Dexmedetomidine enhances the efficacy of 0.25% ropivacaine for postoperative analgesia in pediatric caudal epidurals

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ABSTRACT

Background & Objectives: Caudal epidural block is one of the safe, reliable and effective technique in pediatric patients but single shot caudal epidural block has short duration of analgesia that can be prolonged by addition of adjuvants like opioids, clonidine, neostigmine, ketamine or α₂ agonists along with local anesthetic agents. This prospective randomized study was conducted to assess the efficacy of addition of dexmedetomidine (1µg/kg) to caudal 0.25% ropivacaine (1ml/kg) for postoperative analgesia.

Methodology: Sixty American Society of Anesthesiologists physical status I and II pediatric patients aged 6 months to 6 years were randomly allocated into two groups with 30 patients in each group: Group R (n = 30) received caudal 0.25% ropivacaine 1 ml/ kg and normal saline (0.5 ml) while Group RD received caudal 0.25% ropivacaine 1 ml/kg + dexmedetomidine 1 µg/kg (0.5 ml). Postoperative pain (FLACC pain score), duration of analgesia, rescue analgesic requirement, postoperative sedation scores, and hemodynamic changes along with complications were recorded.

Results: The duration of analgesia was significantly longer in Group RD (797.00 ± 59.20 min) compared to Group R (363.30 ± 31.44 min), (p < 0.0001). The total number of doses of rescue analgesic required were lesser in Group RD in comparison to Group R .The patients in Group RD achieved higher sedation scores than Group R, which was highly significant (p < 0.0001). In adverse effects, the incidence of postoperative agitation (6.66%), and PONV (3.33%) were seen only in Group R when compared to Group RD.

Conclusion: Dexmedetomidine (1 µg/kg) can be used as an adjuvant to single shot caudal epidural using 0.25% ropivacaine (1 ml/kg) for effective postoperative analgesia in pediatric patients as it significantly prolonged the duration of analgesia along with reduced rescue analgesic requirement and minimal side effects.

Key words: Caudal epidural; Ropivacaine; Dexmedetomidine; Postoperative analgesia; Pediatric; Rescue analgesic

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INTRODUCTION

The concept of postoperative analgesia in pediatric patients has evolved and improved in recent years. Caudal epidural block is one of the most popular, reliable, safe and effective technique that can be used alone or in combination with general anesthesia for both intra and postoperative analgesia in pediatric patients undergoing various infraumbilical surgeries.¹,² The advantages of caudal epidural block include the reduced intraoperative requirement of various general and inhalational anesthetic agents.
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as well as opioids in postoperative period, attenuates the stress response associated with surgery, provides adequate postoperative analgesia along with rapid recovery.3

The single shot caudal epidural block is associated with short duration of analgesia which is the main disadvantage of this technique. But various methods have evolved to prolong the duration of analgesia including the addition of adjuvants like opioids, clonidine, neostigmine, ketamine or α2 agonists along with local anesthetic agents in caudal block.4-6

Ropivacaine, an amide local anesthetic, structurally related to bupivacaine, is usually preferred over bupivacaine, as it provides adequate postoperative analgesia along with lesser motor blockade which is desirable in pediatric patients and proved to be more suitable for caudal epidural analgesia, especially during day care surgeries.7

Dexmedetomidine, a highly selective α2 agonist, has eight times higher affinity for α2 adrenergic receptors than clonidine which is responsible for its sedative, anxiolytic and analgesic properties with minimal respiratory depression. Many studies has been done on clonidine as an additive in caudal block but there are limited studies on dexmedetomidine (1µg/kg) as an adjuvant to local anesthetic in caudal block.8-9

So we hypothesized that dexmedetomidine would provide prolonged postoperative analgesia with minimal adverse effects when used in a dose of 1 µg/kg dose as an adjuvant in caudal epidural block in pediatric patients. This prospective, randomized study was undertaken to assess the efficacy of addition of dexmedetomidine (1 µg/kg) to caudal 0.25% ropivacaine (1 ml/kg) in prolonging the duration of postoperative analgesia as primary objective while rescue analgesic requirement, postoperative sedation, hemodynamic changes with adverse effects as secondary objectives in pediatric patients undergoing various infraumbilical surgeries.

**METHODOLOGY**

This prospective, randomized study was conducted on sixty American Society of Anesthesiologists (ASA) physical status I and II pediatric patients between 6 months to 6 years of age who underwent various elective infraumbilical surgeries at our institute after approval from local institutional ethical committee and written informed consent from the parents. Patients with known allergy to any of the study drugs, coagulation disorders, infection at the site of caudal block, patients having history of developmental delay, any neurological disease or skeletal deformities, and parental refusal were excluded from the study.

