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EFFECTO ANTIBACTERIANO Y ANTIFUNGICO DE LA BUPIVACAINA EN LA ANALGESIA DE LAS HERIDAS QUIRURGICAS



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[Al final del trabajo se encuentran Preguntas y Respuestas sobre esta ponencia; mismas preguntas –no todas- que se incluirán en el examen final del **6CVMA 2009**]



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- Effect of local anesthetics on the postoperative inflammatory response

Since the introduction of cocaine in 1884, local anesthetics have been used as a mainstay of pain management. However, numerous studies over the past several decades have elucidated the supplemental role of local anesthetics as antimicrobial agents. In addition to their anesthetic properties, medications such as bupivacaine and lidocaine have been shown to exhibit bacteriostatic, bactericidal, fungistatic, and fungicidal properties against a wide spectrum of microorganisms.

Local anesthetics as antimicrobial agents

Johnson et al. (1) made a comprehensive literature search using MEDLINE 1950-present for in vitro and in vivo studies pertaining to the antimicrobial activity of various local anesthetics on a broad range of bacterial and fungal pathogens. Studies testing the effect on microbial growth inhibition of local anesthetics alone and in combination with other agents, such as preservatives and other medications, as well as the effect of conditions such as concentration and temperature, were included for review. Outcome measures included colony counts, area-under-the-curve and time-kill curve calculations, minimum inhibitory concentrations, and post-antibiotic effect. Evidence suggests that local anesthetics as a class possess inherent antimicrobial properties against a wide spectrum of human pathogens. Multiple local anesthetics at concentrations typically used in the clinical setting (e.g., bupivacaine 0.125%-0.75%; lidocaine 1%-3%) inhibit the growth of numerous bacteria and fungi under various conditions. Different local anesthetics showed various degrees of antimicrobial capacity; bupivacaine and lidocaine, for example, inhibit growth to a significantly greater extent than does ropivacaine. Greater concentrations, longer exposure, and higher temperature each correlate with a proportional increase in microbial growth inhibition. Addition of other agents to the anesthetic solutions, such as preservatives, opioids, or intravenous anesthetics such as propofol, modify the antimicrobial activity via either synergistic or antagonistic action. Limited studies attribute the mechanism of action of antimicrobial activity of local anesthetics to a disruption of microbial cell membrane permeability, leading to leakage of cellular components and subsequent cell lysis. Local anesthetics not only serve as agents for pain control, but possess antimicrobial activity as well. In such a capacity, local anesthetics can be considered as an adjunct to traditional antimicrobial use in the clinical or laboratory setting. Additionally, caution should be exercised when administering local anesthetics prior to diagnostic procedures in which culture specimens are to be obtained, as the antimicrobial activity of the local anesthetic could lead to false-negative results or suboptimal culture yields.

1. Johnson SM, Saint John BE, Dine AP. Local anesthetics as antimicrobial agents: a review. *Surg Infect (Larchmt)* 2008 Apr; 9(2): 205-13

Combined silver sulfadiazine and bupivacaine in wound treatment

In situ photopolymerized semi-interpenetrating networks (sIPNs) composed of poly(ethylene glycol) and gelatin are promising multifunctional matrices for a regenerative medicine approach to dermal wound treatment. In addition to previously demonstrated efficacy in critical defects, sIPNs also function as drug delivery matrices for compounds loaded as either soluble or covalently linked components. Simultaneous release of silver sulfadiazine and bupivacaine from the sIPN would provide multiple-hit management of dermal wounds that minimizes infection, and manages pain along with sIPN absorption of exudates and facilitation of epidermal regrowth. Kleinbeck et al. (1) characterized the release of soluble silver sulfadiazine and bupivacaine and compared it with an established release model. Efficacy of released silver sulfadiazine was confirmed in vitro on *Staphylococcus aureus*, methicillin resistant *S. aureus*, and *Pseudomonas aeruginosa*. Bupivacaine loaded without silver sulfadiazine showed incomplete release, whereas simultaneous loading with silver sulfadiazine facilitated 100% bupivacaine release. Silver sulfadiazine released at 98% without bupivacaine and 96% with bupivacaine. Silver sulfadiazine released onto bacterial cultures inhibited all three strains dose dependently. sIPNs effectively release bupivacaine and silver sulfadiazine while maintaining the antimicrobial activity of

silver sulfadiazine. Drug loaded sIPNs have potential to improve wound management by providing multi-drug delivery along with an effective wound treatment.

1. Kleinbeck KR, Bader RA, Kao WJ. Concurrent in vitro release of silver sulfadiazine and bupivacaine from semi-interpenetrating networks for wound management. *J Burn Care Res.* 2009 Jan-Feb; 30(1):98-104

Antimicrobial activity of local anaesthetics used for dental analgesia

Pelz et al. (1) analyzed the antimicrobial activity of local anaesthetics used for dental analgesia. Seven local anaesthetics and their active anaesthetic components [Ultracaine D-S (articaine hydrochloride), Carbostesin (bupivacaine hydrochloride), Scandicaine (mepivacaine hydrochloride), Xylonest (prilocaine hydrochloride), Xylocaine (lidocaine hydrochloride), Hostacaine (butanilcaine phosphate) and Novocaine (procaine hydrochloride)] were tested for their antimicrobial activity against 311 bacterial strains from 52 different species and 14 *Candida albicans* strains. The tested pathogens were members of the oral flora, and partly members of the skin and intestinal flora. Additionally, the antimicrobial activity of methyl-4-hydroxybenzoate, sodium disulfite, adrenaline hydrogen tartrate and adrenaline (the preservative and vasoconstrictive components of the anaesthetics) was tested. For determination of MIC and minimal bactericidal concentration (MBC), the agar dilution method using Wilkins-Chalgren agar was applied. The trade preparation Ultracaine D-S showed the most prominent antimicrobial activity with regard to both MIC and MBC. Ultracaine D-S and its active substance, articaine hydrochloride, showed similar MIC values, suggesting that the antimicrobial activity is mainly caused by the anaesthetic component. Novocaine showed the lowest antimicrobial activity and did not inhibit 35 of the species tested. The MIC values of all local anaesthetics were between 0.25 and 16 mg ml⁻¹. The routinely applied concentration of Ultracaine D-S was roughly four times higher, and of Hostacaine was two times higher, than the MBC values for the tested bacteria, whereas for the other anaesthetics, the MBC values were not reached or exceeded with the concentrations used. The MIC range of the preservatives was 0.5-1.0 mg ml⁻¹ for methyl-4-hydroxybenzoate and 0.2-0.5 mg ml⁻¹ for sodium disulfite. The articaine MIC values were two to three serial dilution steps lower, and the butanilcaine MIC values one to two serial dilution steps lower, than the MIC of the preservatives. The mepivacaine mean MIC values were slightly lower for *Fusobacterium nucleatum*, *Prevotella intermedia*, *Porphyromonas gingivalis* and *Staphylococcus aureus*, but higher for *Streptococcus intermedius*, compared with the preservative methyl-4-hydroxybenzoate. The same result was found with *Streptococcus intermedius* and lidocaine. Screening of 20 MIC values of 4 pure anaesthetic substances and the corresponding preservative found 2/20 instances where the MICs of the preservatives against 5 representative species (67 strains) were lower, indicating that the antimicrobial effect was mainly due to the preservative, but 18/20 results where the pure anaesthetic component showed greater antimicrobial effects compared with the preservative. The in vitro results for Carbostesin, Scandicaine and especially for Novocaine indicate that a local disinfection should be done prior to injection of the anaesthetics. Due to the results obtained with nosocomial strains (*Escherichia coli*, *S. aureus* and *Pseudomonas*), disinfection of the mucous membranes should be performed routinely in immunocompromised patients, regardless of the anaesthetic used.

