JOURNAL OF CONTEMPORARY MEDICINE

DOI: 10.16899/gopctd.531288 J Contemp Med 2019;9(1):21-26

Original Article / Orjinal Araştırma



The effect of intraoperative fluid volume on postoperative vomiting in pediatric patients undergoing otorhinolaryngological surgery

Kulak burun boğaz cerrahisi geçiren pediatrik hastalarda intraoperatif uygulanan sıvı volümünün postoperatif kusmaya etkisi

Sinan Yılmaz,¹ Dilek Yılmaz²

¹Department of Anaesthesiology and Reanimation, Adnan Menderes University Faculty of Medicine, Aydın, Turkey ²Department of Pediatrics, Adnan Menderes University Faculty of Medicine, Aydın, Turkey

Abstract

Introduction: Intravenous fluid therapy is recommended in international guidelines to prevent the postoperative nause and vomiting in children. But the proper amount of fluid therapy is not clear yet. The aim of this observational study is to evaluate the effect of intraoperative intravenous fluid administration on postoperative vomiting in children after adenoidectomy, tonsillectomy and adenotonsillectomy.

Methods: 160 children, aged between 2-10 years, undergoing elective adenoidectomy, tonsillectomy and adenotonsillectomy under general anaesthesia were randomized to administration of intraoperative infusions of low-volume (group 1=10 ml/kg/h) or high volume (group 2=20/ml/kg/h) 0.9% NaCl solution. A standardized anaesthesia protocol was performed. The vomiting and pain scores of all patients were evaluated.

Results: The frequency of vomiting in patients who received limited fluid in group 1 was significantly higher than those in group 2 at first and 15th minute in post-anesthesia care unit (PACU). The Children's Hospital East Ontario Pain Scale (CHEOPS) scores at 1st and 15th minutes of PACU were significantly higher in group 2 than in group 1 (p=0.021, p=0.026) However, no significant difference was found between the two groups regarding CHEOPS scores at the further time-points.

Discussion and Conclusion: Our results suggest that intraoperative administration of 0.9% NaCl solution at a rate of 20 ml/kg/ h can be useful in reducing mild vomiting complaint in the postoperative first and 15th minutes in children undergoing adenoidectomy, tonsillectomy, and adenotonsillectomy

Keywords: Adenotonsillectomy; children; intravenous fluid; postoperative vomiting

Özet

Amaç: Çocuklarda postoperatif bulantı ve kusmayı önlemek için, uluslararası kılavuzlarda intravenöz sıvı tedavisi önerilmektedir. Fakat, sıvı tedavisinin uygun miktarı henüz belli değildir. Bu gözlemsel çalışmanın amacı, adenoidektomi, tonsillektomi ve adenotonsillektomi yapılan çocuklarda intraoperatif intravenöz sıvı uygulamasının postoperatif kusma üzerine etkisini değerlendirmektir.

Gereç ve Yöntem: Genel anestezi altında elektif adenoidektomi, tonsillektomi ve adenotonsillektomi yapılacak, 2-10 yaş arası 160 çocuk, intraoperatif infüzyon uygulamasına göre, düşük volümlü (grup 1=10 ml/kg/s) veya yüksek volümlü (grup 2=20 ml/kg/s) %0.9 NaCl solüsyonu olarak randomize edildi. Standart bir anestezi protokolü uygulandı. Tüm hastaların kusma ve ağrı skorları değerlendirildi.

Bulgular: Anestezi sonrası bakım ünitesinde (PACU) birinci ve 15. dakikadaki kusma sıklığı, kısıtlı sıvı alan grup 1 hastalarda grup 2 hastalardan anlamlı derecede yüksekti. Anestezi sonrası bakım ünitesinde (PACU) 1. ve 15. dakikada çocuk hastanesi doğu ontario ağrı ölçeği (CHEOPS) skorları, grup 2'de grup 1'den anlamlı yüksek bulundu (p=0.021, p=0.026). Ancak, iki grup arasında CHEOPS skorlarıyla ilgili daha sonraki zamanlarda anlamlı bir fark bulunmadı.