The patients were randomly allocated into two groups with 30 patients in each group: Group R (ropivacaine group) and Group RD (ropivacaine + dexmedetomidine) using computer generated tables of random numbers and allocation concealment was done using sequentially numbered closed opaque sealed envelope technique. A trained anesthesiologist, who was not involved in the study process, prepared the syringes loaded with the study drugs for caudal block and the another anesthesiologist who administered the drug and observed the patient thereafter was unaware about the contents of the loaded syringes for the purpose of double blinding so both the anesthesiologist who prepared the drugs as well as the observer who assessed the results were blinded. The dose was calculated according to the each patient’s body weight, loaded using an insulin syringe rounded off to the closest unit and diluted with normal saline to make it 0.5 ml.

Group R: Received caudal 0.25% ropivacaine 1ml/ kg and normal saline (0.5 ml)

Group RD: Received caudal 0.25% ropivacaine 1ml/ kg + dexmedetomidine 1 µg/kg (0.5 ml)

All the patients had undergone thorough preoperative evaluation on the day before surgery and were kept nil per oral 6 hours for solid food and 2 hours for clear fluid before taking for surgery. After arrival of the patients in operation theatre, a 22 or 24G intravenous (IV) cannula was secured on the dorsum of hand and ringer lactate was started. All the patients were premedicated with midazolam 0.05 mg/kg IV, 10 min prior to induction. ASA standard monitoring was used and all baseline vital parameters including heart rate (HR), noninvasive blood pressure (NIBP), electrocardiogram (ECG), oxygen saturation (SpO2) and respiratory rate (RR) were recorded. Induction of anesthesia was achieved using sevoflurane (8%) in oxygen and nitrous oxide (50:50) on spontaneous ventilation. After achieving adequate depth of anesthesia, an appropriate sized laryngeal mask airway (LMA) was inserted. After induction of anesthesia and LMA insertion the patient was placed in the lateral decubitus position. Under all aseptic precautions, the caudal block was given using 23G needle with appropriate drugs according to group allocation. The time of caudal block was noted and patients were turned again to supine position. Thereafter intraoperative anesthesia was maintained with sevoflurane in oxygen/N2O (50:50). The sevoflurane concentration was adjusted
according to maintain the hemodynamic changes < 20% of the baseline values. Both sevoflurane and N₂O were discontinued at the time of skin closure before completion of the surgery. LMA was removed after thorough suction of oral cavity during emergence from anesthesia and completion of surgery. Emergence or recovery time (the time taken from discontinuation of sevoflurane to opening the eyes on calling the patient’s name) was also noted. All the patients were shifted to postanesthesia care unit for observation. The various hemodynamic parameters including heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP) and oxygen saturation (SpO₂) were recorded at baseline and then at every 5 min till the end of surgery.

The postoperative pain was assessed by using the pediatric observational FLACC (Face; Legs; Activity; Cry; Consolability) pain scale ¹⁰ with its 0–10 score range, each patient’s pain intensity was assessed hourly till 8 hours, then 2 hourly upto 24 hours after the caudal block. If the FLACC pain score was noted at any time to be ≥ 4, syrup paracetamol (15 mg/kg) was administered as a rescue analgesic to achieve the FLACC pain score of ≤ 3. The duration of analgesia (from time of caudal block to the time at which FLACC score was ≥ 4) was recorded. The total number of doses of rescue analgesic required in 24 hours after the caudal block in postoperative period were also recorded.

Postoperative sedation score was assessed using Ramsay sedation scale.¹¹ The assessment of sedation was done hourly up to 4 h after the completion of surgery.

Ramsay 1- Anxious, agitated, restless
Ramsay 2- Cooperative, oriented, tranquil
Ramsay 3- Responsive to commands only
Ramsay 4- Brisk response to light glabellar tap or loud auditory stimulus
Ramsay 5- Sluggish response to light glabellar tap or loud auditory stimulus
Ramsay 6- No response to light glabellar tap or loud auditory stimulus

Various adverse effects or complications such as postoperative nausea and vomiting (PONV), postoperative agitation, respiratory depression, urinary retention, hypotension and bradycardia were also noted and treated accordingly. Respiratory depression was defined as a decrease in SpO₂ of less than 95% which was managed using oxygen supplementation. Hypotension and bradycardia were defined as reduction in blood pressure and heart rate by more than 20% of their baseline values. Hypotension and bradycardia were treated by fluid boluses and mephentermine and atropine respectively. Ondansetron was given to treat PONV. Delayed emergence or recovery time was defined as time taken to get shifted the patient outside the operation theatre more than 20 min after completion of the surgery. Failure of caudal block was defined as any increase in HR and/ or MAP more than 20% of the baseline values.

Statistical analysis:
The sample size was calculated to be 30 in each group to detect a significant difference in the mean time to first rescue analgesic requirement (mean duration of analgesia) and reduction in total analgesic requirement during 24 hours period in both groups with a α error of 0.05.⁴,⁵ All the numerical data were expressed as mean ± SD (standard deviation) whereas the categorical data were expressed as numbers or frequency (%). Statistical analysis were performed by help of SPSS software version 16.0 (SPSS Inc, Chicago, IL, USA). Standard qualitative and quantitative tests were used to compare the data (e.g. unpaired and paired Student’s t- test, chi-square test). A p-value of < 0.05 was considered as statistically significant.