1. Pelz K, Wiedmann-Al-Ahmad M, Bogdan C, Otten JE. Analysis of the antimicrobial activity of local anaesthetics used for dental analgesia. *J Med Microbiol.* 2008 Jan; 57 (Pt 1): 88-94

Ropivacaine poor antimicrobial effect

Aydin et al. (1) investigated the antimicrobial effects of different concentrations of ropivacaine, bupivacaine, lidocaine and prilocaine on *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Candida albicans*. All local anaesthetic dilutions were exposed to microorganisms for 0, 30, 60, 120, 240 min at room temperature. The inoculums taken from diluted suspensions were reinoculated on blood agar and incubated for 18-24 h at 35 degrees C and then the colonies were counted. Ropivacaine did not inhibit any of the microorganisms tested. Bupivacaine reduced the viable cells of *P. aeruginosa* at 0.5% and 0.25% solutions. Lidocaine 5% and 2% and prilocaine 2.0% dilutions reduced the viable cells of all microorganisms tested. Prilocaine 1.0% reduced the viable cells of *E. coli*,

S. aureus and *P. aeruginosa*. Lidocaine 1% reduced only the viable cells of *P. aeruginosa* and prilocaine 0.5% reduced only *E. coli*. It was concluded that Ropivacaine had no antimicrobial effect on microorganisms tested. Bupivacaine showed poor antimicrobial effectiveness. Lidocaine and prilocaine had more powerful antimicrobial effects than the other two local anaesthetics.

1. Aydin ON, Eyigor M, Aydin N. Antimicrobial activity of ropivacaine and other local anaesthetics. *Eur J Anaesthesiol.* 2001 Oct.; 18(10): 687-94

Bactericidal activity of 0.5% bupivacaine with preservatives on microorganisms in the human skin flora

Sakuragi et al. (1) studied the bactericidal activity of 0.5% bupivacaine with 0.08% methyl para-oxybenzoate and 0.02% propyl para-aminobenzoate as preservatives and of the preservatives alone at 37 degrees C and at room temperature on two strains of methicillin-resistant *Staphylococcus aureus*, two strains of methicillin-susceptible *S. aureus*, and one strain each of *Staphylococcus epidermidis* and *Escherichia coli*. The pathogen was exposed to 0.5% bupivacaine with preservatives or to the preservatives alone for 1, 3, 6, 12, and 24 hours at 37 degrees C and at room temperature. The inocula from these suspensions were cultured for 48 hours at 37 degrees C after the antimicrobial activity of bupivacaine was inactivated by 1:1,000 dilution with physiological saline. The 1- through 12-hour exposures of four strains of *S. aureus* to 0.5% bupivacaine with preservatives at room temperature reduced the mean colony count by 24.2%, 49.2%, 71.3%, and 89.6%, respectively, and the exposure at 37 degrees C reduced the count by 74.1%, 95.2%, 99.9%, and 99.8%, respectively. The differences for 1- through 12-hour exposures were significant ($P < .001$). The percentage kill in the strains of *E. coli* and *S. epidermidis* was significantly higher than that in the strains of *S. aureus* at all exposure times at room temperature (*E. coli*, $P < .001$; *S. epidermidis*, $P < .0001$) and at 1- and 3-hour exposures at 37 degrees C (*E. coli*, $P < .001$; *S. epidermidis*, $P < .0001$). The bactericidal activity of the preservatives was markedly lower than that of 0.5% bupivacaine with preservatives ($P < .0001$). The bactericidal activity of 0.5% bupivacaine with preservatives is stronger at body temperature than at room temperature; the bactericidal activity may be due, to a large extent, to bupivacaine rather than to the preservatives; and *S. aureus* is more resistant to the bactericidal activity of bupivacaine than are *S. epidermidis* and *E. coli*.

1. Sakuragi T, Ishino H, Dan K. Bactericidal activity of 0.5% bupivacaine with preservatives on microorganisms in the human skin flora. *Reg Anesth* 1997 Mar-Apr; 22(2): 178-84

Bactericidal activity of clinically used local anesthetics on *Staphylococcus aureus*

The rate of onset of antimicrobial activity of local anesthetics is unknown. Similarly, whether the activity is bactericidal or bacteriostatic is also unknown. Sakuragi et al. (1) investigated the rate and potency of the antimicrobial activity of 0.125%, 0.25%, and 0.5% bupivacaine, 2.0% mepivacaine and 2.0% lidocaine with preservatives, and 2.0% lidocaine without preservatives on two strains of methicillin-resistant *Staphylococcus aureus*. The pathogen was exposed to each local anesthetic for 1, 3, 6, 12, and 24 hours at room temperature. The inocula from these suspensions were diluted to 1:1,000 with physiological saline to inactivate the antimicrobial activity of the local anesthetics and then were cultured for 24 hours at 37 degrees C on agar plates. Lower colony counts were observed with a 3-hour or longer exposure to 0.5% bupivacaine in both strains of *S. aureus* ($P < .05$). The 3-hour exposure reduced the count by approximately 60%, the 6-hour exposure by 70%, and the 24-hour exposure by more than 99%. The bactericidal activity was lowest with 0.125% bupivacaine and 2.0% mepivacaine. Antimicrobial activity was observed shortly after exposure of *S. aureus* to local anesthetics and appeared to be bactericidal rather than bacteriostatic. However, the observed bactericidal activity, although it developed rapidly, may be insufficient to account for the low incidence of epidural infection related to epidural cannulation.

1. Sakuragi T, Ishino H, Dan K. Bactericidal activity of clinically used local anesthetics on *Staphylococcus aureus*. *Reg Anesth* 1996 May-Jun; 21(3): 239-42

Preservatives bacteriostatic activity

In order to study the antibacterial activity of local anesthetics quantitatively, Noda et al. (1) procured their minimum inhibitory concentration (MIC), killing curves and postantibiotic effect (PAE), using the standard colony of *Staphylococcus aureus* ATCC 25923, *Staphylococcus epidermidis* ATCC 14990 and *Pseudomonas aeruginosa* NCTC 10490. Both bupivacaine and lidocaine had bactericidal activity at a clinical concentration. MIC of the former was lower than that of the latter, and it means that bupivacaine has a greater antibacterial activity than lidocaine. At the same concentration, the commercial solutions, such as Xylocaine and Marcain, which contain preservatives, showed a greater antibacterial activity than the pure anesthetic solutions which contain no preservatives. However, the preservatives had no bactericidal activity, but weak bacteriostatic activity.

