

# **RECOMMENDATIONS**

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From the current study, we recommend the following:

1. The addition of dexmedetomidine to intrathecal bupivacaine can be a good alternative to the use of intrathecal fentanyl in spinal anaesthesia.
2. Further studies on large scale of patients and different age groups should be promoted to support the efficacy and safety of adding dexmedetomidine to intrathecal bupivacaine in spinal anaesthesia.
3. Further studies on different doses of dexmedetomidine should be promoted to reach the optimum dose for the use in addition to intrathecal bupivacaine in spinal anaesthesia.

# REFERENCES

## REFERENCES

1. McConchie I, McGeachie J, Healy TE, Cohen PJ. Practice of Anesthesia. 6<sup>th</sup> ed. Vol 34. London, Boston, Sydney Auckland: Wylie and Churchill-Davidson's, 1995. 708-34.
2. Pearce JM. Henry Gray's Anatomy. Clin Anat 2009; 22: 291-5.
3. Putz R. The detailed functional anatomy of the ligaments of the vertebral column. Ann Anat 1992; 174: 40-7.
4. Ellis H. Anatomy for anaesthetists. The lumbar spine and sacrum. Anaesthesia 1962; 17: 38-46.
5. Bernards CM. Sophistry in medicine: lessons from the epidural space. Reg Anesth Pain Med 2005; 30: 56-66.
6. Blomberg RG. Fibrous structures in the subarachnoid space: a study with spinaloscopy in autopsy subjects. Anesth Analg 1995; 80: 875-9.
7. Parkinson D. Human spinal arachnoid septa, trabeculae, and "rogue strands". Am J Anat 1991; 192: 498-509.
8. Salinas FV, Sueda LA, Liu SS. Physiology of spinal anaesthesia and practical suggestions for successful spinal anaesthesia. Best Pract Res Clin Anaesthesiol 2003; 17: 289-303.
9. Butterworth J. Physiology of spinal anesthesia: what are the implications for management? Reg Anesth Pain Med 1998; 23: 370-3.
10. McCrae AF, Wildsmith JA. Prevention and treatment of hypotension during central neural block. Br J Anaesth 1993; 70: 672-80.
11. Marinacci AA. Neurological aspects of complications of spinal anesthesia with medicolegal implications. Bull Los Angel Neuro Soc 1960; 25: 70-92.
12. Auroy Y, Narchi P, Messiah A, Litt L, Rouvier B, Samii K. Serious complications related to regional anesthesia: results of a prospective survey in France. Anesthesiology 1997; 87: 479-86.
13. Rigler ML, Drasner K, Krejcie TC, Yelich SJ, Scholnick FT, DeFontes J, et al. Cauda equina syndrome after continuous spinal anesthesia. Anesth Analg 1991; 72: 275-81.
14. Bromage PR. Spinal opiate analgesia: its present role and future in pain relief. Ann Chir Gynaecol 1984; 73:183-9.
15. Horlocker TT, McGregor DG, Matsushige DK, Schroeder DR, Besse JA. A retrospective review of 4767 consecutive spinal anesthetics: central nervous system complications. Perioperative Outcomes Group. Anesth Analg 1997; 84: 578-84.
16. Lybecker H, Djernes M, Schmidt JF. Postdural puncture headache (PDPH): onset, duration, severity, and associated symptoms. An analysis of 75 consecutive patients with PDPH. Acta Anaesthesiol Scand 1995; 39: 605-12.
17. Chinachoti T, Tritrakarn T. Prospective study of hypotension and bradycardia during spinal anesthesia with bupivacaine: incidence and risk factors, part two. J Med Assoc Thai 2007; 90: 492-501.

18. Kane RE. Neurologic deficits following epidural or spinal anesthesia. *Anesth Analg* 1981; 60: 150-61.
19. Strichartz GR, Sanchez V, Arthur GR, Chafetz R, Martin D. Fundamental properties of local anesthetics. II. Measured octanol:buffer partition coefficients and pKa values of clinically used drugs. *Anesth Analg* 1990; 71: 158-70.
20. Ferreira AA. Pharmacology of local anesthetics. *Anu Bras Odontol* 1974; 3: 41-2, 44, 46.
21. Scott DB, Jebson PJ, Boyes RN. Pharmacokinetic study of the local anaesthetics bupivacaine (Marcain) and etidocaine (Duranest) in man. *Br J Anaesth* 1973; 45: 1010-2.
22. Kerckamp HE, Gielen MJ. Cardiovascular effects of epidural local anaesthetics. Comparison of 0.75% bupivacaine and 0.75% ropivacaine, both with adrenaline. *Anaesthesia* 1991; 46: 361-5.
23. Fozzard HA, Lee PJ, Lipkind GM. Mechanism of local anesthetic drug action on voltage-gated sodium channels. *Curr Pharm Des* 2005; 11: 2671-86.
24. Copeland SE, Ladd LA, Gu XQ, Mather LE. The effects of general anesthesia on whole body and regional pharmacokinetics of local anesthetics at toxic doses. *Anesth Analg* 2008; 106: 1440-9.
25. Bachmann MB, Biscopig J, Schurg R, Hempelmann G. Pharmacokinetics and pharmacodynamics of local anesthetics. *Anaesthesiol Reanim* 1991; 16: 359-73.
26. Sugimoto M, Uchida I, Mashimo T. Local anaesthetics have different mechanisms and sites of action at the recombinant N-methyl-D-aspartate (NMDA) receptors. *Br J Pharmacol* 2003; 138: 876-82.
27. Klein SM, Greengrass RA, Steele SM, D'Ercole FJ, Speer KP, Gleason DH, et al. A comparison of 0.5% bupivacaine, 0.5% ropivacaine, and 0.75% ropivacaine for interscalene brachial plexus block. *Anesth Analg* 1998; 87: 1316-9.
28. Weiniger CF, Golovanevski M, Sokolsky-Papkov M, Domb AJ. Review of prolonged local anesthetic action. *Expert Opin Drug Deliv* 2010; 7: 737-52.
29. White JL, Durieux ME. Clinical pharmacology of local anesthetics. *Anesthesiol Clin North America* 2005; 23: 73-84.
30. Fink BR, Cairns AM. Lack of size-related differential sensitivity to equilibrium conduction block among mammalian myelinated axons exposed to lidocaine. *Anesth Analg* 1987; 66: 948-53.
31. Fink BR, Cairns AM. Differential slowing and block of conduction by lidocaine in individual afferent myelinated and unmyelinated axons. *Anesthesiology* 1984; 60: 111-20.
32. Raymond SA, Steffensen SC, Gugino LD, Strichartz GR. The role of length of nerve exposed to local anesthetics in impulse blocking action. *Anesth Analg* 1989; 68: 563-70.
33. Fink BR. 1992 Labat Lecture. Toward the mathematization of spinal anesthesia. *Reg Anesth* 1992; 17: 263-73.