Sonuç: Sonuçlarımız, intraoperatif 20 ml/kg/saat % 0.9 NaCl solüsyonu uygulamasının, adenoidektomi, tonsillektomi ve adenotonsillektomi uygulanan çocuklarda, postoperatif birinci ve 15. dakikalarda hafif kusma şikayetini azaltmada yararlı olabileceğini desteklemektedir.

Anahtar Sözcükler: Adenotonsillektomi; çocuklar; intravenöz sıvı; postoperatif kusma.

Corresponding (*İletişim*): Sinan Yılmaz, Adnan Menderes Üniversitesi Tıp Fakültesi, Anesteziyoloji ve Reanimasyon Anabilim Dalı, Aydın, Turkey E-mail (*E-posta*): dr_snnylmz@hotmail.com



A denoidectomy and tonsillectomy are the most frequently performed otorhinolaryngology operations in children. ^[1] Postoperative nausea and vomiting (PONV) are seen in 25-30% of these patients, and this incidence may increase up to 80% in children under risk.^[2,3] PONV is the most critical and common complication after adenoidectomy and tonsillectomy and causes postoperative delay in the patient's exit from operation room.

Postoperative gastrointestinal dysfunction (PGD) is defined as the inability to tolerate enteral foods postoperatively which were well-tolerated before surgery.^[3] Ischemic, metabolic, neurogenic, pharmacological or mechanical factors have been reported to play role in the development of PGD, pathogenesis of which is unclear.^[3] Generally accepted opinion is that decrease in the perfusion of the microvilli and the development of intestinal ischemia in the perioperative period due to hypovolemia is the underlying mechanism. Nevertheless, the intestinal ischemia improves within 3 days postoperatively.

The drugs used in antiemetic prophylaxis have many side effects, and they are often inadequate in preventing vomiting as well as increasing the cost.^[4] However, it is known that providing adequate hydration during the perioperative period can prevent PONV. Although there are many studies on fluid therapy in adults, the number of studies in children is limited.^[4,5] In this study, we aimed to investigate the effect of fluid support with 0.9% NaCI intraoperatively on the incidence of PONV in children undergoing adenoidectomy, tonsillectomy or adenotonsillectomy.

Materials and Method

This study was conducted with 160 children between 2-10 years of age who underwent elective adenoidectomy, tonsillectomy, and adenotonsillectomy under general anesthesia, American Society of Anesthesiology (ASA) I-II, between January 1, 2018, and May 31, 2018. The study was approved by the local ethics committee of our University (2017/1280). The informed consent form was obtained from the parents of each patient. Results from the power analysis based on a research of Elgueta, M.F. et al.^[4] revealed that a minimum sample size of 77 cases in each group was required in order to obtain an effect size of 20% (difference between vomiting rates) and power of 80% with a p value of less than 0.05. The study was designed as a observational, randomized and double-blind study. This trial was registered with ClinicalTrials.gov. (NCT03485443).

Children under antiemetic or opioid therapy preoperatively, and those with drug hypersensitivity history, neurological disease, diabetes mellitus, congestive heart failure, gastroesophageal reflux or obesity were not included in the study. Previous nausea-vomiting history, risk factors, and family history of PONV were questioned in all participants.

All children were premedicated with 0.3 mg/kg midazolam orally 30 min before induction of general anesthesia. In the operating room, after routine monitorization, general anesthesia was induced with 8% sevoflurane in 100% oxygen by

a face mask under spontaneous ventilation. Before tracheal intubation, fentanyl 1µg/kg and rocuronium 0.6 mg/kg were administered to all patients. Then, anesthesia was maintained with 40% mixture of oxygen/nitrous oxide and 2% sevoflurane.