1. Noda H, Saionji K, Miyazaki T. Antibacterial activity of local anesthetics. *Masui* 1990 Aug; 39(8):994-1001

Influence of local anesthetics on human leucocyte functions

Okuno et al. (1) examined the influence of local anesthetics (pure bupivacaine and lidocaine with no preservative) on human leukocyte functions. (a) The effect of bupivacaine on the phagocytosis of granulocyte was studied by bioassay. (b) The effect of lidocaine on the appearance of iC3b receptor (CR3) of granulocyte and monocyte (which is an important cell-adhesion-factor) was examined using flowcytometry. (c) The influence of lidocaine on phagocytosis of granulocyte and monocyte and on respiratory burst of granulocyte was examined using flowcytometry. (d) The influence of lidocaine on phagocytosis and that on respiratory burst were compared. These studies revealed that both phagocytosis and respiratory burst were inhibited by lidocaine, and the inhibition of respiratory burst was stronger than the inhibition of phagocytosis by local anesthetics' immunosuppressive effects. It was concluded that the balance of immunosuppressive action due to antimicrobial action and bactericidal ability of local anesthetics determined the occurrence of local bacterial infection.

1. Okuno S, Noda H, Kugimiya T, Saionji K. The influence of local anesthetics on human leukocyte functions studied by micro whole blood collection and flowcytometry. *Masui* 1996 Mar; 45(3):317-25

Antibacterial activity of epidural infusions

The incidence of epidural abscess following epidural catheterisation appears to be increasing, being recently reported as one in 1000 among surgical patients. Coghlan et al. (1) designed a study to investigate the antibacterial activity of various local anaesthetics and additives, used in epidural infusions, against a range of micro-organisms associated with epidural abscess. The aim was to determine which, if any, epidural infusion solution has the greatest antibacterial activity. Bupivacaine, ropivacaine and levobupivacaine crystals were dissolved and added to Mueller-Hinton Agar in concentrations of 0.06%, 0.125%, 0.2%, 0.25%, 0.5% and 1%. Fentanyl, adrenaline and clonidine were also mixed with agar in isolation and in combination with the local anaesthetics. Using a reference agar dilution method, the minimum inhibitory concentrations were determined for a range of bacteria. Bupivacaine showed antibacterial activity against *Staphylococcus aureus*, *Enterococcus faecalis* and *Escherichia coli* with minimum inhibitory concentrations between 0.125% and 0.25%. It did not inhibit the growth of *Pseudomonas aeruginosa* at any of the concentrations tested. Levobupivacaine and ropivacaine showed no activity against *Staphylococcus aureus*, *Enterococcus faecalis* and *Pseudomonas aeruginosa*, even at the highest concentrations tested, and minimal activity against *Escherichia coli* (minimum inhibitory concentrations 0.5% and 1% respectively). The presence of fentanyl, adrenaline and clonidine had no additional effect on the antibacterial activity of any of the local anaesthetic agents. The low concentrations of local anaesthetic usually used in epidural infusions have minimal antibacterial activity. While the clinical implications of this in vitro study are not known, consideration should be given to increasing the concentration of bupivacaine in an epidural infusion or to administering a daily bolus of 0.25% bupivacaine to reduce the risk of epidural bacterial growth.

1. Coghlan MW, Davies MJ, Hoyt C, Joyce L, Kilner R, Waters MJ. *Anaesth Intensive Care* 2009 Jan, 37(1): 66-9

Antibacterial activity of levobupivacaine vs. bupivacaine

Hodson et al. (1) compared the antibacterial activity of bupivacaine with levobupivacaine against a range of bacteria implicated in epidural infection to determine whether any differences existed between the two drugs. Concentrations of 0.125%, 0.25% and 0.5% bupivacaine and levobupivacaine were inoculated with suspensions of either *Staphylococcus epidermidis*, *Staphylococcus aureus* or *Enterococcus faecalis*. After incubation, the mixtures were plated onto blood agar and colony counts were recorded after a further period of incubation. The minimum bactericidal concentration of local anaesthetic against the three bacteria studied was found to be 0.25% for bupivacaine and 0.5% for levobupivacaine showing racemic bupivacaine to have a more potent antibacterial action than levobupivacaine. This finding suggests that the dextrobupivacaine isomer of racemic bupivacaine has a more potent antibacterial action than the levobupivacaine isomer.

1. Hodson M, Gajraj R, Scott NB. A comparison of the antibacterial activity of levobupivacaine vs. bupivacaine: an in vitro study with bacteria implicated in epidural infection. *Anaesthesia* 1999 Jul; 54(7):699-702

Sufentanil modifies the antibacterial activity of bupivacaine and ropivacaine

Tamanai-Shacoori et al. (1) investigated the effect on the growth of *Escherichia coli* (*E. coli*), *Staphylococcus aureus* (*S. aureus*), and *Enterococcus faecalis* (*E. faecalis*) of bupivacaine at a final concentration of 0.77 mg.mL(-1), ropivacaine at 1.2 mg.mL(-1), and sufentanil at 0.38 and 0.5 microg.mL(-1) (alone or in combination with bupivacaine and ropivacaine). The strains were diluted to approximately 3×10^4 cfu.mL(-1) in Mueller-Hinton broth. The anesthetics (0.5 mL) were incubated with the bacterial suspensions (0.5 mL) for 24 hr at 37 degrees C. Bupivacaine inhibited the growth of *E. coli* (59 +/- 0.8%; $P < 0.05$) and *S. aureus* (22 +/- 3.6%; $P < 0.05$). Ropivacaine also inhibited the growth of *E. coli* (41 +/- 1.2%; $P < 0.05$) and *S. aureus* (25.5 +/- 4.1%; $P < 0.05$). Both anesthetics were ineffective against *E. faecalis*. Sufentanil only inhibited *S. aureus* (13.8 +/- 3.1%; $P < 0.05$) at a concentration of 0.5 microg.mL(-1). Sufentanil modified the antibacterial activity of bupivacaine and ropivacaine. It increased the inhibitory effect of bupivacaine on *E. faecalis* and *S. aureus* by 10 +/- 2.1% ($P < 0.05$) and on *E. coli* by 7% ($P < 0.05$). Sufentanil did not increase the inhibitory effect of ropivacaine on the growth of *S. aureus*. On the other hand, sufentanil reduced the inhibitory effect of ropivacaine on *E. coli* by 11% ($P < 0.05$). Both bupivacaine and ropivacaine alone or combined with sufentanil inhibited the growth of *E. coli* and *S. aureus*. *E. faecalis* was partially sensitive to a bupivacaine + sufentanil mixture. Sufentanil had a partial synergistic effect on bupivacaine and a partial antagonistic effect on ropivacaine's antibacterial activity.

