United States Veterans Administration Postoperative pain guidelines. Reg Anesth Pain Med. 2003;28:279–88.
32. American Society of Anesthesiologists Task Force on Acute Pain Management. Practice guidelines for acute pain management in the perioperative setting: An updated report by the American Society of Anesthesiologists Task Force on Acute Pain Management. Anesthesiology. 2004;100:1573–81.
33. Allvin R, Brasseur L, Crul B, Dhal J, Lehmann K, Nicosia F, et al. European minimum standards for the management of post- operative pain. EuroPain Task Force. Pegasus Healthcare Intl, UK, 1998.
34. Tramer MR. A rational approach to the control of post- operative nausea and vomiting: Evidence from systematic reviews. Part I. Efficacy and harm of antiemetic interventions, and methodological issues. Acta Anaesthesiol Scand. 2001;45:4–13.
35. Apfel CC, Bacher A, Biedler A, Danner K, Danzeisen O, Eberhart LH, et al. A factorial trial of six interventions for the prevention of postoperative nausea and vomiting. Duke 4. Anaesthesist. 2005;54:201–9.
36. Koivuranta M, Läärä E, Snare L, Alahuhta S. A survey of postoperative nausea and vomiting. Anaesthesia. 1997;52:443–9.
37. Pierre S, Benais H, Pouymayou J. Apfel's simplified score may favourably predict the risk of postoperative nausea and vomiting. Can J Anaesth. 2002;49:237–42.
38. Gan TJ, Meyer TA, Apfel CC, Chung F, Davis PJ, Habib AS, Society for Ambulatory Anesthesia, et al. Society for Ambu- latory Anesthesia guidelines for the management of post- operative nausea and vomiting. Anesth Analg. 2007;105:1615–28.
39. Scuderi PE, James RL, Harris L, Mims 3rd GR. Multimodal antiemetic management prevents early postoperative vomiting after outpatient laparoscopy. Anesth Analg. 2000;91:1408–14.