ORIGINAL ARTICLE

Comparison between Different Anaesthesia Techniques for Protecting Renal Function in Children Undergoing Radical Nephrectomy

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ABSTARCT

Background and Aim: Most primary renal neoplasms are caused by renal cell carcinomas (RCCs). There is a high risk of morbidity and mortality following radical nephrectomy due to acute kidney injury (AKI). It is crucial to detect and prevent this complication as early as possible. The present study aimed to anesthesia comparison after radical nephrectomy for kids: a study with different anesthesia techniques.

Patients and Methods: This retrospective study was carried out on 84 children of the age up to 12 years undergoing radical nephrectomy in the department of Anaesthesiology, Chaudhary Muhammad Akram Hospital (CMA) Lahore during three years, from August 2019 to July 2022. Prior to study conduction, ethical approval was taken from research and ethical committee. Patients were allocated to three different groups: Group-D (Dexmedetomidine group), Group-C (Caudal group), and Group-P (Placebo group). Children were evaluated by taking history, physical examination, and laboratory examinations such as liver function, CBC, kidney functions, and coagulation profile. SPSS version 28 was used for data analysis.

Results: A total of 84 children investigated with different anesthesia techniques. Each group was assigned 28 children undergoing radical nephrectomy. A significant difference did not appear between the three groups in terms of serum creatinine at any of the times of measurement. Group D showed significant lower values for cystatin C and NGAL compared with group C and group P regardless of the measurement period. In all three studied groups, there were no significant differences in age, gender, or weight of the patients (p> 0.05). Comparatively to the other two groups, the Dex Group had significantly higher urine output, more sedation, and lower objective pain scores.

Conclusion: Clinical prediction schemes using cystatin C and NGAL biomarkers showed that dexmedetomidine prevents AKI in children undergoing renal replacement therapy. The Dex Group had significantly higher urine output, more sedation, and lower objective pain scores as compare to the other two groups. Furthermore, dexmedetomidine provides renal protection and sedation as well as analgesia.

Keywords: Radical nephrectomy; Dexmedetomidine; Cystatin C; Children

INTRODUCTION

Renal cell carcinomas (RCCs) contributes to the majority of primary renal neoplasms (80-85%), however, RCCs are resistant to nonsurgical treatments such as hormonal therapy, chemotherapy, and radiation. Therefore, radical nephrectomy still remains the primary treatment method for RCCs. Urological operations are regarded to be significant risk for perioperative renal disease [3], with nephrectomy being the most likely risk of causing acute kidney injury (AKI). Postoperative AKI in RCC patients is a significant risk factor for new-onset chronic kidney disease (CKD) following radical nephrectomy. Preventing postoperative AKI is critical for reducing the occurrence of CKD following nephrectomy [4]. AKI is often diagnosed using blood urea nitrogen and serum creatinine values. Since they are impacted by several renal and non-renal variables that are unrelated to kidney damage or function [5]. Because it is readily filtered at the glomeruli and virtually entirely reabsorbed and catabolized in the proximal tubular cells, cystatin C is an endogenous measure of renal function [6]. In certain investigations, this measure was found to be superior to creatinine in the early detection of renal impairment [7]. Other investigators, however, have not proven such advantage [8].

Serum neutrophil gelatinase-associated lipocalin (NGAL) is an initial diagnostic for AKI that is highly susceptible, specific, and prognostic in a variety of disease processes. NGAL is a tubular stress marker; its intensity rises substantially in response to tubular damage and rises more than 24 hours before serum creatinine [9]. Dexmedetomidine is a more potent and selective 2-adrenoreceptor agonist than clonidine, with a 2:1-adrenoreceptor ratio of 1600: 1 when compared to clonidine [10]. Dexmedetomidine is a strong and highly selective 2-adrenoceptor agonist with sympatholytic, amnestic, sedative, and analgesic effects that has been characterized as a beneficial and safe adjuvant in many therapeutic applications [11, 12]. Caudal epidural blocking is a well-known and effective approach for providing postoperative analgesia for a variety of surgical operations in children. They also inhibit the transition of acute postoperative pain to chronic pain [13]. As a result, the present study aimed to evaluate the relationship between the selection of general anesthetic agent and long-term renal function following nephrectomy.