1. Tamanai-Shacoori Z, Shacoori V, Vo Van JM, Robert JC, Bonnaure-Mallet M. Sufentanil modifies the antibacterial activity of bupivacaine and ropivacaine. *Can J Anaesth.* 2004 Nov; 51(9):911-4.

Ropivacaine 0.1% with sufentanil 1 microg/mL inhibits in vitro growth of *Pseudomonas aeruginosa* and does not promote multiplication of *Staphylococcus aureus*

Kampe et al. (1) investigated the effect of ropivacaine combined with sufentanil, a mixture frequently used for postoperative epidural analgesia, on the growth of *Staphylococcus aureus* and *Pseudomonas aeruginosa* at room temperature. Aliquots of suspension of *S. aureus* and *P. aeruginosa* in saline were transferred into test tubes containing either a mixture of ropivacaine 0.1% and sufentanil 1 microg/mL (R+S) or saline (SA), with the latter serving as control. At 0, 3, 6, 24, and 48 h after inoculation, 1 mL

of each solution was spread over standard blood agar. The plates were incubated at 22 degrees C for 48 h, and the numbers of colony-forming units (cfu) were counted. The growth ratio for both bacterial strains was calculated as $\text{cfu time } (t(n))/\text{cfu baseline } (t(0))$. The primary efficacy variable was the area under the curve (AUC) in $(\text{cfu } t(n)/\text{cfu } t(0)) \times \text{time}$, based on the growth ratios. The AUC for *P. aeruginosa* was significantly less in R+S than in SA ($P = 0.028$). Multiplication of *P. aeruginosa* (growth ratio >1) was observed for at least 6 h after inoculation in SA. Growth of *P. aeruginosa* was significantly less in R+S than in SA at 3 h ($P = 0.043$) and 24 h ($P = 0.012$) after inoculation. The AUC for *S. aureus* did not differ significantly between R+S and SA ($P = 0.74$). Neither R+S nor SA promoted multiplication of *S. aureus*. Forty-eight hours after inoculation, growth of *S. aureus* was significantly less in R+S than in SA ($P < 0.0001$). It was concluded that R+S inhibited growth of *P. aeruginosa* and did not promote multiplication of *S. aureus* when compared with SA. This laboratory study demonstrated that compared with saline, ropivacaine 0.1% with 1 microg/mL of sufentanil inhibited growth of *Pseudomonas aeruginosa* and did not promote multiplication of *Staphylococcus aureus* at room temperature. With respect to bacterial infection with these two strains, the mixture seems to be safe for continuous epidural administration if prepared under aseptic conditions and after alcohol hand rub.

1. Kampe S, Poetter C, Buzello S, Wenchel HM, Paul M, Kiencke P, Kasper SM. Ropivacaine 0.1% with sufentanil 1 microg/mL inhibits in vitro growth of *Pseudomonas aeruginosa* and does not promote multiplication of *Staphylococcus aureus*. *Anesth Analg*. 2003 Aug;97(2):409-11

Levobupivacaine hydrochloride and sufentanil have no antimicrobial effect at 25 degrees C in vitro

Levobupivacaine in combination with sufentanil may be used for labour or postoperative regional analgesia. Guillier et al. (1) investigated the in vitro antimicrobial effect of levobupivacaine and sufentanil against common micro-organisms encountered during regional anaesthesia. Standardized suspensions of *Staphylococcus aureus*, *Staphylococcus epidermidis* and *Escherichia coli* were incubated for 1, 3, 6 and 24 h at 25 degrees C, with saline (as control), sufentanil 0.5 or 0.75 microg mL⁻¹, levobupivacaine hydrochloride 5.6 mg mL⁻¹ and concentrations of 1.4, 2.8 and 5 mg mL⁻¹ of levobupivacaine hydrochloride with sufentanil 0.5 microg mL⁻¹. Colony counts were compared after 24 h incubation at 37 degrees C. No bacterial growth was observed on any bacterial strain for any solution tested throughout the experiment. These results suggest that solutions of levobupivacaine combined with sufentanil may be used for 24 h at room temperature during regional anaesthesia with no risk of bacterial growth.

1. Guillier M, Boselli E, Bouvet L, Freney J, Renaud FN, Chassard D, Allaouchiche B. Levobupivacaine hydrochloride and sufentanil have no antimicrobial effect at 25 degrees C in vitro. *Eur J Anaesthesiol*. 2007 Jul;24(7):634-9

Synergy between *Staphylococcus aureus* and *Pseudomonas aeruginosa* in a rat model of complex orthopaedic wounds

Hendricks et al. (1) observed an interaction in animals inoculated concomitantly with *Staphylococcus aureus* and *Pseudomonas aeruginosa* during a study of the efficacy of surfactants for disinfection of orthopaedic wounds. This led them to investigate whether synergy could be demonstrated between *Staphylococcus aureus* and *Pseudomonas aeruginosa* in a rat model of complex orthopaedic wounds. A wire was implanted into the spinous process of a lumbar vertebra of Sprague-Dawley rats through a dorsal incision. Animals were divided into two groups: group one was inoculated with either *Staphylococcus aureus* or *Pseudomonas aeruginosa*, and group two received a polymicrobial inoculation with both test organisms in varying concentrations. After inoculation, the wounds were irrigated and closed. On postoperative day 14, all animals were killed and specimens from the wounds were cultured.

The number of colony-forming units (CFU) of *Staphylococcus aureus* or *Pseudomonas aeruginosa* needed to cause infection in 50% of the animals (ID₅₀) was determined with use of the Reed-Muench method. The infection rate associated with each inoculum combination was calculated, and the two groups were compared. The ID₅₀ was 2.8×10^4 CFU for *Staphylococcus aureus* and 4.8×10^5 CFU for *Pseudomonas aeruginosa*. The combination of 10^3 CFU of *Staphylococcus aureus* with low concentrations (10^2 , 10^3 , or 10^4 CFU) of *Pseudomonas aeruginosa* yielded infection rates that were higher than those found with either organism alone at the same concentrations. The combination of 10^3 CFU of *Staphylococcus aureus* and 10^3 CFU of *Pseudomonas aeruginosa* yielded a 75% infection rate, which was significantly higher ($p = 0.004$) than that associated with 10^3 CFU of either organism alone. As the *Pseudomonas aeruginosa* concentration was increased (to 10^5 , 10^6 , and 10^7 CFU), this trend reversed, and the infection rate decreased to 33% ($p = 0.004$). Low concentrations of *Pseudomonas aeruginosa* (0 to 10^5 CFU) combined with 10^6 CFU of *Staphylococcus aureus* yielded infection rates ranging from 83% to 100%. At the higher concentrations of *Pseudomonas aeruginosa* (10^6 and 10^7 CFU), however, the infection rate again decreased, to 33% ($p = 0.005$). Only *Staphylococcus aureus* was isolated from the cultures of the specimens from the animals that had received a polymicrobial inoculum. Synergy between *Staphylococcus aureus* and *Pseudomonas aeruginosa* was demonstrated when low levels of each organism were present in the wound. As the *Pseudomonas aeruginosa* concentration was increased, the infection rates fell well below what would be anticipated, suggesting that low concentrations of *Pseudomonas aeruginosa* enhance the ability of *Staphylococcus aureus* to cause infection in this orthopaedic wound model. At the same time, the presence of *Staphylococcus aureus* in the ratios tested decreased the rate of infection by *Pseudomonas aeruginosa*. *Staphylococcus aureus* is a pathogen commonly seen in orthopaedic patients. The pathogenicity of *Staphylococcus aureus* was shown to be increased in the presence of anaerobic bacteria. This study demonstrated synergy between *Staphylococcus aureus* and *Pseudomonas aeruginosa*, at low concentrations, in a wound model while at the same time showing that *Staphylococcus aureus* lowers the rate of *Pseudomonas aeruginosa* infection.