The patients were randomized with the help of random numbers obtained by computer and were divided into two groups. Group 1 consisted of patients to receive low volume (10 ml/ kg/h) of 0.9% NaCl and patients to receive high volume (20 ml/ kg/h) of 0.9% NaCl formed group 2. Patients and anesthesiologists were blinded to the group information where patients were involved. All children were administered i.v. paracetamol 10 mg/kg for postoperative analgesia during anesthesia. The residual neuromuscular blockade was reversed with a mixture of neostigmine 0.04 mg/kg and atropine 0.02 mg/kg. 0.9% NaCl solution infusion was stopped after tracheal extubation and all children were transferred to post-anesthesia care unit (PACU). Evaluation of nausea and vomiting was performed by a four-point scale; 0: No nausea and/or vomiting, 1: mild nausea and/or vomiting which does not require treatment, 2: nausea and/or vomiting requiring treatment and 3: vomiting resistant to antiemetic treatment. All children's retching efforts (nausea and / or vomiting) was noted at the 1st, 15th, and 30th, minutes of PACU and at the 1st, 4th, and 6th hours of clinical follow-up by a researcher who was blind to the patient's group information. When vomiting was detected at any time, postoperative vomiting was accepted as 'positive'. Besides, antiemetic treatment (i.v metoclopramide 0.15 mg/kg) was administered to all patients with vomiting scale score ≥ 2 points. No child was allowed to take intravenous or oral fluid in the PACU. The children who participated in the study were evaluated in PACU for postoperative complications.

Trained PACU nurses evaluated the pain severity of all children according to the Children's Hospital East Ontario Pain Scale (CHEOPS) (Table 1).^[6] Also, CHEOPS scores of all children were recorded at the 1st, 15th, and 30th minutes of PACU and at the 1st, 4th, and 6th hours of clinical follow-up by a researcher who was blind to the patient's group information. When CHEOPS score was determined \geq 8 points, 1 mg/kg meperedine was administered. In patients who did not develop any surgical complication, oral intake was allowed 6 hours after surgery.

Statistical analysis

The Kolmogorov-Smirnov test was used to assess the normality of distribution in numeric variables. For the numeric variables that were normally distributed, the comparison between two groups was conducted by independent sample t-test and descriptive statistics was presented as the mean±standard deviation. For the numeric variables that were not normally distributed, the comparison between two groups was conducted by Mann–Whitney U test and descriptive statistics were presented as median (interquartile range). To analyze the categorical data, the Chi-square test was used and descriptive statistics were presented as frequency (%). The logistic regression with a forward stepwise variable selection

Table 1. Modified Children's Hospital of Eastern Ontario Pain Scale (CHEOPS)						
Score	0	1	2			
Cry	No cry	Crying, moaning	Scream			
Facial	Smiling	Neutral	Grimace			
Verbal	Positive statement	Negative statement	Suffering from pain			
Torso	Neutral	Variable, taot, upright	Streched			
Legs	Neutral	Kicking	Streched, continuous move			

Table 2. Demographic data

	Group 1 (10 ml kg⁻¹ h⁻¹) (n=80)	Group 2 (20 ml kg ⁻¹ h ⁻¹) (n=80)	р
Sex n (%)			
Male	51 (63.7%)	52 (65%)	0.869
Female	29 (36.3%)	28 (35%)	
Age (year) (mean±sd)	5.4±2.3	5.6±2.5	0.543
Weight (kg) median (IQR)	19 (11.5)	18.7 (9)	0.921
Height (cm)	111.2±19.4	112.2±20.6	0.641
Surgery n(%)			
Adenoidectomy	56 (70%)	56 (70%)	
Tonsillectomy	4 (5%)	2 (2.5%)	0.683
Adenotonsillectomy	20 (25%)	22 (27.5%)	
Duration of the surgery (min.) (mean±sd)	41±16.6	40.8±15.6	0.870
Total fluid (ml) median (IQR)	110 (98.8)	255 (207)	0.001
Fasting time (hour) (mean±sd)	8.8±1.6	9.2±1.7	0.219

IQR: interquartile range

was used to predict vomiting. A p value of less than 0.05 was considered as statistically significant.