34. Drachman D, Strichartz G. Potassium channel blockers potentiate impulse inhibition by local anesthetics. *Anesthesiology* 1991; 75: 1051-61.
35. Kozlov SP, Svetlov VA, Luk'ianov MV. Pharmacology of local anesthetics 1992; 17: 263-73.
36. Kozlov SP, Svetlov VA, Luk'ianov MV. Pharmacology of local anesthetics and clinical aspects of segmental blocking. II. Spinal anesthesia. *Anesteziol Reanimatol* 1998; 54: 37-42.
37. Pitkanen M, Haapaniemi L, Tuominen M, Rosenberg PH. Influence of age on spinal anaesthesia with isobaric 0.5% bupivacaine. *Br J Anaesth* 1984; 56: 279-84.
38. Bandi E, Weeks S, Carli F. Spinal block levels and cardiovascular changes during post-Cesarean transport. *Can J Anaesth* 1999; 46: 736-40.
39. Holman SJ, Robinson RA, Beardsley D, Stewart SF, Klein L, Stevens RA. Hyperbaric dye solution distribution characteristics after pencil-point needle injection in a spinal cord model. *Anesthesiology* 1997; 86: 966-73.
40. Urmev WF, Stanton J, Bassin P, Sharrock NE. The direction of the Whitacre needle aperture affects the extent and duration of isobaric spinal anesthesia. *Anesth Analg* 1997; 84: 337-41.
41. Janik R, Erdmann K, Wahl J. Spinal anesthesia with hyperbaric tetracaine and bupivacaine: velocity of spread, analgesic effect and motor blockade in various positions and injection volumes. *Reg Anaesth* 1986; 9: 110-5.
42. Russell IF, Holmqvist EL. Subarachnoid analgesia for caesarean section. A double-blind comparison of plain and hyperbaric 0.5% bupivacaine. *Br J Anaesth* 1987; 59: 347-53.
43. Wildsmith JA, McClure JH, Brown DT, Scott DB. Effects of posture on the spread of isobaric and hyperbaric amethocaine. *Br J Anaesth* 1981; 53: 273-8.
44. Sidhu SK, Shaw S, Wilkinson JD. A 10-year retrospective study on benzocaine allergy in the United Kingdom. *Am J Contact Dermat* 1999; 10: 57-61.
45. Chen AH. Toxicity and allergy to local anesthesia. *J Calif Dent Assoc* 1998; 26: 683-92.
46. Tsujimoto A, Ikeda M. Central nervous system toxicity of local anesthetics. *Hiroshima Daigaku Shigaku Zasshi* 1977; 9: 127-34.
47. Clarkson CW, Hondeghem LM. Mechanism for bupivacaine depression of cardiac conduction: fast block of sodium channels during the action potential with slow recovery from block during diastole. *Anesthesiology* 1985; 62: 396-405.
48. Ryu HY, Kim JY, Lim HK, Yoon J, Yoo BS, Choe KH, et al. Bupivacaine induced cardiac toxicity mimicking an acute non-ST segment elevation myocardial infarction. *Yonsei Med J* 2007; 48: 331-6.
49. Albright GA. Cardiac arrest following regional anesthesia with etidocaine or bupivacaine. *Anesthesiology* 1979; 51: 285-7.
50. Wan QX, Bo YL, Li HB, Li WZ. Effects of mixture of lidocaine and ropivacaine at different concentrations on the central nervous system and cardiovascular toxicity in rats. *Chin Med J (Engl)* 2010; 123: 79-83.

51. Moore DC, Crawford RD, Scurlock JE. Severe hypoxia and acidosis following local anesthetic-induced convulsions. *Anesthesiology* 1980; 53: 259-60.
52. Spence AG. Lipid reversal of central nervous system symptoms of bupivacaine toxicity. *Anesthesiology* 2007; 107: 516-7.
53. Scott DB. Evaluation of clinical tolerance of local anaesthetic agents. *Br J Anaesth* 1975; 47: 128-31.
54. Courtney KR, Kendig JJ, Cohen EN. Frequency-dependent conduction block: the role of nerve impulse pattern in local anesthetic potency. *Anesthesiology* 1978; 48: 111-7.
55. Irwin W, Fontaine E, Agnolucci L, Penzo D, Betto R, Bortolotto S, et al. Bupivacaine myotoxicity is mediated by mitochondria. *J Biol Chem* 2002; 277: 12221-7.
56. Aniteye EA, Edwin F, Tettey MM, Frimpong-Boateng K. Post-thoracotomy Horner syndrome associated with extrapleural infusion of bupivacaine. *Interact Cardiovasc Thorac Surg* 2009; 9: 310.
57. Lund PC, Cwik JC. Propitocaine (Citanest) and Methemoglobinemia. *Anesthesiology* 1965; 2: 569-71.
58. Bakshi U, Chatterjee S, Sengupta S, Gupta D. Adjuvant Drugs In Central Neuraxial Analgesia- A Review. *The Internet Journal of Anesthesiology*. 2009; 26:1.
59. Jordan VSB, Tung A. Dexmedetomidine: Clinical Update. *Seminars in Anesthesia, Preoperative Medicine and Pain* 2002; 21: 265-74.
60. Arcangeli A, D'Alo C, Gaspari R. Dexmedetomidine use in general anaesthesia. *Curr Drug Targets* 2009; 10: 687-95.
61. Gertler R, Brown HC, Mitchell DH, Silvius EN. Dexmedetomidine: a novel sedative-analgesic agent. *Proc (Bayl Univ Med Cent)* 2001; 14: 13-21.
62. Mantz J, Josserand J, Hamada S. Dexmedetomidine: new insights. *Eur J Anaesthesiol* 2011; 28: 3-6.
63. MacDonald E, Kobika BK, Scheinin M. Gene targeting homing in on alpha-2 adrenoceptor subtype function. *Trends Pharmacol Sci* 1997; 18: 211-9.
64. Bousquet P, Dontenwill M, Grenay H. Imidazoline receptors in cardiovascular and metabolic diseases. *J Cardiovasc Pharmacol* 2000; 35: S21-5.
65. Kagawa K, Mammoto T, Hayashi Y. The effect of imidazoline receptors and alpha-2 adrenoceptors on the anesthetic requirement (MAC) for halothane in rats. *Anesthesiology* 1997; 87: 963-7.
66. Afonso J, Reis F. Dexmedetomidine: current role in anesthesia and intensive care. *Rev Bras Anesthesiol* 2012; 62: 118-33.
67. Tawfeeq NA, Halawani MM, Al-Faridi K, Aal-Shaya WA, Taha WS. Traumatic brain injury: neuroprotective anaesthetic techniques, an update. *Injury* 2009; 40(Suppl 4): S75-81.
68. Farag E, Argalious M, Sessler DI, Kurz A, Ebrahim ZY, Schubert A. Use of alpha(2)-Agonists in Neuroanesthesia: An Overview. *Ochsner J* 2011; 11: 57-69.

69. Basar H, Akpınar S, Dogancı N, Buyukkocak U, Kaymak C, Sert O, et al. The effects of preanesthetic, single-dose dexmedetomidine on induction, hemodynamic, and cardiovascular parameters. *J Clin Anesth* 2008; 20: 431-6.
70. Kabukcu HK, Sahin N, Temel Y, Titiz TA. Hemodynamics in coronary artery bypass surgery: effects of intraoperative dexmedetomidine administration. *Anaesthesist* 2011; 60: 427-31.
71. Heesen M, Dietrich GV, Detsch O. The in-vitro effect of alpha-2 agonists on thrombocyte function and density of thrombocyte alpha-2 receptors. *Anaesthesist* 1996; 45: 255-8.
72. Menegaz RG, Kapusta DR, Mauad H, de Melo Cabral A. Activation of alpha(2)-receptors in the rostral ventrolateral medulla evokes natriuresis by a renal nerve mechanism. *Am J Physiol Regul Integr Comp Physiol* 2001; 281: R98-R107.
73. Hegan JJ, Leslie RA, Ptel S. Orexin A activates locus coeruleus cell firing and increases arousal in rat. *Proc Natl Acad USA* 1996; 14: 10911-6.
74. Maze M, Virtanen R, Daunt D. Effects of Dex, a novel imidazole sedative-anesthetic agent, on adrenal steroidogenesis: in vivo and in vitro studies. *Anesth Analg* 1991; 73: 204-8.
75. Kunisawa T, Nagata O, Nagashima M, Mitamura S, Ueno M, Suzuki A, et al. Dexmedetomidine suppresses the decrease in blood pressure during anesthetic induction and blunts the cardiovascular response to tracheal intubation. *J Clin Anesth* 2009; 21: 194-9.
76. Akin A, Bayram A, Esmoğlu A, Tosun Z, Aksu R, Altuntas R, et al. Dexmedetomidine vs midazolam for premedication of pediatric patients undergoing anesthesia. *Paediatr Anaesth* 2012; 22: 871-6.
77. Candiotti KA, Bergese SD, Bokesch PM, Feldman MA, Wisemandle W, Bekker AY. Monitored anesthesia care with dexmedetomidine: a prospective, randomized, double-blind, multicenter trial. *Anesth Analg* 2010; 110: 47-56.
78. Deeter KH, King MA, Ridling D, Irby GL, Lynn AM, Zimmerman JJ. Successful implementation of a pediatric sedation protocol for mechanically ventilated patients. *Crit Care Med* 2011; 39: 683-8.
79. Dasta JF, Kane-Gill SL, Pencina M, Shehabi Y, Bokesch PM, Wisemandle W, et al. A cost-minimization analysis of dexmedetomidine compared with midazolam for long-term sedation in the intensive care unit. *Crit Care Med* 2010; 38: 497-503.
80. Wunsch H, Kahn JM, Kramer AA, Rubenfeld GD. Use of intravenous infusion sedation among mechanically ventilated patients in the United States. *Crit Care Med* 2009; 37: 3031-9.
81. Siobal MS, Kallet RH, Kivett VA, Tang JF. Use of dexmedetomidine to facilitate extubation in surgical intensive-care-unit patients who failed previous weaning attempts following prolonged mechanical ventilation: a pilot study. *Respir Care* 2006; 51: 492-6.
82. Bloom FE, Kupper DJ. *Psychopharmacology-The Fourth Generation of Progress*. 4<sup>th</sup> ed. Lippincott Williams and Wilkins, 1995.