1. Hendricks KJ, Burd TA, Anglen JO, Simpson AW, Christensen GD, Gainor BJ. Synergy between *Staphylococcus aureus* and *Pseudomonas aeruginosa* in a rat model of complex orthopaedic wounds. *J Bone Joint Surg Am.* 2001 Jun; 83-A(6):855-61

Sequential irrigation with common detergents: a promising new method for decontaminating orthopedic wounds

This investigation (1) sought to determine the capacity of irrigation solutions in decontaminating orthopedic wounds challenged with a polymicrobial inoculum. Rats were divided into two groups, a control group and a treatment group. After creation of a dorsolumbar incision and placement of a wire through the spinous process, rats were inoculated with *Staphylococcus aureus* and *Pseudomonas aeruginosa*. Wounds were irrigated with control or treated solutions. At 2 weeks, cultures were obtained. There were statistically significant differences between groups regarding total number of culture positive sites ($P < 0.001$), culture-positive animals ($P = 0.02$), and quantitative cultures ($P < 0.02$). Sequential irrigation with surfactants lowers bacteria counts recovered from polymicrobial wounds.

1. Burd T, Christensen GD, Anglen JO, Gainor BJ, Conroy BP, Simpson WA. Sequential irrigation with common detergents: a promising new method for decontaminating orthopedic wounds. *Am J Orthop.* 1999 Mar; 28(3): 156-60

The use of detergent irrigation for musculoskeletal wounds

The primary purpose of irrigation is to remove bacterial contaminants from the wound. Surfactants do that by disrupting the bonds of the organism to the surface. The use of this wound care strategy was studied in a series of investigations spanning several years. In vitro experiments revealed that surfactant irrigation was superior to saline or antibiotic solutions for removal of adherent bacteria from metallic surfaces, from bone, and from bovine muscle. An in vivo model of the complex orthopedic wound was developed. The superiority of surfactant irrigation over saline or antibiotic solution was demonstrated in animal wounds containing metal, bone injury, and soft tissue damage. Specificity of different surfactant irrigations for various bacterial species was demonstrated. A sequential surfactant irrigation protocol was developed and shown effective in the polymicrobial wound with established infection (1).

1. Anglen JO, Gainor BJ, Simpson WA, Christensen G. The use of detergent irrigation for musculoskeletal wounds. *Int Orthop*. 2003;27(1):40-6

Topical antibiotic irrigation in the prophylaxis of operative wound infections in orthopedic surgery

Although the orthopedic literature on the clinical use of topical antibiotics is sparse, the effectiveness of topical antibiotics has been shown well enough in vitro and in the surgical literature to justify strong consideration of their use in orthopedic procedures.. Saline irrigation should not be relied upon to reduce bacterial contamination completely, although it does remove debris, foreign material, and clot, which often contain bacteria, from the surgical wound. Topical antibiotic agents used for irrigation should have a broad spectrum of antimicrobial activity. Triple antibiotic solution (neomycin, polymyxin, and bacitracin) provides the most complete coverage against the organisms most likely to cause infections in both clean and contaminated orthopedic surgical cases. These agents should be allowed to remain in the wound for at least 1 minute before their removal. Further studies of topical antibiotic irrigation in orthopedic surgery are needed to demonstrate the most effective antibiotic(s) and technique of administration.. There is evidence to suggest that the more often an irrigant is used, the more effective it is in preventing infection. The use of bacitracin as an irrigant should probably be avoided in patients previously exposed to that agent. Antibiotic-containing solutions should be utilized with pulsatile lavage systems. Saline alone may drive previously administered antibiotics from bone, leaving insufficient local antibiotic levels (1).

1. Dirschl DR, Wilson FC. Topical antibiotic irrigation in the prophylaxis of operative wound infections in orthopedic surgery. *Orthop Clin North Am*. 1991 Jul;22(3):419-26.

Topical irrigation with polymyxin and bacitracin for spinal surgery

Savitz et al. (1) evaluated constant irrigation with saline containing 50,000 units each of polymyxin and bacitracin in a regimen of antimicrobial prophylaxis for clean spinal surgery at two community hospitals with a zero infection rate. The focus was on the bactericidal effects of prophylactic topical antibiotics by assessing random contamination in neurosurgical wounds from: 1) the flora of the integument and nares of the operating team, 2) the surgical apparel, 3) the patient's skin, 4) air-borne organisms in the operating theater, and 5) the surgeon's gloves. Based on individual biotyping of bacteria and antimicrobial sensitivity testing, no consistent source or pattern could be uncovered for the organisms recovered from the operative site. Relying on longitudinal data, the incidence of intraoperative bacterial growth with continuous saline lavage was reduced from 64 to 4% when the combination of topical polymyxin and bacitracin was added. Although the virtual elimination of bacterial growth in the surgical

site was accomplished, the efficacy of topical antibiotics in the prevention of wound infection remains unproven.

1. Savitz SI, Savitz MH, Goldstein HB, Mouracade CT, Malangone S. Topical irrigation with polymyxin and bacitracin for spinal surgery. *Surg Neurol.* 1998 Sep; 50(3):208-12

When should old therapies be abandoned? A modern look at old studies on topical ampicillin

Charalambous et al. (1) sought to determine whether topical ampicillin can reduce the rate of wound infections in clean contaminated surgical wounds (appendectomy, colorectal surgery). All randomized controlled trials examining the use of topical ampicillin in appendectomy and colorectal surgery published in English were identified via a Medline, Advanced Medline, and Cochrane Controlled Trials Register search and a meta-analysis performed. Results. Topical ampicillin vs. no antibiotic prophylaxis in clean contaminated wounds significantly reduced surgical wound infection rates (Odds Ratio (OR)=0.084, 95% CI, 0.04-0.16, P<0.0001). Topical ampicillin vs. no antibiotic prophylaxis in contaminated wounds also reduced surgical wound infection (OR=0.262, 95% CI, 0.14-0.51, P<0.0001). Topical ampicillin combined with systemic antibiotics vs. systemic antibiotics alone did not reduce surgical wound infection rate (OR=0.927, 95% CI, 0.27-1.72, P=0.90). Topical ampicillin significantly reduces the rate of surgical wound infections in clean contaminated surgery. A significant but smaller effect is seen in appendectomies where the appendix is gangrenous or perforated. Topical ampicillin did not confer any additional benefit when systemic antibiotics are used. While ampicillin may no longer be an effective agent, topical application of antibiotics is effective. A meta-analysis of studies using topical ampicillin for the prevention of infection in clean contaminated wound suggests that topical ampicillin is effective, but no incremental benefit is seen with systemic antibiotics.