Results

A total of 160 children (n=103, 64% male) were included in the study and were randomized into two groups. Each group consisted of 80 children. There was no difference between the two groups in terms of demographic data (Table 2). 85% of the children who participated in the study were older than 3 years of age. The proportion of children older than 3 years was similar between the two groups (86% vs 83%, p=0.825). The most frequently performed surgical operation was adenoidectomy (70%) (Table 2). The study groups were similar in terms of the type of surgery performed (p=0.683). In addition, the duration of surgery was comparable between the groups (p=0.870). The mean fasting time of whole study population was 9.0 \pm 1.6 hours and that of the two study groups was similar (Table 2).

28% (n=45) of the children who participated in the study had vomiting at any time postoperatively. The frequency of vomiting was in patients who received limited fluid in group 1 was significantly higher than those in group 2 (29/80 vs. 16/80, p=0.022) (Figure 1). In addition, only 7 (4.3%) children in the whole study sample required antiemetic treatment due to vomiting.



Figure 1. Comparison of the vomiting rate of both study groups at any time.

In the evaluation of vomiting in PACU according to time, at the first minute in PACU, we observed that the rate of mild vomiting-not requiring treatment, vomiting requiring treatment, vomiting resistant to antiemetic treatment were higher in group 1 compared to those in group 2 (17.5%, 2.5% and 1.3% vs. 8.8%, 2.5%, and 0%, respectively). Besides, in both groups, only mild-no treatment required was observed at the 15th minute, and vomiting rate was higher in group 1 than in group



Figure 2. Comparison of nausea and vomiting severity between groups according to time-points.





2 (22.5% vs. 5%, p=0.001, Figure 2). In addition, there was no significant relation between nausea-vomiting and gender in both study groups (p=0.624 and p=0.519 for groups 1 and 2, respectively). In the PACU, 84.4% of the children did not experience any problem. 11 children had agitation, 9 had sore throat, 2 had bronchospasm, 2 had epistaxis and 1 had cough complaint during PACU follow-up.

The CHEOPS score was ≥ 8 points in 86.9% (n=139) of all children at any time, and the difference in CHEOPS scores of the two groups was not statistically significant (p=0.061). The median (IQR) CHEOPS scores at 1st and 15th minutes of PACU were significantly higher in group 2 than in group 1 [1st and 15th minutes are 4 (3) points and 3 (4) v.s 2 (3) points and 3 (3) points, p=0.021 and p=0.026, respectively). However, no significant difference was found between the two groups regarding CHEOPS scores at the further time-points (Figure 3).

According to logistic regression analysis, the patient's age older than 3 years (OR=4.372, Cl 1.127-16.955, p=0.033) and the CHEOPS score \geq 8 points (OR=3.996, Cl 1.35-11.827,

Table 3. Results of logistic regression analysis for vomiting					
Parameters	Vomiting (n=160)				
	OR (95% CI)	р			
Age (≥3 years)	4.372 (1.127–16.955)	0.033			
CHEOPS (≥8)	3.996 (1.35–11.827)	0.012			
Groups (20 ml kg ⁻¹)	0.361 (0.168–0.776)	0.009			

CI: Confidence interval; CHEOPS: Children's Hospital East Ontario Pain Scale.

p=0.012) were independent factors to increase nausea-vomiting, while intraoperative 20 ml kg⁻¹ fluid administration (group 2) (OR=0.361, CI 0.168-0.776, p=0.009) was independently related with decrease in nausea-vomiting (Table 3). Moreover, gender, body weight, type of surgery, duration of surgery (\geq 30 min) and fasting time (>8 hours) did not have a significant effect on nausea-vomiting.