83. Guo TZ, Jiang JY, Butterman AE. Dexmedetomidine injection into the locus coeruleus produces antinociception. *Anesthesiology* 1996; 84: 873-81.
84. Levanen J, Makela ML, Scheinin H. Dexmedetomidine premedication attenuates ketamine-induced cardiostimulatory effects and post-anesthetic delirium. *Anesthesiology* 1995; 82: 1117-5.
85. Eisenach JC, Shafer SL, Bucktin BA. Pharmacokinetics and pharmacodynamics of intraspinal dexmedetomidine in sheep. *Anesthesiology* 1994; 80: 1349-59.
86. Eisenach JC. Alpha-2 agonists and analgesia. *Exp Opin Invest Drugs* 1994; 3: 1005-10.
87. Eisenach JC, De Kock M, Klimscha W. Alpha 2 adrenergic agonists for regional anesthesia. *Anesthesiology* 1996; 85: 655-74.
88. Fairbanks CA, Wilcox GL. Spinal antinociceptive synergism between morphine and clonidine persist in mice made acutely or chronically tolerant to morphine. *J Pharmacol Exp Ther* 1999; 288: 1107-16.
89. Li X, Eisenach JC. Alpha 2a adrenoceptor stimulation reduces capsaicin induced glutamate release from spinal cord synaptosomes. *J Pharmacol Exp Ther* 2001; 299: 939-44.
90. Blandszun G, Lysakowski C, Elia N, Tramer MR. Effect of perioperative systemic alpha2 agonists on postoperative morphine consumption and pain intensity: systematic review and meta-analysis of randomized controlled trials. *Anesthesiology* 2012; 116: 1312-22.
91. Arain SR, Ruehlow RM, Uhrich TD, Ebert TJ. The efficacy of dexmedetomidine versus morphine for postoperative analgesia after major inpatient surgery. *Anesth Analg* 2004; 98: 153-8.
92. Unlugenc H, Gunduz M, Guler T, Yagmur O, Isik G. The effect of pre-anaesthetic administration of intravenous dexmedetomidine on postoperative pain in patients receiving patient-controlled morphine. *Eur J Anaesthesiol* 2005; 22: 386-91.
93. Karhuvaara S, Kallio A, Scheinin M, Anttila M, Salonen JS, Scheinin H. Pharmacological effects and pharmacokinetics of atipamezole, a novel alpha 2-adrenoceptor antagonist. *Br J Clin Pharmacol* 1990; 30: 97-106.
94. Yazbek-Karam VG, Aouad MM. Perioperative uses of dexmedetomidine. *MEJ Anaesth* 2006; 18: 1043-56.
95. Aho M, Erkola O, Kallio A, Scheinin H, Korttila K. Comparison of dexmedetomidine and midazolam sedation and antagonism of dexmedetomidine with atipamezole. *J Clin Anesth* 1993; 5: 194-203.
96. Scheinin H, Aantaa R, Anttila M, Hakola P, Helminen A, Karhuvaara S. Reversal of the sedative and sympatholytic effects of dexmedetomidine with a specific alpha2-adrenoceptor antagonist atipamezole: A pharmacodynamic and kinetic study in healthy volunteers. *Anesthesiology* 1998; 89: 574-84.
97. Karhuvaara S, Kallio A, Salonen M, Tuominen J, Scheinin M. Rapid reversal of alpha 2-adrenoceptor agonist effects by atipamezole in human volunteers. *Br J Clin Pharmacol* 1991; 31: 160-5.

98. Brunton LL, Laso JS, Parker KL. 11<sup>th</sup> ed. Goodman & Gilman's the pharmacological basis of therapeutics. New York: McGraw-Hill, 2006. 854-5.
99. Janicki PK, Parris WC. Clinical pharmacology of opioids. In: Smith H (ed). Drugs for Pain. Philadelphia: Hanley & Belfus, Inc., 2003. 97-118.
100. Reves JG, Glass P, Lubarsky DA, Matthew D, Martinez-Ruiz R. Intravenous anesthetics. In: Miller RD (ed). Miller's Anesthesia. 7<sup>th</sup> ed. Ch. 26. Philadelphia: Churchill-Livingston, 2009.
101. Bailey PW, Snnith BE. Continous epidural injection of fentanyl for postoperative analgesia. *Anaesthesia* 1980; 35: 1002-6.
102. Satoh M, Minami M. Molecular pharmacology of opioid receptors. *Pharmacol Ther* 1995; 68: 343-64.
103. McCleane G, Smith H. Opioids for persistent noncancer pain. *Med Clin N Am* 2007; 91: 177-97.
104. Enneking FK. Local anesthetics and additives. *Anesth Analg* 2001; 92(Suppl): 32-6.
105. Baily PL, Stanley TH. Pharmacology of the IV narcotics or anaesthetics. 3<sup>rd</sup> ed. In: Miller RD (ed). *Anaesthesia*. New York, Edinburgh, London: Churchill Livingstone, 1990. 287-315.
106. Adams JU, Tallarida RJ, Geller EB, Adler MW. Isobolographic superadditivity between delta and mu opioid agonists in the rat depends on the ratio of compounds, the mu agonist and the analgesic assay used. *J Pharmacol Exp Ther* 1993; 266: 1261-7.
107. Synder SH. Opiate receptors in the brain. *New Engl J Med* 1977; 256-66.
108. Carr DB, Cousins MJ. Spinal route of analgesia: Opioids and future options. In: Cousins MJ, Bridenbaugh PO (eds). *Neural blockade in clinical anesthesia and management of pain*. Vol 24. Philadelphia: Lippincott-Raven, 1998. 59-67.
109. Wong KC. Narcotics are not expected to produce unconsciousness and amnesia. *Anesth Analg* 1983; 62: 625-6.
110. Tanaka M, Watanabe S, Matsumiya N. Enhanced pain management for postgastrectomy patients with combined epidural morphine and fentanyl. *Can J Anaesth* 1997; 44: 1047-52.
111. Cooper DW, Ryall DM, McHardy FE, Lindsay SL, Eldabe SS. Patients controlled extradural analgesia with bupivacaine, Fentanyl, or a mixture of both, after cesarean section. *Br J Anaesth* 1996; 76: 611-5.
112. Barash PG, Cullin BF, Stoelting RK. Opioids. In: John TA (ed). *Handbook of Clinical Anaesthesia*. 3<sup>rd</sup> ed. Philadelphia, New York: Lippincott, 1997. 158-76.
113. Senntag H, Larsen R, Brock Schneider B. Myocardial blood flow and oxygen consumption during high dose fentanyl anaesthesia in patients with coronary artery disease. *Anesthesiology* 1081; 56: 414-22.
114. Tanaka M, Watanabe S, Ashimura H, Akiyoshi Y, Nishijima Y, Sato S, et al. Minimum effective combination dose of epidural morphine and fentanyl for post-hysterectomy analgesia: A randomized, prospective, double-blind study. *Anesth Analg* 1993; 77: 942-6.

