The Pharma Innovation

ISSN: 2277- 7695
CODEN Code: PIHNBQ
ZDB-Number: 2663038-2
IC Journal No: 7725

Received: 27-11-2013
Accepted: 27-01-2014

Vol. 2 No. 12. 2014
Online Available at www.thepharmajournal.com

THE PHARMA INNOVATION - JOURNAL

Surgical stress metabolic markers dynamics in different kinds of anesthesiological management of surgeries on rectal cancer

Ivan I. Titov [*1], Khrystyna I. Popivnyak [1], Marta B. Grynovska [1]

1. Department of Anesthesiology and Intensive Care. Ivano-Frankivsk, National Medical University, Ukraine. [E-mail: titovdoc@rambler.ru]

Surgeries on rectal cancer are a strong stress-provoking factor, which triggers excessive glucose and cortisol release into the bloodstream. This justifies research on how to improve anesthesiological protection of the patients from surgical stress and provide adequate postoperative analgesia to reduce the number of complications and improve outcome. The patients were randomly divided into control group and 2 test groups, who underwent surgeries on rectal cancer and received IV and combined anesthesia respectively. Blood samples for glucose and cortisol were drawn at different stages of research. Obtained results were statistically verified. Glucose and cortisol level dynamics suggests there is a difference between anesthesia kind and efficacy of surgical stress prevention.

Keyword: epidural anesthesia, ropivacaine, surgical stress, rectal cancer, cortisol, glucose.

1. Introduction

Approximately 6 millions of cancer cases are diagnosed annually and more than 4 million have lethal outcome, which accounts for 10% of global lethal outcome [1]. According to WHO, 20 millions of new cancer cases will be diagnosed annually by 2020 [2, 3].

Currently there is a lack of comprehensive knowledge in the anesthesiological management of surgical oncology in Ukraine. Therefore, the relevance of research on adequate anesthesiological management of rectal cancer surgeries and postoperative analgesia is obvious. [4, 5]. In the course of surgical intervention glucose and cortisol are released into the bloodstream as a natural response to stress. Measurement of these values provides a quick and objective assessment of the degree of stress as well as treatment adequacy and efficacy [6].

We have studied glucose and cortisol level dynamics at different stages of surgical intervention in 2 test groups, who underwent standard anesthesiological management: IV anesthesia with endotracheal intubation and mechanical ventilation (I group) and spinal with superficial general anesthesia, endotracheal intubation and mechanical ventilation (II group).

2. Materials and Methods

120 patients with rectal cancer have been observed: 72 (60%) male patients and 48 (40%) female patients. Age range 45-69 years. The patients were randomly divided in 2 groups. The I group (n=50) received IV anesthesia (propofol+fentanyl) with muscle relaxation (atracurium besilate) and mechanical ventilation, postoperative analgesia was achieved through the use of opioid analgesics. The II group (n=50) received prior colloid infusion (Refortan 6% 500 ml + Sterofundin 500 ml) 15 ml/kg body weight. Then with the use of disposable "Espocan" (B|Braun, Germany), a puncture with L_2-L_3 access was performed in a seated position. Epidural space was reached and 15 mg

bupivacaine was injected intrathecally (Marcain Spinal Heavy 0.5%, Astrazeneca, UK) with subsequent catheterization of epidural space. Epidural catheter was left in place along the vertebral column and to the left shoulder. Induction and maintenance of anesthesia was achieved with propofol (Propofol Lipuro 1%, B|Braun, Germany) and atracurium besylate (Intuban, Farmac, Ukraine) at doses corresponding to bispectral index 40-60 (BIS Vista, USA- „Xenko" Ukraine). Mechanical ventilation device „Bryz" (Burevisnyk, Ukraine) was used for normal ventilation mode, P_{et} CO_2 38-40 mm.Hg. Opioid analgesics (fentanyl) were not prescribed intraoperatively. Analgesia was achieved through spinal anesthesia. Surgical intervention duration was about 90-100 minutes. Postoperative analgesia was achieved with local anesthetic ropivacaine (Naropin, Astrazeneca, UK), which has been introduced epidurally in the ICU for 5 days. Obtained results were statistically verified by means of Student's t-criterion.

3. Results

Blood glucose levels in patients of control group were within normal limits. However, there has been a statistically significant difference between median baseline values in control group and median baseline values in two test groups. The contrastive analysis with the help of Kruskal-Wallis test showed that baseline values of the control group were lower than those of the test groups. Furthermore, blood samples of the control group were drawn during routine appointment with general practitioner and blood samples of the two test groups were drawn prior to surgery on the same day. This suggests that hyperglycemia in the two test groups was in the first place triggered by strong psychological and emotional stress in patients undergoing surgery on rectal cancer as the outcome of surgical intervention was unknown.

According to Mann-Whitney criterion there was no statistically credible difference between baseline values of two test group.