METHODOLOGY

This retrospective study was carried out on 84 children undergoing radical nephrectomy in the department of Anaesthesiology, Chaudhary Muhammad Akram Hospital (CMA) Lahore during three years, from August 2019 to July 2022. Prior to study conduction, ethical approval was taken from research and ethical committee. Patients were allocated to three different groups: Group-D (Dexmedetomidine group), Group-C (Caudal group), and Group-P (Placebo group). Children were evaluated by taking history, physical examination, and laboratory examinations such as liver function, CBC, kidney functions, and coagulation profile. Patients taking two agonists, had acute kidney injury (creatinine clearance less than 90 ml/min), had sustained intraoperative, or were using intraoperative diuretics to address oliguria were excluded. Puncture site risk was higher in those with skin lesion, bleeding and clotting abnormalities, and congenital heart disease. Participants were categorized into three comparable groups (each with 28 patients) at random: Dexmedetomidine (D) group, where Dex. 0.8 g/kg was administered intravenously over 10 minutes as a loading dose, followed by 0.4 g/kg/h infusion. Group (C): caudal group, and Placebo (P) group. Normal laboratory procedures were utilized for creatinine clearance levels and baseline serum creatinine were acquired 24 hours earlier. Additionally, baseline levels of serum NGAL and serum cystatin C were acquired using commercially available kits.

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During anesthesia, all the participants established stringent replacement of fluid in accordance with established fluid replacement administration recommendations. At the conclusion of operation, children were positioned supine, oral secretion was aspirated, anesthesia was terminated, and 100% oxygen was administered. SPSS version 28.0 was used to analyze the data. The mean \pm standard deviation was used to describe quantitative data. The qualitative data was described using the frequency and percentage. P-values of 0.05 were deemed significant, while P-values of 0.01 regarded highly significant.

RESULTS

A total of 84 children investigated with different anesthesia techniques. Each group was assigned 28 children undergoing radical nephrectomy. A significant difference did not appear between the three groups in terms of serum creatinine at any of the times of measurement. Group D showed significant lower values for cystatin C and NGAL compared with group C and group P regardless of the measurement period. In all three studied groups, there were no significant differences in age, gender, or weight of the patients (p> 0.05). Comparatively to the other two groups, the Dex Group had significantly higher urine output, more sedation, and lower objective pain scores. Assessing renal function using common parameters such as creatinine clearance and serum creatinine revealed no statistically significant variation among three study groups measured at different periods (p > 0.05) as shown in Table-I. Nevertheless, the preoperative baseline levels of cystatin C among groups were investigated and found comparable (p = 0.07), and reduced significantly in the Dex. Group compared to the others, there was insignificant association in groups C and P as shown in Table-II. Table III shows a comparison of the sedation scores in the three investigated groups at various follow-up periods.

Table-1: creatinine clearance and serum creatinine compared in three groups

Parameters Preoperative 12 hrs. Post-operative 12 hrs. Post-operative 24 hrs. Serum Creatinine (Mean ± SD) 0.791 ± 0.159 0.790 ± 0.141 0.789 ± 0.140 Group C 0.792 ± 0.143 0.793 ± 0.123 0.785 ± 0.131 Group D 0.790 ± 0.141 0.787 ± 0.132 0.787 ± 0.132 Group P 0.790 ± 0.141 0.787 ± 0.132 0.787 ± 0.132 Creatinine clearance (Mean ± SD) 106.87 ± 10.512 106.67 ± 10.153 106.52 ± 10.892 SD) 108.84 ± 11.273 108.34 ± 11.153 108.13 ± 13.251 108.16 ± 11.852 Group D Group P 0 0.782 ± 12.681 108.13 ± 13.251 108.16 ± 11.852					
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Table-2: NGAL and cystatin C compared in groups