115. Ballantyne JC, Carr DB, deFerranti S, Suarez T, Lau J, Chalmers TC, et al. The comparative effects of postoperative analgesic therapies on pulmonary outcome: Cumulative meta-analysis of randomized, controlled trials. *Anesth Analg* 1998; 86: 596-612.
116. Christian CM, Waller JL, Moldehouer CC. Postoperative rigidity following fentanyl anaesthesia. *Anesthesiology* 1983; 58: 275-7.
117. Stanley TH, Berman J, Green O, Robertson D. Plasma catecholamine and cortisol responses to fentanyl-oxygen anaesthesia for coronary artery operations. *Aaesthesia* 1980; 53: 250-3.
118. Jaffe JH, Marten WR. Opioid analgesics and antagonists. 6<sup>th</sup> ed. In: Gelman AG, Goodman LS, Gilman A (eds). *The Pharmacological basis therapeutics*. New York: MacMillan, 1980. 513-27.
119. Stoelting RK, Miller RD. Intravenous anesthetics, in basics of anesthesia. 4<sup>th</sup> ed. Churchill-Livingstone, 2000. 58-69.
120. Dolin SJ. Drugs and pharmacology. In: Padfield NL (ed). *Total intravenous anesthesia*. Oxford: Butterworth Heinemann, 2000. 13-35.
121. Ganellin CR, David J. *Dictionary of Pharmacological Agents*. 1996; 1396.
122. Sirohi S, Dighe SV, Madia PA, Yoburn BC. The relative potency of inverse opioid agonists and a neutral opioid antagonist in precipitated withdrawal and antagonism of analgesia and toxicity. *J Pharmacol Exp* 2009; 330: 513-9.
123. Wolfe TR, Bernstone T. Intranasal drug delivery: an alternative to intravenous administration in selected emergency cases. *J Emerg Nurs* 2004; 30: 141-7.
124. Shukla D, Verma A, Agarwal A, Pandey HD, Tyagi C. Comparative study of intrathecal dexmedetomidine with intrathecal magnesium sulfate used as adjuvants to bupivacaine. *J Anaesth Clin Pharmacol* 2011; 27: 495-9.
125. Gupta R, Bogra J, Verma J, Kohli M, Kushwaha JK, Kumar S. Dexmedetomidine as an intrathecal adjuvant for postoperative analgesia. *India J Anaesth* 2011; 55: 347-51.
126. Al-Ghanem SM, Massad IM, AL-Mustafa MM, Al-Zaben KR, Qudaisat IY, Qatawneh AM, et al. Effect of adding dexmedetomidine versus fentanyl to intrathecal bupivacaine on spinal block characteristics in gynecological procedures. *AM J Appl Sci* 2009; 6: 882-7.
127. Sriwatanakul K, Kelvie W, Lasagna L, Calimlim JF, Weis OF, Mehta G. Studies with different types of visual analogue scales for measurement of pain. *Clin Pharmacol Ther* 1998; 34: 234-9.
128. Kleinman W, Mikhail M. Spinal, epidural, & caudal blocks. In: Morgan GE, Mikhail MS, Murray MJ (eds). *Clinical anesthesiology*. 4<sup>th</sup> ed. New York: Lange Medical Books, 2006.
129. Bromage PR. A comparison of the hydrochloride and carbon dioxide salts of lidocaine and prilocaine in epidural analgesia. *Acta Anesthesiol Scand Suppl* 1965; 16: 55-69.
130. Liu LL, Gropper MA. Postoperative analgesia and sedation in the adult intensive care unit. A guide to drug selection. *Drugs* 2003; 63: 755-67.

131. Miller, RD et al. Miller's Anesthesia. 7th ed. London: Churchill Livingstone, 2009. 1616-8.
132. Abdelhamid SA, El-Lakany MH. Intrathecal dexmedetomidine: Useful or not? *J Anesth Clin Res* 2013; 4: 9.
133. Sunil BV, Sahana KS. Comparison of dexmedetomidine and magnesium sulfate as adjuvants with hyperbaric bupivacaine for spinal anesthesia: A double blind controlled study. *J Med Sci Clin Res* 2013; 1: 117-24.
134. Sunil BV, Sahana KS, Jajee PR. Comparison of dexmedetomidine, fentanyl and magnesium sulfate as adjuvants with hyperbaric bupivacaine for spinal anaesthesia: A double Blind Controlled Study. *IJRTSAT* 2013; 9: 14-9.
135. Sunil BV, Sahana KS, Jajee PR. Dexmedetomidine as an adjuvant with hyperbaric bupivacaine for spinal anaesthesia: a double blind controlled study. *JEMDS* 2013; 2: 7604-11.
136. Kanazi GE, Aouad MT, Jabbour-Khoury SI, Al Jazzar MD, Alameddine MM, Al-Yaman R, et al. Effect of low-dose dexmedetomidine or clonidine on the characteristics of bupivacaine spinal block. *Acta Anaesthesiol Scand* 2006; 50: 222-7.
137. Ogan SF, Job OG, Enyindah CE. Comparative effects of single shot intrathecal bupivacaine with dexmedetomidine and bupivacaine with fentanyl on labor outcome. *ISRN Anesthesiology* 2012; 816984.
138. Mahendru V, Tewari A, Katyal S, Grewal A, Singh MR, Katyal R. A comparison of intrathecal dexmedetomidine, clonidine and fentanyl as adjuvants to hyperbaric bupivacaine for lower limb surgery: A double blind controlled study. *J Anaesthesiol Clin Pharmacol* 2013; 29: 496-502.
139. Smith MS, Schumbra UB, Wilson KH, Page SO, Hulette C, Light AR, et al. Alpha 2 adrenergic receptor in human spinal cord: Specific localized expression of mRNA encoding alpha-2 adrenergic receptor subtypes at four distinct levels. *Brain Res Mol Brain Res* 1995; 34: 109-17.
140. Smith C, Brinbaum G, Carter JL, Greenstein J, Lublin FD. Tizanidine treatment of spasticity caused by multiple sclerosis: results of a double-blind, placebo-controlled trial. *US Tizanidine Study Group. Neurology.* 1994; 44: 34-43.
141. Yaksh TL, Reddy SV. Studies in primate on the analgesic effects associated with intrathecal actions of opiates, alpha-adrenergic agonists, and baclofen. *Anesthesiology* 1981; 54: 451-67.
142. Al-Mustafa MM, Abu-Halaweh SA, Aloweidi AS, Murshidi MM, Ammari BA, Awwad ZM, et al. Effect of dexmedetomidine added to spinal bupivacaine for urological procedures. *Saudi Med J* 2009; 30: 365-70.
143. Hala EA, Shafie MA, Youssef H. Dose-related prolongation of hyperbaric bupivacaine spinal anesthesia by dexmedetomidine. *Ain Shams J Anesthesiol* 2011; 4: 83-95.
144. Talke P, Tayefeh F, Sessler DI, Jeffrey R, Noursalehi M, Richardson C. Dexmedetomidine does not alter the sweating threshold, but comparably and linearly reduces the vasoconstriction and shivering thresholds. *Anesthesiology* 1997; 87: 835-41.