After induction and skin incision blood samples were repeatedly drawn in patients of both test groups. It showed a statistically significant difference with lower values in patients of the second test group, who received with spinal and superficial general anesthesia. Moreover, blood glucose levels in patients of the abovementioned group at the most traumatic stage of the surgery (surgical exposure site) were 6.39±1.87 mmol/l, which is the upper limit of the normal value. Blood samples were repeatedly drawn in patients of both test groups at the end of surgical intervention during the wound bandaging. Difference between two test groups was established according to Mann-Whitney (W=29.0; P=4.96E-10) criterion, which indicates that the patients of the second test group, who received combined anesthesia (spinal and superficial general anesthesia).

Patients of the first test group who received general IV multicomponent anesthesia showed hyperglycemia (8,14±1,70 mmol/l), which, considering the first test group glucose levels at this stage, suggests inadequate patient protection from surgical stress with negative metabolic consequences, represented by elevated blood sugar.

Table 5.1: Blood glucose (mmol/l) dynamics in control and test groups

Blood sampling stage	Blood glucose (mmol/l), M±SD; Me (0,5L; 0,5U)			Statistical comparison criteria	
	Control group, n=50	Group I (IV anesthesia+ mechanical ventilation) n=50	Group II (combined spinal and epidural anesthesia +mechanical ventilation) n=50	Kruskal-Wallis	Mann-Whitney
Baseline values	4,11±0,66; 4,12	8,76±2,36; 8,5	8,99±2,29; 8,9	TS=79,0 P=0,00	W=484,0 P=0,62

	(3,6; 4,52)	(7,2; 10,5)	(7,5; 11,2)		
Beginning of the surgery (after surgical exposure)	-	8,67±1,89; 8,35 (7,2; 9,3)	6,39±1,87; 6,1 (5,2; 7,4)	-	W=154,0 P=0,00001
End of the surgery (wound bandaging)	-	8,14±1,70 7,6 (6,9; 9,4)	5,52±0,73 5,57 (5,1; 6,1)	-	W=29,0 P=4,96E-10
24 hours after surgery	-	6,84±1,32 6,55 (6,1; 7,4)	5,17±0,43 5,1 (4,9; 5,3)	-	W=79,5 P=4,23E-8

TS - Test Statistics

24 hours after the surgical intervention a statistically significant difference in blood glucose levels in both test groups, which is proved by Mann-Whitney criterion (Table 5.1). II test group values as previously were within normal limits.

The control group blood cortisol level was within normal limits. However, a statistically significant difference was observed between median baseline values of the control and test groups according to Kruskal-Wallis test (Fig. 5.1).

A significant decrease in cortisol level was observed in control group patients during routine appointment with general practitioner blood sampling. On the contrary, three times higher cortisol levels in patients of both test groups were observed during blood sampling shortly before the surgery. This suggests an expressed response to stress, anxiety and fear, associated with unknown outcome of the surgery on rectal cancer and possible postoperative complications. (Table 5.2).

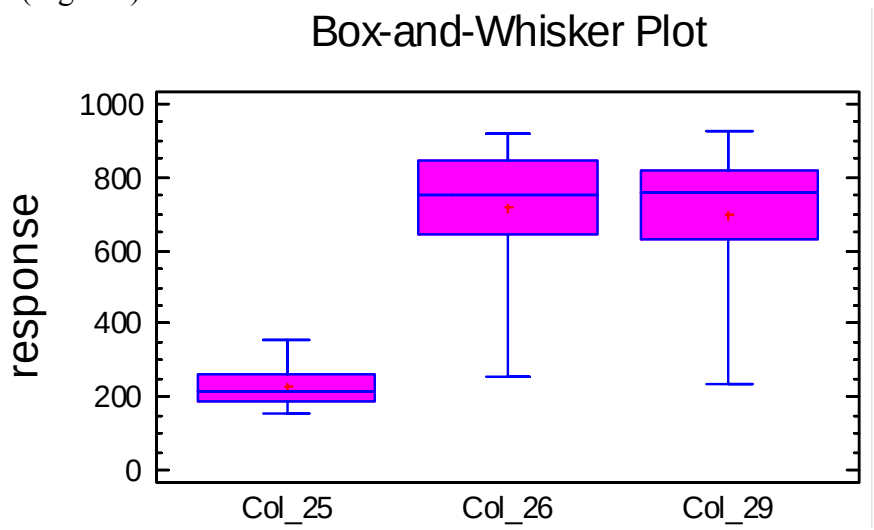

Fig 5.1: Median blood serum cortisol values in patients of control and test groups

According to Mann-Whitney criterion, there was no statistically credible difference between baseline values of both test groups.

After induction and skin incision a blood sample was repeatedly drawn in patients of both tests groups for cortisol level detection. It has been established that patients of the I test group, who received IV anesthesia with mechanical ventilation, showed a statistically credible decrease in cortisol level (TS=3.6; P=0.003), median decrease 159.8 (105.2; 220.2) ng/ml. II group patients showed a similar tendency. A considerable, statistically credible decrease in cortisol level was observed if compared to reference values (CT=3.6; P=0.003), median decrease 392.2 (361.0; 421.9) ng/ml.