Parameters	Preoperative	Post-operative 12 hrs.	Post-operative 24 hrs.
NGAL (Mean ± SD)			
Group C	70.72 ± 8.45	131.72 ± 10.132	151.52 ± 8.275
Group D	68.67 ± 9.752	63.85 ± 15.825	56.42 ± 16.233
Group P	69.89 ± 8.836	153.62 ± 14.167	176.21 ± 8.156
Cystatin C (Mean ±			
SD)	0.974 ± 0.161	0.996 ± 0.163	0.987 ± 0.247
Group C	1.041 ± 0.164	0.625 ± 0.068	0.642 ± 0.057
Group D	1.063 ± 0.134	1.214 ± 0.125	1.286 ± 0.187
Group P			

Table-3: sedation score compared in studies groups

Follow-up period (minutes)	Group C	Group D	Group P	P-value
5	1.89 ± 0.23	0.7 ± 0.045	0.45 ± 0.05	0.001
15	1.31 ± 0.114	0.46 ± 0.03	0.30 ± 0.031	0.0012
30	1.03 ± 0.09	0.31 ± 0.034	0.17 ± 0.021	0.001
60	0.91 ± 0.083	0.13 ± 0.012	0.09 ± 0.016	0.005

DISCUSSION

The present study mainly compared three different anesthesia techniques for children protecting renal function undergoing radical nephrectomy and found that Dexmedetomidine reduces AKI in children receiving renal replacement treatment, according to

clinical prediction methods based on cystatin C and NGAL biomarkers. In comparison to the other two groups, the Dex Group had considerably greater urine production, more sedation, and lower objective pain levels. Dexmedetomidine also offers renal protection, sedation, and analgesia. Regardless of the testing time, group D had significantly lower cystatin C and NGAL levels than groups C and P. There were no significant variations in patient age, gender, or weight across the three study groups. The Dex Group had considerably larger urine output, more sedation, and lower objective pain levels than the other two groups. In a research similar to ours, Lee et al. [14] carried out their study on 72 patients and evaluated the Dex. Effects on renal function undergoing substitution of cardiac valve by cardiopulmonary bypass. Patients were arbitrarily assigned to the Dex. group, which received 0.6 g/kg/hr 15 minutes before induction, followed by 0.2 g/kg/hr until the conclusion of the operation, or the Placebo group, which received equivalent treatment with normal saline. The results of traditional renal function testing did not differ significantly.

A convenient choice of anesthetic strategy can influence a variety of patient outcomes. Although no standard technique has been proven to be superior to others, one of the key goals of this type of surgery is to preserve children's renal function following radical nephrectomy [15]. Hoste et al. [16] found that after induction, Dex. was injected and maintained for 4 hours postoperatively. In comparison to placebo and was linked with urine production increase but had no effect on renal function.

These findings were consistent with those of Balkanay et al. [17], who discovered that dexmedetomidine intraoperative infusion at 0.4 g/kg/h rate keeps blood pressure and HR within acceptable ranges for a longer period of time than the placebo group. The reduction in blood pressure and HR is consistent with the findings of Suriyachote et al. [18], who compared dexmedetomidine to fentanyl in bariatric surgery, demonstrating that dexmedetomidine attenuates various stress responses, through sympatholytic activity during surgery and maintains hemodynamic stability.

With high concentrations or rapid infusion rates, dexmedetomidine can produce a rise in blood pressure and a reduction in HR [19-21]. The activation of 2-adrenoceptors on vascular smooth muscle is considered to cause vasoconstriction, higher blood pressure, and a reflex drop in HR [22, 23]. There was no drop in HR or rise in blood pressure during the bolus infusion in the current research. This shows that the first 1 g/kg loading infusion for 10 minutes is not fast and may not result in high blood dexmedetomidine concentrations.

Novaes et al. [24] conducted a study on individuals scheduled for nephrectomy or prostatectomy that agreed with our findings. Patients were separated into two groups for a blind infusion of dexmedetomidine 0.5 g/kg for the first 20 minutes, trailed by 0.7 g/kg/h until the 0.9% saline. There were no significant differences in postoperative mean serum creatinine and creatinine clearance values between the dexmedetomidine and control groups. Postoperative mean serum cystatin C levels did not differ significantly between groups at any point and remained within the normal range in both groups.