# **PROTOCOL**

أوافق  
8

**A COMPARATIVE STUDY OF INTRATHECAL  
DEXMEDETOMIDINE AND FENTANYL AS ADDITIVES TO  
BUPIVACAINE**

دراسة مقارنة لإعطاء ديكسميديتوميدين أوفينتانييل كعقاقير مضافة لعقار البوبيبيفاكين تحت الأم الجافية

أوافق

Protocol of a thesis submitted  
to the Faculty of Medicine  
University of Alexandria  
In partial fulfillment of the  
requirements of the degree of  
**Master of Anaesthesia  
and Surgical Intensive Care**  
by

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خطة بحث مقدمة  
لكلية الطب  
جامعة الإسكندرية  
إيفاء جزئيا  
لشروط الحصول على درجة  
الماجستير فى التخدير  
والعناية المركزة الجراحية  
من

وفاء حسن أحمد  
بكالوريوس الطب و الجراحة  
طبيب مقيم  
مستشفيات جامعة الإسكندرية  
قسم التخدير  
و العناية المركزة الجراحية  
كلية الطب  
جامعة الإسكندرية  
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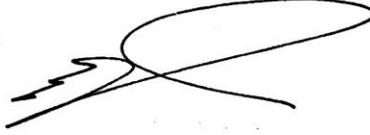


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For his experience in spinal anaesthesia

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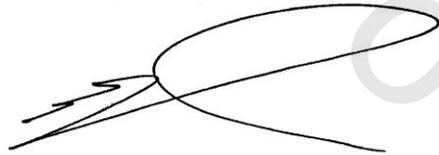
## INTRODUCTION

Lower abdominal and lower limb surgeries may be performed under local, regional (spinal or epidural) or general anaesthesia, but neuraxial blockade is the preferred mode of anaesthesia. Spinal block is still the first choice because of its rapid onset, superior blockade, low risk of infection as from catheter in situ, less failure rates, and cost effectiveness, but has the drawbacks of shorter duration of block and lack of postoperative analgesia. <sup>(1)</sup>

The choice of local anaesthetic agent and its concentration is determined by the anticipated duration of the surgical procedure and the balanced need for sensory and motor block. <sup>(2)</sup>

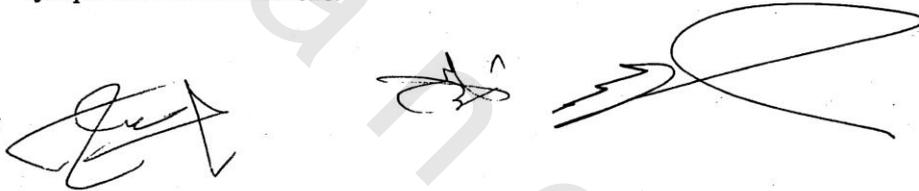
Bupivacaine is an amide local anaesthetic with slow onset and long duration of action (lasting 2-2.5 hours). <sup>(3)</sup> Large doses of intrathecal bupivacaine were associated with severe hypotension and delayed recovery of the motor block. <sup>(4)</sup>

In recent years, the use of intrathecal adjuvants has gained popularity with the aim of prolonging the duration of block, better success rate, patient satisfaction, decreased resource utilization compared with general anaesthesia, and faster recovery. The quality of the spinal anaesthesia has been reported to be improved by the addition of opioids (such as morphine, fentanyl, and sufentanyl). Other drugs (such as dexmedetomidine, clonidine, magnesium sulfate, neostigmine, ketamine and midazolam) have been studied to improve the quality of spinal anaesthesia, but uptill now there is no single drug with no side effects. <sup>(5)</sup>



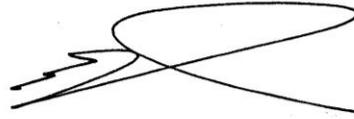
Fentanyl is one of the short acting narcotic analgesics with potent morphine-like action. It produces many of its clinical effects rapidly after intrathecal administration. <sup>(6)</sup> Neuroaxial administration of lipophilic opioids such as, fentanyl and sufentanyl tends to provide a rapid onset of analgesia and their rapid clearance from cerebrospinal fluid (CSF) may limit cephalic spread and the development of certain side effects such as, delayed respiratory depression. <sup>(7)</sup>

Dexmedetomidine, a new highly selective alpha 2 agonist, is under evaluation as a neuraxial adjuvant as it is supposed to provide stable hemodynamic conditions, good quality of intraoperative and prolonged postoperative analgesia with minimal side effects. It is FDA (Food and Drug Administration) approved as a short term sedative for mechanically ventilated intensive care unit patients. <sup>(8)</sup> The analgesic action of intrathecal alpha 2 adrenoceptor agonist is supposed to be by depressing the release of C-fiber transmitters and by hyperpolarization of post-synaptic dorsal horn neurons. <sup>(9)</sup>



## AIM OF THE WORK

The aim of this study is to compare the addition of either dexmedetomidine or fentanyl to intrathecal bupivacaine as regards: the onset and duration of sensory and motor block, hemodynamic effects, postoperative analgesia and adverse effects of either drugs.

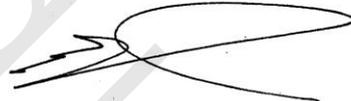


## PATIENTS

The present study will be carried out on 60 patients (approved to be sufficient by the department of statistics, High Institute of Public Health, University of Alexandria), aged 18-50 years old, of both sexes, of height ranging from 160-190cm<sup>(1)</sup>, with American Society of Anaesthesiologists (ASA) I and II health status, admitted to the Alexandria Main University Hospitals and scheduled for elective lower abdominal or lower limb surgeries.

Exclusion criteria will include:

1. Pregnant and lactating females.
2. Patients allergic to studied medications.
3. Patients with heart block & dysrhythmias.
4. Hypertensive patients.
5. Patients on therapy with adrenergic receptor antagonist, calcium channel blocker, &/or angiotensin converting enzyme (ACE) inhibitor.
6. Patients with opium addiction & sedative drugs consumption.
7. Patients with contraindications for spinal anaesthesia.



Patients will be randomly categorized by closed envelope method in a double blinded study into three equal groups (20 patients each): <sup>(10)</sup>

- **Group B:** Patients will receive 3ml (15mg) of 0.5% hyperbaric bupivacaine + 0.5ml of normal saline intrathecally.
- **Group F:** Patients will receive 3ml (15mg) of 0.5% hyperbaric bupivacaine + 0.5ml (25 microgram) of preservative free fentanyl intrathecally. <sup>(11)</sup>
- **Group D:** Patients will receive 3ml (15mg) of 0.5% hyperbaric bupivacaine + 0.5ml (5 microgram) of diluted, preservative free dexmedetomidine intrathecally. <sup>(12,13)</sup>

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## METHODS

After the approval of the local ethical committee, consent will be taken from each patient confirming his/her acceptance of intrathecal anaesthesia, after knowing the technique and its possible complications.

### Pre-operative screening of all patients will include:

- History taking.
- Complete physical examination.
- Laboratory investigation:
  1. Complete Blood Picture.
  2. Prothrombin time, activated partial thromboplastin time and INR.
  3. Liver enzymes: Aspartate transaminase, Alanine transaminase.
  4. Serum urea and creatinine.
  5. Fasting Blood Sugar.

Patients will be premedicated by H<sub>2</sub> antagonist (ranitidine 50mg, intramuscularly, 2 hours preoperatively). Before commencing regional anaesthesia, standard monitoring will be established using multichannel monitor (Hewlett-Packard, Viridia 24, Germany) as follow:

- Electrocardiogram (ECG) for heart rate and rhythm. (Beat/min).
- Non-invasive measurement of arterial blood pressure. (Mean blood pressure in mmHg).
- Oxygen saturation. (SpO<sub>2</sub>%).