Discussion

In this observational study, we demonstrated that i.v fluid supplement (20 ml/kg/h 0.9% NaCl) administered intraoperatively in children undergoing adenoidectomy and/or tonsillectomy is useful in reducing the mild vomiting complaints in the first 15 minutes after surgery. Postoperative nausea-vomiting has been reported in 25-30% of children undergoing surgery and this incidence increases up to 80% in children at risk.^[2,3] In accordance with the literature, we observed the rate of PONV in 28.1% of our study population.

Different results have been reported in the literature on PONV and intraoperative fluid administration in adults and children because the volume and content of the fluid and the time of administration were different in each study. In addition, different types of surgical procedures and different opioid treatments might have resulted in different outcomes.^[7-9] In adults who will undergo thyroidectomy, administration of 30 ml/kg sodium lactate fluid has not been shown to reduce the incidence of PONV and it has been stated that antiemetic treatment is still needed. In another study conducted with adults, it was reported that the administration of 20 ml/kg isotonic electrolyte fluid for 30 minutes before the surgical procedure in patients undergoing short ambulatory surgery under general anesthesia had no effect on postoperative nausea-vomiting at the post-op 30th minute, 60th minute and at discharge.^[9]

Unlike adults, it has been reported that intraoperative additional fluid administration in children is generally useful in preventing PONV.^[4,10] Total body fluid (TBF), extracellular fluid (ECF) and metabolism rates of children are higher than adults. ^[5,10,11] Therefore, the prolonged duration of fluid restriction and insensible fluid loss in children cause hypovolemia more frequently and in a shorter time than in adults.^[5] Consequently, children are more risky than adults in terms of PONV development. In children undergoing strabismus surgery which bears a higher risk for vomiting, the administration of ringer lactate solution at a rate of 30 ml/kg has been shown to reduce the frequency of PONV during postop first 24-hour.^[10] However, another study reported that i.v hydration or home hydration for 24 hours after adenoidectomy did not reduce PONV.^[12] In our study, the rate of vomiting up to postop first 15th minute was found to be less frequent in children who received in-traoperative 0.9% NACI at a rate of 20 ml/kg/h compared to those who received 10 ml/kg/h. However, it was remarkable that most of the PONV detected in the group 1 who received 0.9% NACI at low volume was in the form of nausea and/or mild vomiting not requiring treatment. In addition, there was no difference between the groups regarding the need for antiemetic treatment.

In studies showing that intravenous fluid replacement reduces the incidence and severity of PONV, some mechanisms have been proposed to explain this benefit.^[3,7,8] It has been reported that high volume fluid supplementation in the perioperative period increases the intravascular volume and maintains intestinal mucosal perfusion.[3,4,7,13] In 60 patients undergoing major surgery, it was shown that intestinal perfusion was maintained with perioperative colloidal fluid treatment, and the rate of intestinal hypoperfusion, revealed by gastric tonometry evaluation, decreased from 56% to 7%.^[14] However, there are also publications which suggest that the administration of excess volume (30 ml/kg) may lead to undesirable side effects. ^[15-17] In our study, we did not detect any problems in the postoperative period due to the fluid volume administered. However, the volume of fluid we administered to children in group 2 (20 ml/kg/h) was less than the amount of 'excess volume' (30 ml/kg/h) defined in the literature. We think that the low vomiting rate in the early postoperative period (in the first 15 min), especially in the higher fluid volume group (group 2), may be related to the maintenance of intestinal perfusion.

Preoperative prolonged fasting period and overnight fluid restriction may cause unwanted side effects in children.^[3,18] In particular, hypoperfusion and ischemia of the intestinal mucosa may cause PONV.^[2,3,5,15] It is also known that PONV has a strong association with antidiuretic hormone (ADH), which is released in the postoperative period.^[2] In our study, although we did not make a specific evaluation on the mechanism of PONV development, the mean fasting period of both groups was about 9 hours. Our result was slightly longer than the fasting time recommended by the guidelines. But, the lack of any significant difference between that of groups made the groups similar in terms of these risk factors.