1. Charalambous CP, Tryfonidis M, Swindell R, Lipsett AP. When should old therapies be abandoned? A modern look at old studies on topical ampicillin. *J Infect.* 2003 Oct; 47(3):203-9

Significant reduction in stereotactic and functional neurosurgical hardware infection after local neomycin/polymyxin application

Hardware infection is a common occurrence after the implantation of neurostimulation and intrathecal drug delivery devices. Miller et al. (1) investigated whether the application of a neomycin/polymyxin solution directly into the surgical wound decreases the incidence of perioperative infection. Data from all stereotactic and functional hardware procedures performed at the Oregon Health & Science University over a 5-year period were reviewed. All patients received systemic antibiotic prophylaxis. For the last 18 months of the 5-year period, wounds were additionally injected with a solution consisting of 40 mg neomycin and 200,000 U polymyxin B sulfate diluted in 10 ml normal saline. The primary outcome measure was infection of the hardware requiring explantation. Six hundred fourteen patients underwent hardware implantation. Among 455 patients receiving only intravenous antibiotics, the infection rate was 5.7%. Only 2 (1.2%) of 159 patients receiving both intravenous and local antibiotics had an infection. The wounds in both of these patients were compromised postoperatively: 1 patient had entered a swimming pool, and the other had undergone a general surgery procedure that exposed the hardware. If these patients are excluded from analysis, the effective infection rate using a combined intravenous and local antibiotic prophylaxis is 0%. There were no complications due to toxicity. The combination of local neomycin/polymyxin with systemic antibiotic therapy can lead to a significantly lower rate of postoperative infection than when systemic antibiotics are used alone.

1. Miller JP, Acar F, Burchiel KJ. Significant reduction in stereotactic and functional neurosurgical hardware infection after local neomycin/polymyxin application. *J Neurosurg.* 2009 Feb; 110(2):247-50

Antimicrobial activity of bupivacaine and morphine

Antimicrobial activity of bupivacaine and morphine against 10 microbial strains was studied with an agar dilution method (1). The strains tested were Escherichia coli (ATCC 25922), Pseudomonas aeruginosa (ATCC 27853), Staphylococcus aureus (ATCC 25923), and one of each of the clinical isolates of Staphylococcus epidermidis (a multiresistant strain), Staphylococcus epidermidis (a sensitive strain), Streptococcus pneumoniae, Streptococcus pyogenes (A), Streptococcus faecalis, Bacillus cereus, and Candida albicans. The antimicrobial effect of bupivacaine was tested at concentrations of 0.5, 1.25, 2.5, and 5 mg/ml (0.05%, 0.125%, 0.25%, and 0.5%). Bupivacaine at a concentration of 2.5 mg/ml inhibited the growth of the sensitive S. epidermidis strain, S. pyogenes, and S. pneumoniae, and all of the others except P. aeruginosa at a concentration of 5 mg/ml. Morphine 0.2 and 2 mg/ml (0.02 and 0.2%) did not inhibit any of the strains.

1. Rosenberg PH, Renkonen OV. Antimicrobial activity of bupivacaine and morphine. Anesthesiology. 1985 Feb;62(2):178-9

Antimicrobial activity of bupivacaine and pethidine

The antimicrobial activity of bupivacaine and pethidine in concentrations commonly used in epidural practice was studied by an agar dilution method against ten common micro-organisms (1). Both drugs showed increasing microbe inhibition with increasing drug concentrations. Bupivacaine at common epidural concentrations inhibited eight of the ten organisms and pethidine inhibited six. These findings confirm previous reports of microbe inhibition by bupivacaine, and in addition demonstrate a similar but slightly lesser activity by pethidine. Antimicrobial activity of epidural drugs can be regarded as a desirable property with clinical implications.

1. Grimmond TR, Brownridge P. Antimicrobial activity of bupivacaine and pethidine. Anaesth Intensive Care. 1986 Nov;14(4):418-20

Use of prehospital dressings in soft tissue trauma: is there any conformity or plan?

Acute soft tissue wounds are commonly seen in the prehospital setting. In January 2007 a questionnaire-based study was undertaken to evaluate the early management of such injuries. All 13 UK ambulance services were contacted, as well as 2 voluntary ambulance services. The questionnaire considered the implementation of a wound treatment policy and staff training, immediate wound management including haemostasis, cleansing, analgesia, dressings and the use of antibiotics. The response rate was 100%. Only 27% of services had a wound treatment policy in place, but all services implemented staff training. All services regularly achieved haemostasis of wounds using a combination of pressure and elevation. Regular cleansing was performed by 47% of services and those that did so used normal saline or water. All ambulance services administered analgesics. The most commonly used analgesics were Entonox and intravenous morphine. Other analgesics administered were paracetamol and ibuprofen. No local anaesthesia was used. Dressings were applied regularly by all services; 13 different types of dressings were in regular use. This study confirmed that there is currently no national standard protocol for early acute wound management in the prehospital care setting. The key areas for improvement are cleansing, simplification of dressings and the introduction of standardised protocols and teaching.

1. Jones AP, Allison K, Wright H, Porter K. Use of prehospital dressings in soft tissue trauma: is there any conformity or plan? Emerg Med J. 2009 Jul;26(7):532-4.

Bupivacaine and Kaltostat reduces post-operative donor site pain

A prospective double blind controlled trial was carried out to examine the differences in post-operative split skin graft donor site pain between sites dressed with three differently treated types of dressing; a dry calcium alginate dressing (Kaltostat Britcair), a saline moistened Kaltostat dressing and a bupivacaine hydrochloride (0.5%) moistened Kaltostat dressing. There was a significant reduction in post-operative pain in the Kaltostat and bupivacaine group (group 3) at 24 and 48 h when compared to the other two groups ($p < 0.04$). There was no difference in ease of removal of dressings or the quality of wound healing on day 10 between the three groups. This study demonstrates a significant reduction in post-operative pain in bupivacaine soaked Kaltostat without reducing the beneficial effects of Kaltostat on donor site healing (1).