They will be given intravenous lactated Ringer's solution 10 ml/kg as volume preload. Spinal anaesthesia will be performed in the sitting position at the L3-4 interspace with midline or paramedian approach by using a 25 gauge Quinke's



spinal needle with all aseptic precautions. Injection will be according to the following groups:

- Group B: Patients will receive 3ml (15mg) of 0.5% hyperbaric bupivacaine + 0.5ml of normal saline intrathecally.
- Group F: Patients will receive 3ml (15mg) of 0.5% hyperbaric bupivacaine + 0.5ml (25 microgram) of preservative free fentanyl intrathecally.
- Group D: Patients will receive 3ml (15mg) of 0.5% hyperbaric bupivacaine + 0.5ml (5 microgram) of diluted, preservative free dexmedetomidine intrathecally.

Injection will be given over 10-15 sec, immediately after completion of the injection patients will lie supine. Low flow oxygen (4L/minute) will be administered via oxygen mask.

#### MEASUREMENTS

The following parameters will be measured:

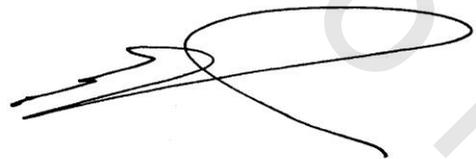
**I. Patient data:**

- 1- Patient's age (years).
- 2- Patient's height (cm).

**II. Duration of the operation: (minutes).**

**III. Hemodynamic measurements:**

- 1-Heart rate (HR in beat / min).
- 2-Non-invasive measurement of mean arterial blood pressure (MABP in mmHg).
- 3-Oxygen saturation (SpO<sub>2</sub> %).



All previous parameters will be continuously monitored and recorded at the following periods:

- 1- Before spinal anaesthesia.
- 2- Immediate after spinal analgesia and every 15 minutes, for 90 min and at the end of surgery.
- 3- Every hour for 6 hours postoperative.

#### IV. Assessment of sensation:

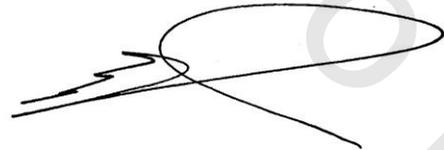
All durations will be calculated considering the time of spinal injection as time zero.

Sensory analgesia will be assessed by iced cubes to measure the following:

- 1- Onset of sensory analgesia (defined as time in minutes to reach highest sensory level) tested every minute after intrathecal injection till reaching the highest level).
- 2- Sensory level of analgesia (defined as segmental level of highest sensory analgesia).
- 3- Duration of analgesia (defined as the time in minutes it takes for sensory level to decrease to dermatomal level S1) measured from the highest obtained sensory level every 15 minutes. <sup>(1)</sup>

Postoperatively:

- 4- Pain intensity will be evaluated by using a visual analogue scale (VAS) starting from the first pain experienced by the patient till the end of study with 0 corresponding to no pain and 10 to the worst pain imaginable, it will be assessed at the first, second, fourth, sixth, eighth, hour and every four hours till 24 hours. <sup>(14)</sup>



5- Time for first request of analgesia (defined as the time elapsed from the time of spinal injection till reaching VAS>4) will be recorded and treated by intramuscular diclofenac sodium in a dose of 1mg/kg to be repeated if needed after 12 hours but if pain persists after one hour from the first dose, 25 mg pethidine will be given intravenously.<sup>(10)</sup>

6- The total analgesic dose of both diclofenac sodium and pethidine taken within the first 24 hours will be recorded.

**V. Assessment of motor function:**

Motor blockade will be evaluated as follows:

1- Onset of motor block. (Defined as time in minutes from the end of drug injection intrathecally until patient is unable to move hip, knee and ankle)<sup>(15)</sup> tested every minute after intrathecal injection.

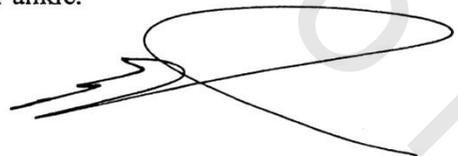
2- Duration of motor block in minutes will be recorded from the time of the onset of the block to the time when the patient will be able to lift their legs in bed against gravity (Bromage-score 0) tested every 15 min. This is according to the following modified Bromage-score:<sup>(16)</sup>

0: The patient is able to move the hip, knee and ankle.

1: The patient is unable to move the hip but is able to move the knee and ankle.

2: The patient is unable to move the hip and knee but able to move the ankle.

3: the patient is unable to move hip, knee or ankle.



**VI. Side effects:**

The incidence of adverse effects such as hypotension, bradycardia, nausea, vomiting, shivering, pruritus, respiratory depression and sedation will be recorded.

Hypotension, defined as a decrease of systolic blood pressure by more than 30% from baseline or fall below 90mmHg, will be treated by intravenous fluids and intravenous increments of 5mg ephedrine. Total ephedrine dose will be recorded.

Bradycardia, defined as heart rate less than 50bpm, will be treated by 0.6mg of intravenous atropine

Respiratory depression, defined as respiratory rate <10, will be assessed for any needed airway support.

Sedation will be assessed by Ramsay Sedation Score.<sup>(17)</sup> This will also be assessed for any needed airway support.

Score	Response
1	Anxious or restless or both
2	Cooperative, oriented and tranquil
3	Responding to commands
4	Brisk response to stimulus
5	Sluggish response to stimulus
6	No response to stimulus

These side effects will be assessed at the first, second, fourth, sixth, eighth, hour and every four hours till 24 hours.



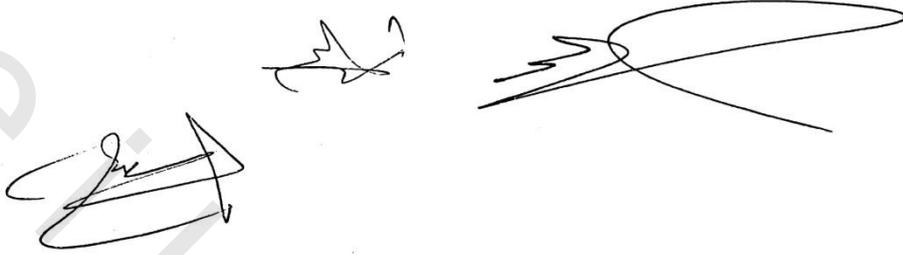
## RESULTS

The results of this study will be tabulated and statistically analyzed according to the collected data to fulfill the aim with the aid of different ways of presentation: numerical, mathematical and graphical.



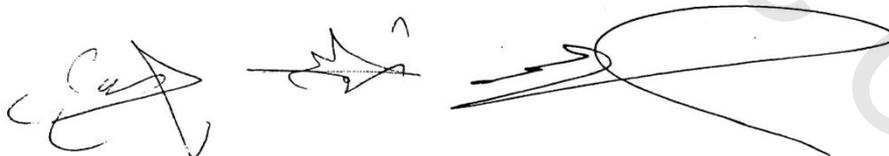
## DISCUSSION

Findings will be discussed in view of the results of the work and their scientific significance.

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## REFERENCES

1. Shukla D, Verma A, Agarwal A, Pandey HD, Tyagi C. Comparative study of intrathecal dexmedetomidine with intrathecal magnesium sulfate used as adjuvants to bupivacaine. *J Anaesth Clin Pharmacol* 2011; 27:495-9.
2. Tetzlaff JF. Spinal, epidural and caudal blocks in: Morgan GE, Mikhail MS (Ed): *Clinical Anesthesiology* 1996; 16:211-44.
3. Tuominen M. Bupivacaine spinal anaesthetics. *Acta Anaesthesiol Scand* 1991; 35:1.
4. Chung CJ, Bae SH, Chae K Y, Chin YJ. Spinal anaesthesia with 0.25% hyperbaric bupivacaine for cesarean section: effects of volume. *Br J Anaesth* 1996; 77:145-9.
5. Kalso E, Poyhia R, Rosemberg P. Spinal antinociceptive by dexmedetomidine, a highly selective 2-adrenergic agonist. *Pharmacol Toxicol* 1991; 68:140-3.
6. Ummenhofer WC, Arends RH, Shen DD, Bernards CM. Comparative spinal distribution and clearance kinetics of intrathecally administered morphine, fentanyl, alfentanil and sufentanil. *Anesthesiology* 2000; 92:739-53.
7. Hamber EA, Viscomi CM: Intrathecal lipophilic opioids as adjuncts to surgical spinal anesthesia. *Reg Anesth Pain Med* 1999; 24:255.
8. Venn RM, Grounds RM. Comparison between dexmedetomidine and propofol for sedation in the intensive care unit: Patient and clinician perceptions. *Br J Anaesth* 2001; 87:684-90.
9. Eisanach JC, De Kock M, Klimscha W. Alpha 2 adrenergic agonists for regional anesthesia. *Anesthesiology* 1996; 85:655-74.