There was significant distinction between the two groups in serum NGAL levels after 24 and 48 hours in the current investigation. Traditional renal function tests, such as blood urea nitrogen, serum creatinine, urine output, and creatinine clearance rate assessments, may miss the development of acute kidney failure in the first 48 hours after surgery.

Jaakola et al. [25] investigated the impact of Dex. on infants having AKI with congenital heart surgery and found that children received an injection of Dex. (1 g/kg) until 12 hours following the procedure. When compared to the placebo group, the Dex. group had significantly reduced serum creatinine levels.

In the current study, the Dex. group had significantly greater sedation scores than the other two groups. This came as no surprise given Dex's sedative characteristics. Kumar et al. [26] concluded that a single Dex. Dosage administered over 20 minutes might deliver enough analgesia and sedation with no concurrent respiratory depression, which is consistent with our findings.

CONCLUSION

The present study found that **c**linical prediction schemes using cystatin C and NGAL biomarkers showed that dexmedetomidine prevents AKI in children undergoing renal replacement therapy. The Dex Group had significantly higher urine output, more sedation, and lower objective pain scores as compare to the other two groups. Furthermore, dexmedetomidine provides renal protection and sedation as well as analgesia.

REFERENCES

- Hassan Saeed ELHoshy & Islam Mohamed ELBardan (2022) Comparison between different anaesthesia techniques for protecting renal function in children undergoing radical nephrectomy, Egyptian Journal of Anaesthesia, 38:1, 401-408, DOI:10.1080/11101849.2022.2092301.
- Priye S, Jagannath S, Singh D, et al. Dexmedetomidine as an adjunct in postoperative analgesia following cardiac surgery: a randomized, double-blind study. Saudi J Anaesth. 2015 Oct;9(4):353.
- Loomba RS, Villarreal EG, Dhargalkar J, et al. The effect of dexmedetomidine on renal function after surgery: a systematic review and meta-analysis. J Clin Pharm Ther. 2021 Sep 12;47(3):287–297.
- Cho JS, Shim JK, Soh S, et al. Perioperative dexmedetomidine reduces the incidence and severity of acute kidney injury following valvular heart surgery. Kidney Int. 2016 Mar 1;89(3):693–70.
- Bai Y, He H, Zhang P, et al. Effects of dexmedetomidine on immune function, renal function and inflammatory factors of patients undergoing percutaneous nephrolithotomy under general anesthesia. Exp Ther Med. 2021 Apr 1;21(4):1–9.
- Zdziechowska M, Gluba-Brzózka A, Poliwczak AR, et al. Serum NGAL,KIM-1, IL-18, L-FABP: new biomarkers in the diagnostics of acute kidney injury (AKI) following invasive cardiology procedures. Int Urol Nephrol. 2020 Nov;52(11):2135–2143.
- Benzer M, Alpay H, Baykan Ö, et al. Serum NGAL, cystatin C and urinary NAG measurements for early diagnosis of contrast-induced nephropathy in children. Ren Fail. 2016 Jan 2;38(1):27–34.
- Corbacioglu SK, Cevik Y, Akinci E, et al. Value of plasma neutrophil gelatinase-associated lipocalin (NGAL) in distinguishing between acute kidney injury (AKI) and chronic kidney disease (CKD). Turk J Emerg Med. 2017 Sep 1;17(3):85–88.
- Lundblad M, Lönnqvist PA. Adjunct analgesic drugs to local anaesthetics for neuroaxial blocks in children. Curr Opin Anesthesiol. 2016 Oct 1;29(5):626–631.
- Tandon M, Singh A, Saluja V, et al. Validation of a new "objective pain score" vs. "numeric rating scale" for the evaluation of acute pain: a comparative study. Anesth Pain Med. 2016 Feb;6(1). DOI:10.5812/aapm.32101.
- Li X, Zhang C, Dai D, et al. Efcacy of dexmedetomidine in prevention of junctional ectopic tachycardia and acute kidney injury after pediatric cardiac surgery: a meta-analysis. Congenit Heart Dis. 2018 Sep;13 (5):799–807.