1. Butler PE, Eadie PA, Lawlor D, Edwards G, McHugh M. Bupivacaine and Kaltostat reduces post-operative donor site pain. *Br J Plast Surg.* 1993 Sep;46(6):523-4

Infection risk from the use of continuous local-anesthetic infusion pain pumps in aesthetic and reconstructive abdominal procedures

A retrospective chart review evaluated 159 patients who underwent abdominoplasty (with or without suction-assisted lipectomy), panniculectomy, or a transverse rectus abdominis myocutaneous (TRAM) flap for breast reconstruction. Information was collected on descriptive and demographic information, and the incidence of postoperative infection. Of the 159 patients who underwent abdominal procedures, 100 (62.9%) received the pain pump for postoperative pain control. None of those 100 patients developed an infection. Fifty-nine patients did not receive a pain pump, and 2 of those patients (3.3%) developed an infection. Overall, 1.3% (2 of 159) of patients in this study developed a postoperative infection. There is no increase in the risk of postoperative infection with the use of continuous local-anesthetic infusion pain pumps used after aesthetic and reconstructive abdominal procedures (1).

1. Hovsepian RV, Smith MM, Markarian MK, Sahba K, Paul MD, Evans GR, Wirth GA. Infection risk from the use of continuous local-anesthetic infusion pain pumps in aesthetic and reconstructive abdominal procedures. *Ann Plast Surg.* 2009 Mar;62(3):237-9

Continuous-infusion local anesthetic pain pump use and seroma formation with abdominal procedures: is there a correlation?

Seroma formation is the most commonly occurring complication in plastic surgery abdominal procedures. Continuous local anesthetic pain pump delivery systems are often used to decrease postoperative pain. An unreported concern with use of these devices in abdominal procedures is the effect of continuous fluid infiltration of the surgical site and a possible increase in the incidence of seroma formation. Smith et al. (1) performed a retrospective chart review to evaluate all patients ($n = 159$) who underwent abdominal procedures (abdominoplasty, panniculectomy, and transverse rectus abdominis myocutaneous flap harvest) over a 3-year period. Patient charts were evaluated for sex, age, body mass index, procedure performed, surgeon, operation length, pain pump use, postoperative seroma formation, and any complications. In cases with pain pump use, catheter placement location, anesthetic medication and strength, continuous-infusion rate, and duration of pain pump use were also reviewed. If a postoperative seroma formation was identified, treatment and outcomes were also recorded. The overall seroma formation rate was 11.3 percent (18 of 159 patients). Other complications occurred at a rate of 2.5 percent (four of 159). The incidence of seroma was 11.0 percent (11 of 100) in patients with pain pump use versus 11.9 percent (7 of 59) in those who did not use a pain pump. There

was no statistically significant difference ($p = 0.9$) in the incidence of seroma formation between those who did and did not use a pain pump device.

1. Smith MM, Hovsepian RV, Markarian MK, Degelia AL, Paul MD, Evans GR, Wirth GA. Continuous-infusion local anesthetic pain pump use and seroma formation with abdominal procedures: is there a correlation? *Plast Reconstr Surg.* 2008 Nov; 122(5): 1425-30

Continuous infusion pump system for postoperative pain control at muscle-sparing transverse rectus abdominis musculocutaneous (TRAM) flap donor sites

Heller et al. (1) assessed the efficacy of a continuous infusion pump system for postoperative pain control at muscle-sparing transverse rectus abdominis musculocutaneous (TRAM) flap donor sites. In this prospective, randomized, double-blind trial, a dual-catheter continuous infusion pump system was placed in the muscle-sparing TRAM flap donor-site area in all patients. Bupivacaine (0.375%; continuous infusion pump group) or isotonic saline (control group) was infused at 4 ml/hour. All patients also had a patient-controlled anesthesia system delivering intravenous narcotics on demand. Pain scores, patient satisfaction, narcotic use, milestones of surgical recovery, and side effects of narcotics were compared between the two groups. Forty-eight patients were included in the study (23 continuous infusion pump patients and 25 control patients). The continuous infusion patients used less mean patient-controlled anesthesia narcotic during the first 2 postoperative days (78.0 mg versus 42.7 mg; $p = 0.019$) and transitioned earlier to oral narcotics than did control patients. Patients' overall pain satisfaction scores were significantly better in the continuous infusion group than in the control group. There were no significant differences between groups with regard to overall abdominal pain intensity scores, total narcotic use, length of hospitalization, incidence of narcotic side effects, or milestones of surgical recovery. The continuous infusion pump system appears to be a safe and effective method for postoperative donor-site pain management in TRAM flap breast reconstruction patients and should be considered for postoperative donor-site pain management. However, continuous infusion pump local anesthetic delivery to the muscle-sparing TRAM flap donor site did not eliminate narcotic use for pain control.

1. Heller L, Kowalski AM, Wei C, Butler CE. Prospective, randomized, double-blind trial of local anesthetic infusion and intravenous narcotic patient-controlled anesthesia pump for pain management after free TRAM flap breast reconstruction. *Plast Reconstr Surg.* 2008 Oct; 122(4): 1010-8

Efficacy of the pain pump catheter in immediate autologous breast reconstruction

Baroody et al. (1) evaluated the efficacy of a slow bupivacaine infusion at postoperative surgical sites in immediate breast reconstruction patients. This prospective study included 16 patients who underwent autologous breast reconstruction with a latissimus dorsi pedicled flap immediately after mastectomy. A two-site infusion kit with dual split-flow catheters was secured at the operative sites before skin closure. A spring-loaded disposable pump then infused 0.25% bupivacaine at a rate of 2.08 cc per catheter per hour for 48 continuous hours. Patient pain levels, nausea/emesis, and oral and intravenous narcotic use were then recorded at 12-hour intervals. Medication use was converted to pain units for results comparison (one pain unit was defined as the equivalent of 10 mg of intravenous morphine). A retrospective control group comprised 16 consecutive patients from December of 1999 to October of 2002 who underwent the same surgery by the same surgeon using oral and intravenous pain medications. The experimental group demonstrated a more than fivefold decrease in the use of oral and intravenous pain medications compared with the historical controls (6.7 versus 1.7 pain units) ($p < 0.001$). The overall pain experienced by the catheter patients was nearly twofold less than the pain experienced by those without the catheter (1.8 versus 3.4 on the visual analog pain scale) ($p < 0.017$). Twenty-eight percent of the experimental group experienced nausea/emesis compared with 61 percent

in the control group. No complications occurred with the use of the pain pump catheter. A 48-hour infusion of 0.25% bupivacaine significantly decreases the need for postoperative narcotics and the over-all pain experience in immediate breast reconstruction patients. This effective form of pain control may alleviate patient concerns of postoperative pain and may safely downstage many plastic surgery procedures, such as immediate breast reconstruction, and many cosmetic procedures to same-day status when the primary indication for admission is pain management.