10. Gupta R, Bogra J, Verma J, Kohli M, Kushwaha JK, Kumar S.  
Dexmedetomidine as an intrathecal adjuvant for postoperative analgesia.  
India J Anaesth 2011; 55:347-51.  
11. <http://www.meppo.com/pdf/drugs/707-FENTANYL-1329751051.pdf>
12. Al-Ghanem SM, Massad IM, AL-Mustafa MM, Al-Zaben KR, Qudaisat IY,  
Qatawneh AM, et al. Effect of adding dexmedetomidine versus fentanyl to  
intrathecal bupivacaine on spinal block characteristics in gynecological  
procedures. AM JApplSci 2009; 6:882-7.  
13. [http://www.precedex.com/wp-content/uploads/Precedex\\_PI.pdf](http://www.precedex.com/wp-content/uploads/Precedex_PI.pdf)
14. Sriwatanakul K, Kelvie W. Studies with different types of visual analogue  
scales for measurement of pain. ClinPharmacolTher 1998; 34:234-9.
15. Morga GE, Mikhail MS, Muray MJ. Spinal, Epidural and caudal  
blocks. Clinical Anesthesiology, 4<sup>th</sup>ed. 2006; 16:289-323.
16. Bromage PR. A comparison of the hydrochloride and carbon dioxide salts of  
lidocaine and prilocaine in epidural analgesia. Acta Anesthesiol Scand Suppl  
1965; 16:55-69.
17. Liu LL, Gropper MA. Postoperative analgesia and sedation in the adult  
intensive care unit. A guide to drug selection. Drugs 2003; 63(8):755-67.

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**SAMPLE SIZE:**

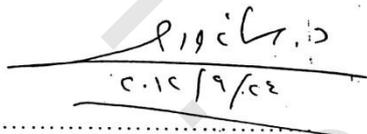
Using a power of 80% to detect a significant difference in mean time for sensory regression to S1 from highest sensory level between a group of patients undergoing lower abdomen or lower limb surgery and receiving dexmedetomidine and others receiving fentanyl = 289 minutes, <sup>(1)</sup> standard deviations are 20 minutes and 12.3 minutes, respectively, alpha error = 0.05, using the sample ratio between groups = 1. The minimal required sample size was found to be 45 which mean 15 for each group.

The total sample will be randomly selected & equally allocated among the study groups.

The sample size was calculated using G power software <sup>(2)</sup>.

**Reference:**

1. Gupta R, Verma R, Bogra J et al. Comparative study of intrathecal dexmedetomidine and fentanyl as adjuvants to bupivacaine. J Anaesth Clin Pharmacoln 2011; 27: 339-43.
2. Daniel W. Biostatistics. A foundation for analysis in the health science. 6th edition, NY: John Wiley and sons, Inc; 1995.

  
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# **ARABIC SUMMARY**

## الملخص العربي

جعلت بساطة أسلوب التخدير الشوكي وموثوقيتها واحدة من التقنيات المفضلة في جراحات أسفل البطن و الأطراف السفلى. ولكن في حالة انتهاء تأثير التخدير الشوكي غير المتوقع في وقت مبكر أو طول مدة العملية يمكن أن يسبب الألم أثناء العملية. و لذلك فإن زيادة جرعة التخدير الموضعي، أو إضافة المواد الأفيونية للتخدير الشوكي قد تكون مفيدة لإطالة مدة التخدير ولكن قد تتسبب في عدم استقرار الديناميكية الدموية، والغثيان، واحتباس البول، وخمول في الجهاز التنفسي وتأخر عودة الحركة في الأطراف السفلى، ولذلك برزت الحاجة إلى عقارات مكملة للعقارات الموضعية.

وكان **الهدف** من هذه الدراسة هو مقارنة إضافة عقار الديكسميديتوميدين أو الفنتانيل إلى عقار البيوبيفاكين في التخدير الشوكي بشأن ما يلي: بداية تأثير العقار على الإحساس والحركة، ومدة تأثيره على الإحساس والحركة وتأثيره على العلامات الحيوية، وتأثيره على تسكين الألم و على حدوث المضاعفات.

وقد أجريت الدراسة على ٦٠ مريضاً داخل مستشفيات جامعة الإسكندرية والمقرر عقدها في جراحات أسفل البطن والأطراف السفلى. تم تقسيمهم إلى ثلاث مجموعات:

المجموعة (ب): تم إعطاء المرضى ٣ ميللي (١٥ مجم) من عقار البيوبيفاكين (عالي الكثافة) ٠,٥% + ٠,٥ ميللي من محلول الملح الطبيعي داخل الأم الجافية.

المجموعة (ف): تم إعطاء المرضى ٣ ميللي (١٥ مجم) من عقار البيوبيفاكين (عالي الكثافة) ٠,٥% + ٠,٥ ميللي (٢٥ ميكروجرام) من عقار الفينتانيول (الخالي من المواد الحافظة) داخل الأم الجافية.

المجموعة (د): تم إعطاء المرضى ٣ ميللي (١٥ مجم) من عقار البيوبيفاكين (عالي الكثافة) ٠,٥% + ٠,٥ ميللي (٥ ميكروجرام) من عقار الديكسميديتوميدين المخفف (الخالي من المواد الحافظة) داخل الأم الجافية.

تم تقييم المرضى قبل إجراء التدخل الجراحي عن طريق السؤال عن التاريخ المرضي و توقع الكشف الاكلينيكي و اجراء التحاليل والفحوصات الطبية.

تم إعطاء المرضى أوية مضادة لحموضة المعدة في تحضيرها قبل العملية. تم توصيل المرضى بأجهزة لقياس العلامات الحيوية قبل إجراء التخدير الشوكي و كانت عبارة عن رسم قلب لمعرفة معدل النبض ، متوسط ضغط الدم الشرياني، نسبة تشبع الدم الشرياني بالأكسجين.

تم إعطاء المرضى محلول رينجر الوريدى (١٠ مللى لكل كيلوجرام). تم إعطاء التخدير الشوكي في وضع الجلوس بين الفقرات القطنية الثالثة و الرابعة في منتصف الجسم أو محاز للوسط بواسطة إبرة بزل (كويكي) مقاس ٢٥ مع أخذ كل إحطياطات التعقيم و تم حقن العقارات، كل حسب مجموعته. تم استلقاء المرضى على ظهورهم عقب إعطاء التخدير الشوكي و تم توصيل الأوكسجين (٤ لتر/الدقيقة) لهم بواسطة قناع الأوكسجين.

تم قياس البيانات التالية:

**بيانات المريض:** ١- السن (بالسنوات) ٢- الطول (بالسنتمترات). **مدة العملية:** (بالدقائق). **العلامات الحيوية (قبل و أثناء و بعد العملية):** معدل النبض، متوسط ضغط الدم الشرياني، نسبة تشبع الدم الشرياني بالأكسجين.