Table 5.2: Blood serum cortisol dynamics in control and test groups

Blood sampling stage	Blood serum cortisol (ng/ml)M±SD; Me (0,5L; 0,5U)			Statistical comparison criteria	
	Control group, n=50	Group I (IV anesthesia + mechanical ventilation, n=50	Group II (spinal anesthesia+ mechanical ventilation), n=50	Kruskal-Wallis	Mann-Whitney
Baseline values	229,0±60,3 215,6 (185,8; 264,4)	720,1±167,1 754,1 (645,8; 842,1)	697,4±187,8 755,2 (628,2; 815,3)	TS=50,2 P=1,24E-11	W=288,0 P=0,64
Beginning of the surgery (after surgical exposure)	-	592,4±111,5 607,5 (524,1; 654,2)	349,7±81,3 345,1 (310,3; 384,7)	-	W=26,0 P=2,9E-8
End of the surgery (wound bandaging)	-	472,3±111,7 468,2 (402,3; 551,3)	253,6±47,3 255,4 (207,5; 274,5)	-	W=21,0 P=1,6E-8

TS - Test statistics

After the surgery blood serum cortisol level in the I test group was gradually decreasing and has reached 472,3±111,7 ng/ml. II test group showed greater decrease in cortisol level at the end of surgery. There was no statistically credible difference between II test group and control group cortisol levels.

Blood cortisol levels dynamics in 2 test groups shows a statistically credible difference. (Table 5.2). Furthermore, patients of II test group, who received combined anesthesia, showed results closer to normal values. A similar tendency was observed at the end of surgical intervention (Table 5.2).

The research shows that blood cortisol levels indicate response to stress. Induction of general and combined (regional+general) anesthesia reduces blood cortisol levels. However, patients of II test group, who received combined anesthesia, showed results closer to normal values. Therefore, according to blood cortisol levels dynamics combined regional (spinal) and general anesthesia can be more effective in prevention of surgical stress and operational stress-related complications (GIT lesions, transitory renal dysfunction, hypercatabolism, cardiovascular disorders).

4. Conclusions

1. Surgeries on rectal cancer are a strong stress-provoking factor, which triggers hyperglycemia and hypercortisolemia.
2. IV anesthesia with total muscle relaxation and mechanical ventilation during abdominoperineal resection, rectal extirpation or anterior resection of rectum fail to provide adequate patient protection from surgical stress.
3. Combined spinal (bupivacaine) and superficial general anesthesia with total muscle relaxation and mechanical ventilation provides a better protection from negative surgical stress according to glucose and cortisol concentration and thus prevents intraoperational and operational stress-related complications (GIT lesions, transitory renal dysfunction, hypercatabolism, cardiovascular disorders).
4. The research will contribute to further investigations of analgesia nociception index dynamics during the surgery on rectal cancer and correlation analysis between blood glucose and cortisol levels.

5. References

1. Ribakov EG. Rectal cancer — modern approach. Coloproctology, 2007; 3 (21): 29 – 38.
2. Cagir B. Rectal cancer. Medical Oncology J., 2009.

3. Saito N. Function Preserving Surgery for lower rectal cancer involving lower urinary tract in male patients.World Journal of Colorectal Surgery: 2008; 1(1), Article 11.
4. Duke J. Anesthesia secrets. Hanley and Belfus inc./Philadelphia, 2nd edition. – 2002.
5. Handbook of spinal anaesthesia and analgesia. BG. Covino, DB. Scott, DH. Lambert. Mediglobe SA, 1994.
6. Vironen J.H., Kairaluoma M. Impact of functional results on quality of life after rectal cancer surgery. Dis Colon Rectum, 2006; 49: 568-578.
7. Christian CK, Kwaan MR, Betensky RA, Breen EM, Zinner MJ, Bleday R. Risk factors for perineal wound complications following abdominoperineal resection. Dis Colon Rectum. 2005;48(1):43–48.
8. Carsin AE , Sharp L, Cronin-Fenton D P.Inequity in colorectal cancer treatment and outcomes: a population-based study. British Journal of Cancer, 2008; 99: 266–274.
9. Feuer A EJ, Thun MJ. Cancer statistics, 2005. CA Cancer J Clin. 2005; 55: 10-30.
10. Manjoney D L, Koplewitz M J, Abrams J S. Factors influencing perineal wound healing after proctectomy. Am J Surg. 1983;145(1):183–189.
11. Ben-Eliyahu S.The promotion of tumor metastasis by surgery and stress: Immunological basis and implications for psychoneuroimmunology. Brain Behav Immun 2003; 17(1):27–36.
12. Gupta GP, Massague J: Cancer metastasis: Building a framework. Cell 2006; 127:679 –95
13. Fedorov FD. Clinical surgical proctology, Moscow Publishers, 1994.