1. Baroody M, Tameo MN, Dabb RW. Efficacy of the pain pump catheter in immediate autologous breast reconstruction. *Plast Reconstr Surg.* 2004 Sep 15; 114(4):895-8

Better prophylaxis against surgical site infection with local as well as systemic antibiotics

Prophylactic systemic antibiotics significantly lower the risk of postoperative infection, and injection of antibiotics directly into the wound cavity has been found to be even more effective. Cavanaugh et al. (1) investigated the efficacy of direct injection of antibiotics into a wound cavity after wound closure, both alone and in combination with systemic administration of antibiotics. They hypothesized that a combination of preoperative systemic administration and postoperative local injection would be the most effective treatment. Rats were divided into six treatment groups: no treatment, local gentamicin, systemic cefazolin, local cefazolin, systemic cefazolin plus local gentamicin, and systemic cefazolin plus local cefazolin. A wound cavity was opened along the femur, an implant was placed, and the wound was inoculated with 2.5×10^8 colony forming units of *Staphylococcus aureus*. Systemic antibiotics were injected subcutaneously thirty minutes before the initial incision. Local antibiotics were injected percutaneously into the wound cavity after closure. The rats were killed at forty-eight hours postoperatively, and quantitative cultures were performed. All groups that received antibiotics showed significantly lower bacterial counts than the no-treatment control group ($p < 0.0003$). Local gentamicin treatment decreased the number of colony-forming-unit isolates by approximately two orders of magnitude as compared with the number in the group treated with systemic cefazolin ($p = 0.00005$) and five orders of magnitude as compared with the number in the control group ($p = 0.00003$). The combination of systemic cefazolin and local gentamicin decreased the bacterial count by approximately seven orders of magnitude as compared with the count in the no-treatment control group and significantly decreased the count as compared with that in the group treated with local gentamicin alone ($p = 0.00006$). The combination of systemic cefazolin and local gentamicin proved to be the most effective regimen. Local injection of gentamicin proved more effective than systemic administration of cefazolin but was not as effective as the combination of both antibiotics. The initially high concentrations of locally applied antibiotic and the utilization of two different classes of antibiotics may have contributed to the observed efficacy.

1. Cavanaugh DL, Berry J, Yarboro SR, Dahners LE. Better prophylaxis against surgical site infection with local as well as systemic antibiotics. An in vivo study. *J Bone Joint Surg Am.* 2009 Aug; 91(8):1907-12

Risk factors for postoperative spinal wound infections after spinal decompression and fusion surgeries

Veeravagu et al. (1) made a multivariate analysis of a prospectively collected database to determine preoperative, intraoperative, and patient characteristics that contribute to an increased risk of postoperative wound infection in patients undergoing spinal surgery. Current literature sites a postoperative infection rate of approximately 4%; however, few have completed multivariate analysis

to determine factors which contribute to risk of infection. This study identified patients who underwent a spinal decompression and fusion between 1997 and 2006 from the Veterans Affairs' National Surgical Quality Improvement Program database. Multivariate logistic regression analysis was used to determine the effect of various preoperative variables on postoperative infection. Data on 24,774 patients were analyzed. Wound infection was present in 752 (3.04%) patients, 287 (1.16%) deep, and 468 (1.89%) superficial. Postoperative infection was associated with longer hospital stay (7.12 vs. 4.20 days), higher 30-day mortality (1.06% vs. 0.5%), higher complication rates (1.24% vs. 0.05%), and higher return to the operating room rates (37% vs. 2.45%). Multivariate logistic regression identified insulin dependent diabetes (odds ratios [OR] = 1.50), current smoking (OR = 1.19) ASA class of 3 (OR = 1.45) or 4 to 5 (OR = 1.66), weight loss (OR = 2.14), dependent functional status (1.36) preoperative HCT <36 (1.37), disseminated cancer (1.83), fusion (OR = 1.24) and an operative duration of 3 to 6 hours (OR = 1.33) or >6 hours (OR = 1.40) as statistically significant predictors of postoperative infection. Using multivariate analysis of a large prospectively collected data from the National Surgical Quality Improvement Program database identified the most important risk factors for increased postoperative spinal wound infection. It demonstrated the high mortality, morbidity, and hospitalization costs associated with postoperative spinal wound infections. The information provided should help alert clinicians to presence of these risks factors and the likelihood of higher postoperative infections and morbidity in spinal surgery patients.

1. Veeravagu A, Patil CG, Lad SP, Boakye M. Risk factors for postoperative spinal wound infections after spinal decompression and fusion surgeries. *Spine (Phila Pa 1976)*. 2009 Aug 1; 34(17): 1869-72

Comparison of surgical wound infection after preoperative skin preparation with 4% chlohexidine and povidone iodine

Antiseptic scrub and paint can reduce bacterial colonization and postoperative wound infection. Two forms of antiseptics, povidone iodine and chlorhexidine, are commonly used in the operating theater. Paocharoen et al. (1) studied the efficacy of the reduction of bacterial colonization and surgical wound infection among these antiseptic. Five hundred surgical patients were randomly divided into two groups. Povidone Iodine and Chlorhexidine were used for skin preparation in group 1 and 2 respectively. Bacterial colonization and postoperative wound infection were examined after skin preparation. Demographic data was analyzed by student's t test; the culture result and surgical wound infection were analyzed by Mantel-Haenszel method for relative risk and 95% CI. There was a significant reduction of bacterial colonization and wound infection after skin preparation in group 2 compared with group 1. Colonization of bacterial and postoperative surgical wound infection were significantly reduced in the chlorhexidine group. Chlorhexidine antiseptic should be the first consideration for preoperative skin preparation.

1. Paocharoen V, Mingmalairak C, Apisarnthanarak A. Comparison of surgical wound infection after preoperative skin preparation with 4% chlohexidine and povidone iodine: a prospective randomized trial. *J Med Assoc Thai*. 2009 Jul; 92(7): 898-902

Effect of local anesthetics on the postoperative inflammatory response

Current knowledge suggests that peripheral inflammation following surgery activates and sensitizes both peripheral and central nervous system. These phenomena involved in the maintenance of the inflammatory response lead to hypersensibility, hyperalgesia and allodynia. Hyperalgesia participates in the general experience of postoperative pain and ALo in the development of chronic pain. A correlation between the ability of treatments to reduce areas of hypersensitivity surrounding the wound after

surgery and their ability to reduce the incidence of chronic pain has been shown. For a long time, local anaesthetics have been used for their capacity to block nociceptive input. They can ALo modulate the inflammatory response following a surgical trauma. By inhibiting the nervous conductivity at the site of the trauma, local anesthetics attenuate the sensitization of the nervous system and therefore the inflammatory phenomena. They ALo exert intrinsic anti-inflammatory properties by modulating the local and systemic liberation of inflammatory mediators. The mechanisms involved are not clearly elucidated. Local, systemic, and spinal inflammatory mechanisms may be influenced by local anesthetics through multiple different mechanisms. The therapeutic implications of effects of local anesthetics on local, systemic, and spinal inflammatory responses merit further study (1).

1. Beloeil H, Mazoit JX. Effect of local anesthetics on the postoperative inflammatory response. *Ann Fr Anesth Reanim.* 2009 Mar; 28(3):231-7.