تم دراسة **الغلق العصبى** عن طريق : قياس بداية فقدان الإحساس، أعلى مستوى لفقدان الإحساس ومدة فقدان الإحساس. كما تم قياس تسكين الألم بعد العملية وتم قياسه عن طريق تحديد درجة الألم باستخدام تدريج المقياس المرئى ، و أيضا تم تقدير المدة التى احتاج المريض بعدها للمسكنات وجرعة المسكنات التى تناولها المريض فى الأربعة والعشرين ساعة الأولى بعد العملية.

دراسة الأثر على **الارتخاء العضلى** عن طريق : قياس بداية فقدان الحركة و مدة فقدان الحركة.

كذلك تم ملاحظة وتسجيل **المضاعفات** التى حدثت أثناء وبعد العملية.

لوحظ من هذه الدراسة الآتى: عدم وجود تغيرات ملحوظة بين المجموعات بالنسبة إلى السن، الطول، الجنس، مدة العملية أو الحالة الصحية العامة.

كان هناك إنخفاض إحصائى ملحوظ فى معدل النبض عند الدقيقة ٤٥ فى المجموعة (د) عن المجموعة (ف) (بدلالة إحصائية=٠,٠٤٥) ، كما تكرر ذلك عند الدقيقة ٦٠ و ٩٠ (بدلالة إحصائية=٠,٠٢٧ و ٠,٠٤٧ بالتوالى) فقط. بمقارنة المجموعة (ف) و (ب) كان الإنخفاض فى المجموعة (ب) عند الدقيقة ٣٠ و ٤٥ (بدلالة إحصائية=٠,٠٤٠ و ٠,٠٤٨ بالتوالى).

بالنسبة لمتوسط ضغط الدم الشرياني كان هناك انخفاض إحصائي في المجموعة (د) عن المجموعة (ف) عند الدقيقة ٤٥ (بدلالة إحصائية=٠,٠٣١) و كان هناك انخفاض إحصائي في المجموعة (ب) عن المجموعة (د) بعد إعطاء التخدير الشوكي و عند الدقيقة ١٥ (بدلالة إحصائية=٠,٠٠٦ و ٠,٠٤٤) وأيضا في المجموعة (ب) عن المجموعة (ف) بعد إعطاء التخدير الشوكي و عند الدقيقة ١٥ (بدلالة إحصائية=٠,٠٠٣ و ٠,٠٥٠ بالتوالي).

لم يكن هناك أى اختلاف إحصائي بين المجموعات بالنسبة لنسبة تشبع الدم الشرياني بالأكسجين.

أما بالنسبة لبدائية فقدان الإحساس فكانت نتائج المجموعة (د) الأسرع بالمقارنة بالمجموعتين الأخرتين (بدلالة إحصائية=٠,٠٠٠)

أما بالنسبة لبدائية فقدان الحركة فكانت نتائج المجموعة (د) الأسرع بالمقارنة بالمجموعتين الأخرتين (بدلالة إحصائية=٠,٠٠) كما كانت نتائج المجموعة (ف) أسرع من المجموعة (ب) (بدلالة إحصائية=٠,٠١٦)

كانت مدة فقدان الإحساس و مدة فقدان الحركة لفترة أطول في المجموعة (د) بالمقارنة بالمجموعة (ف) (بدلالة إحصائية=٠,٠٠٠) و أيضا كانت نتائج المجموعة (ف) أطول من المجموعة (ب) (بدلالة إحصائية=٠,٠٠٠)

كانت قراءات تدرج المقياس المرئي في المجموعة (د) منخفضة عن المجموعتين الأخرتين كما كانت منخفضة في المجموعة (ف) عن المجموعة (ب).

احتاج عدد أقل إلى المسكنات في المجموعة (د) عن في المجموعتين الأخرتين و كان ذلك في وقت متأخر عن المجموعة (ف) و (ب) (بدلالة إحصائية=٠,٠١٣ و ٠,٠٠٢ بالتوالي). احتاج عدد أقل إلى المسكنات في المجموعة (ف) عن المجموعة (ب) و كان ذلك في وقت متأخر عنها (بدلالة إحصائية=٠,٠١٥). لم يكن هناك احتياج لأى مسكنات في المجموعة (د) بنسبة ٧٥% و في المجموعة (ف) ٥٠% و في المجموعة (ب) ١٠%.

احتاجت مرضى المجموعة (د) إلى جرعات أقل من مسكن الديكلوفيناك صوديوم عن المجموعتين الأخرتين (بدلالة إحصائية=٠,٠٣٠ و ٠,٠٠٠ بالتوالي) و كذلك كان احتياج المجموعة (ف) أقل من المجموعة (ب) (بدلالة إحصائية=٠,٠٠٠)

لم يحتاج مرضى المجموعة (د) إلى مسكن البيثيديين. و كذلك كان احتياج مرضى المجموعة (ف) لجرعات أقل من المجموعة (ب) من نفس العقار (بدلالة إحصائية=٠,٠٢٦).

لم يكن هناك أى اختلاف إحصائي بين المجموعات بالنسبة لحدوث المضاعفات و هي قلة معدل النبض، انخفاض في ضغط الدم، الغثيان، القيء، الرعشة، الحكة، هبوط معدل التنفس و انخفاض درجة الوعي. كما لم يكن هناك أى اختلاف إحصائي بين المجموعات بالنسبة لجرعات عقارى الأتروبين و الإفدرين.

#### الاستنتاجات:

١. بداية فقدان الإحساس و الحركة أسرع عند استخدام ٥ ميكروجرام من عقار الديكسميديتوميدين من استخدام ٢٥ ميكروجرام من عقار الفينتانيل داخل الأم الجافية بالإضافة إلى عقار البيوبيفاكين.
٢. مدة فقدان الإحساس و الحركة أطول عند استخدام ٥ ميكروجرام من عقار الديكسميديتوميدين من استخدام ٢٥ ميكروجرام من عقار الفينتانيل داخل الأم الجافية بالإضافة إلى عقار البيوبيفاكين.
٣. أدى استخدام عقار الديكسميديتوميدين داخل الأم الجافية بالإضافة إلى عقار البيوبيفاكين إلى تسكين الألم لفترة أطول بعد انتهاء العملية.
٤. استخدام عقار الديكسميديتوميدين داخل الأم الجافية بالإضافة إلى عقار البيوبيفاكين أدى إلى احتياج أقل من المسكنات في فترة ما بعد العملية.
٥. لم يؤدي استخدام عقار الديكسميديتوميدين أو عقار الفينتانيل داخل الأم الجافية بالإضافة إلى عقار البيوبيفاكين إلى أى حمول في درجة الوعي.
٦. كانت المضاعفات قليلة و مقبولة عند استخدام عقار الديكسميديتوميدين.

#### التوصيات:

- ١- إضافة عقار الديكسميديتوميدين إلى عقار البيوبيفاكين (عالي الكثافة) ٠,٥% يمكن أن يؤخذ في الاعتبار كاستخدام روتيني في التخدير الشوكي لإزالة الألم بالعمليات و بعدها.
- ٢- استكمال الدراسات المستقبلية لمعرفة مدى كفاءة إضافة عقار الفينتانيل مع عقار الديكسميديتوميدين إلى عقار البيوبيفاكين (عالي الكثافة) ٠,٥% في التخدير الشوكي بالنسبة لتحسين إزالة الألم.
- ٣- إمكانية استخدام عقار الديكسميديتوميدين بحدن في مجموعات عمرية مختلفة و في أمراض طبية مختلفة و في فترة الحمل.

# الملخص العربي

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البوبيفاكين تحت الأم الجافية

مقدمة من

وفاء حسن أحمد

بكالوريوس الطب والجراحة - جامعة الإسكندرية، ٢٠٠٧

للحصول على درجة

الماجستير

فى

التخدير والعناية المركزة الجراحية

موافقون

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الأم الجافية

رسالة علمية

مقدمة إلى كلية الطب- جامعة الإسكندرية  
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الماجستير

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