- Zhai M, Kang F, Han M, et al. The effect of dexmedetomidine on renal function in patients undergoing cardiac valve replacement under cardiopulmonary bypass: a double-blind randomized controlled trial. J Clin Anesth. 2017 Aug 1;40:33–38.
- Xie Y, Jiang W, Cao J, et al. Dexmedetomidine attenuates acute kidney injury in children undergoing congenital heart surgery with cardiopulmonary bypass by inhibiting the TLR3/NF-κB signaling pathway. Am J Transl Res. 2021;13(4):2763.
- Volpon LC, Sugo EK, Carlotti AP. Diagnostic and prognostic value of serum cystatin C in critically ill children with acute kidney injury. Pediatr Crit Care Med. 2015 Jun 1;16(5):e125–31.
- 15. Goren O, Matot I. Perioperative acute kidney injury. Br J Anaesth. 2015 Dec 1;115(suppl_2):ii3–14.
- Hoste EA, Bagshaw SM, Bellomo R, et al. Epidemiology of acute kidney injury in critically ill patients: the multinational AKI-EPI study. Intensive Care Med. 2015 Aug;41(8):1411–1423.
- Balkanay OO, Goksedef D, Omeroglu SN, Ipek G. The dose-related effects of dexmedetomidine on renal functions and serum neutrophil gelatinaseassociated lipocalin values after coronary artery bypass grafting: a randomized, triple-blind, placebo-controlled study. Interact Cardiovasc Thorac Surg 2015; 20:209–214.
- Suriyachote P, Indrambarya T, Srisawat N, Vimuktanandana A. The renoprotective effect of intraoperative dexmedetomidine infusion in elective coronary bypass graft. Surgery J Anesthesiol 2014; 40:221– 222.
- Bayram A, Ulgey A, Baykan A, Narin N, Narin F, Esmaoglu A, et al. The effects of dexmedetomidine on early stage renal functions in pediatric patients undergoing cardiac angiography using non-ionic contrast media: a double-blind, randomized clinical trial. Paediatr Anaesth 2014; 24:426–432.
- Ljungberg B, Bensalah K, Canfield S, Dabestani S, Hofmann F, Hora M, et al. EAU guidelines on renal cell carcinoma: 2014 update. Eur Urol 2015;67:913–924.
- Cho JS, Shim JK, Soh S, Kim MK, Kwak YL. Perioperative dexmedetomidine reduces the incidence and severity of acute kidney injury following valvular heart surgery. Kidney Int 2016; 89:693–700.
- Si Y, Bao H, Han L, Shi H, Zhang Y, Xu L, et al. Dexmedetomidine protects against renal ischemia and reperfusion injury by inhibiting the JAK/STAT signaling activation. J Transl Med 2013; 11:141.
- Manasa CR, Padma L, Shivshankar S, Ramanujam R. Evaluation of efficacy of sedative and analgesic effects of single IV dose of dexmedetomidine in post-operative patients. Int J Pharmacol Clin Sci 2013; 2:75–81.
- Novaes MVM, Lavinas PSG, Pires GHD, et al. Renal function after major uro-oncologic surgery and dexmedetomidine infusion. Open J Anesthesiol. 2013;3 (8):356–362.
- Jaakola ML, Salonen M, Lehtinen R, Scheinin H. The analgesic action of dexmedetomidine – a novel α2-adrenoceptor agonist – in healthy volunteers. Pain 1991; 46:281–285.
- Kumar S, Kushwaha BB, Prakash R, Jafa S, Malik A, Wahal R, et al. Comparative study of effects of dexmedetomidine and clonidine premedication in perioperative hemodynamic stability and postoperative analgesia in laparoscopic cholecystectomy. Internet J Anesthesiol 2014;33:1–8.