In 2014 PONV guidelines, four independent risk factors for PONV development were defined in children; >30 min of surgery, patient age >3 years, history of PONV and surgery for strabismus.^[5] To reduce PONV, it is recommended to avoid general anesthesia, preferential use of propofol infusion, avoiding nitrous oxide and volatile anesthetics, keeping the perioperative period as short as possible and adequate hydration.^[5] The risk factors for PONV in our study population were that general anesthesia was applied to all children who participated in our study, the duration of surgery was >30 min, and 85% of the children were older than 3 years of age. However, since the study groups were similar concerning these risk factors, the children in both groups were under similar PONV risk. However, the most frequent risk factor for PONV in children enrolled in our study was that the majority of the children were older than 3 years of age and the CHEOPS score was \geq 8 points. We found that the incidence of PONV was less in patients who received i.v fluid supplementation in higher volume (20 ml/kg//h) intraoperatively. However, PONV was not related with gender, body weight, type and duration of surgery.

If the pain is not relieved adequately in the postoperative period, vomiting occurs frequently after short ambulatory surgical procedures.^[4,5] Therefore, in our study, 86.6% of the children with CHEOPS score ≥8 points at any time in the PACU were treated with i.v. meperidine (1 mg/kg). In addition, all patients received i.v. paracetamol 10 mg/kg during anesthesia for postoperative analgesia purpose. It is also known that the opioids used to decrease the postoperative pain by acting on the chemoreceptor trigger zone while increasing the risk of PONV.^[5] Although the groups were similar in terms of meperedine treatment usage, we observed that the CHEOPS score at the first 15th min was higher in group 2 compared to group 1. Eventually, we think that the high fluid volume given in the intraoperative period was helpful in reducing the development of PONV in the postoperative period in group 2 despite more severe pain with high CHEOPS scores.

Drugs used to prevent PONV after ambulatory surgeries increase operating costs.^[19] In our study, although we found that 0.9% NaCl, given in a rate of 20 ml/kg/h in the intraoperative period, was beneficial in reducing PONV development in the early postop period, the rate of antiemetic treatment use was not different between the two groups. Therefore, we do not think that the intraoperative administration of higher supplemental fluid volume (20 ml/kg/h) in children can be an alternative treatment to antiemetic treatments in preventing PONV.

There were some limitations of our study. Firstly, although all participants underwent standard general anesthesia, the lack of anesthesia duration records was a limitation of the study. Secondly, in our study, 15% of the children were younger than 3 years of age. CHEOPS scores, which we used for vomiting scoring and pain assessment, might not provide adequate assessment, especially in young children.

In conclusion, our results suggest that intraoperative administration of 0.9% NaCl solution at a rate of 20 ml/kg/h can be useful in reducing mild vomiting complaint in the postoperative first 15 minutes in children undergoing adenoidectomy, tonsillectomy, and adenotonsillectomy

Acknowledgements: We thank Prof. Dr. İmran Kurt Ömürlü for statistical analysis.

Conflict of interest: The authors declare no conflict of interest.

References

- 1. Cullen KA, Hall MJ, Golosinskiy A. Ambulatory surgery in the United States,2006. Natl Health Stat Report. 2009;(11):1-25.
- Apfel CC, Läärä E, Koivuranta M, Greim CA, Roewer N. A simplified risk score for predicting postoperative nausea and vomiting: conclusions from cross-validations between two centers. Anesthesiology. 1999;91(3):693-700.
- Mythen MG. Postoperative gastrointestinal tract dysfunction: an overview of causes and management strategies. Cleve Clin J Med. 2009; 76(4): 66–71.
- Elgueta MF, Echevarría GC, De la Fuente N, et al. Effect of intravenous fluid therapy on postoperative vomiting in children undergoing tonsillectomy. Br J Anaesth. 2013;110(4):607-14. doi: 10.1093/bja/aes453.
- Gan TJ, Diemunsch P, Habib AS, et al. Society for Ambulatory Anesthesia. Consensus guidelines for the management of postoperative nausea and vomiting. Anesth Analg. 2014;118(1):85-113. doi: 10.1213/ANE.00000000000002.
- McGrath PJ, Jhonson G, Goodman JT, et al. CHEOPS: A behavioral scale for rating postoperative pain in children. In: Fields HL, Dubner R, Cervero F, editors.Advances in pain research and therapy. vol. 9. New York: Raven Press; 1985:395-402.
- Dagher CF, Abboud B, Richa F, et al. Effect of intravenous crystalloid infusion on postoperative nausea and vomiting after thyroidectomy: a prospective, randomized, controlled study. Eur J Anaesthesiol. 2009; 26(3): 188–91.
- McCaul C, Moran C, O'Cronin D, et al. Intravenous fluid loading with or without supplementary dextrose does not prevent nausea, vomiting and pain after laparoscopy. Can J Anaesth. 2003; 50(5): 440–4.
- 9. Yogendran S, Asokumar B, Cheng DC, et al. A prospective randomized double-blinded study of the effect of intravenous fluid therapy on adverse outcomes on outpatient surgery. Anesth Analg. 1995; 80(4): 682–6.
- 10. Goodarzi M, Matar MM, Shafa M, Townsend JE, Gonzalez I. A prospective randomized blinded study of the effect of intra-

venous fluid therapy on postoperative nausea and vomiting in children undergoing strabismus surgery. Paediatr Anaesth. 2006; 16(1): 49–53.

- Bianchetti MG, Bettinelli A. Differential diagnosis and management of fluid, electrolyte, and acid-base disorders. In: Comprehensive Pediatric Nephrology 1st edn. Geary DF, Schaefer F, eds. Philadelphia: Mosby; 2008. 395-431.
- Egeli E, Harputluoglu U, Ozturk O, et al. Can post-adenotonsillectomy morbidity be reduced by intravenous 24 h hydration in pediatric patients following adenotonsillectomy?. Int J Pediatr Otorhinolaryngol. 2004; 68(8): 1047–51.
- Hayes I, Rathore R, Enohumah K, et al. The effect of crystalloid versus medium molecular weight colloid solution on post-operative nausea and vomiting after ambulatory gynecological surgery - a prospective randomized trial. BMC Anesthesiol. 2012 31;12:15. doi: 10.1186/1471-2253-12-5.
- 14. Mythen MG, Webb AR. Perioperative plasma volume expansion reduces the incidence of gut mucosal hypoperfusion during cardiac surgery. Arch Surg. 1995; 130(4): 423–9.
- 15. Brandstrup B, Tonnesen H, Beier-Holgersen R, et al. Effects of intravenous fluid restriction on postoperative complications: comparison of two perioperative fluid regi-mens: a randomized assessor-blinded multicenter trial. Ann Surg. 2003;238(5): 641–8.
- Lobo DN, Bostock KA, Neal KR, et al. Effect of salt and water balance on recovery of gastrointestinal function after elective colonic resec-tion: a randomised controlled trial. Lancet 2002;359(9320):1812–8.
- Nisanevich V, Felsenstein I, Almogy G, Weissman C, Einav S, Matot I. Effect of intraoperative fluid manage-ment on outcome after intraabdominal surgery. Anesthe-siology 2005;103(1):25–32.
- Sinclair S, James S, Singer M. Intraoperative intravascular volume optimisation and length of hospital stay after repair of proximal femoral fracture: randomised controlled trial. BMJ. 1997 11;315(7113):909-12.
- Diez L. Assessing the willingness of parents to pay for reducing postoperative emesis in children. Pharmacoeconomics 1998; 13(5 Pt 2): 589–95.