RESULTS

Both groups were comparable in terms of mean age, weight, gender and duration of surgery, P > 0.05) (Table 1). The baseline hemodynamic parameters were comparable in both the groups (Figure 1). There were no significant differences in the mean HR, mean SBP, mean DBP, and mean MAP between the two groups at any time interval (p > 0.05)(Figures 1-3).

Group R – Ropivacaine; Group RD – Ropivacaine + Dexmedetomidine

Patients in Group R achieved significantly higher FLACC pain score compared with patients in Group RD. No patient had pain score ≥ 4 till first 4 hours in both the groups. 3 (10%) patients and 20 (66%) patients in Group R had a pain score of ≥ 4 at the end of 5th and 6th hour while none of the patients in group RD had a pain score of ≥ 4 at these time intervals. 20 out of 30 patients in Group R achieved FLACC pain score ≥ 4 at 6th hour after caudal block as compared to none of the patients in Group RD. However, in Group RD 19 out of 30 patients had FLACC pain score ≥ 4 at 14th hour after the caudal block.
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The mean duration of analgesia was longer in Group RD (797.00 ± 59.20 min) compared to Group R (363.30 ± 31.44 min) that was statistically highly significant, p < 0.0001 (Table 2).

The total number of doses of rescue analgesic required were lesser in Group RD as compared to Group R. In Group R, 19 patients (63.33%) required 3 doses of rescue analgesic, whereas none of the patients required 3 doses of rescue analgesic in Group RD. In Group R, 10 (33.33%) patients required 2 doses whereas 1 patient (3.33%) required 1 dose of rescue analgesic. However, in Group RD 4 patients (13.33%) required 2 doses and 26 (86.67%) patients required only one dose of rescue analgesic that was also statistically significant, p < 0.05 (Table 3).

The patients in Group RD achieved higher sedation scores than Group R. At the end of first hour, the patients in Group RD had higher sedation scores, in comparison to patients in Group R which was highly significant, (p < 0.0001). 26 out of 30 patients (86.66%) had sedation score equal to 3 as compared to 7 patient (23.33%) in Group R which was highly significant, (p < 0.0001). At the same time 23 patients (76.66%) in Group R have a sedation score of 2. Similarly, at the end of 2nd hour, 20 patients (66.66%) in Group RD had a sedation score of 3, while at the end of 3rd hour, 2 patients (6.66%) in Group RD had a sedation score of 3. However, in Group R, none of the patients had a sedation score of 3, at the end of 2nd and 3rd hours. At the end of 4th hour, none of the patients in both groups had a RSS of 3 (Table 4).

### Table 1: Demographic data of patients

<table>
<thead>
<tr>
<th>Basic Characteristics</th>
<th>Group R (n = 30)</th>
<th>Group RD (n = 30)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (months)</td>
<td>32.53 ± 15.96</td>
<td>37.83 ± 17.09</td>
<td>0.219*</td>
</tr>
<tr>
<td>Weight (kgs)</td>
<td>11.63 ± 2.88</td>
<td>11.95 ± 2.98</td>
<td>0.677*</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>30/0 (100%/0%)</td>
<td>29/1 (96.67%/3.33%)</td>
<td></td>
</tr>
<tr>
<td>Mean duration of surgery (min)</td>
<td>40.33 ± 11.67</td>
<td>38.33 ± 9.32</td>
<td>0.466*</td>
</tr>
<tr>
<td>Types of surgery(n/%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Herniotomy</td>
<td>23 (76.67%)</td>
<td>25 (83.33%)</td>
<td></td>
</tr>
<tr>
<td>Orchidopexy</td>
<td>3 (10%)</td>
<td>2 (6.67%)</td>
<td></td>
</tr>
<tr>
<td>Urethroplasty</td>
<td>2 (6.67%)</td>
<td>2 (6.67%)</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>2 (6.67%)</td>
<td>1 (3.33%)</td>
<td></td>
</tr>
</tbody>
</table>

*Values expressed as Mean ± SD and number (percentage)

*p > 0.05, not significant; n (%), number (percentage); M/F, Male, Female

Group R – Ropivacaine; Group RD – Ropivacaine + Dexmedetomidine
The recovery time was longer in Group RD (6.20 ± 0.92 min) as compared to Group R (4.23 ± 1.04 min), (p < 0.0001). In adverse effects, the incidence of postoperative agitation (6.66%), and PONV (3.33%) were seen only in Group R, compared to Group RD. The duration of first passage of urine was significantly more in Group RD (287.30 ± 36.29 min) compared to Group R (177.00 ± 16.43 min) (p < 0.0001).

**DISCUSSION**

The concept of postoperative pain relief and its use in the pediatric patients has changed dramatically over the recent years. Caudal epidural blockade is one of the most popular regional blocks used for postoperative analgesia in pediatric age group and has gained popularity nowadays as it allows rapid recovery from anesthesia with effective postoperative analgesia.4,5

This technique is widely used for various surgical procedures either alone or in combination with general anesthesia. Several studies have reported the use of caudal adjuvants like opioids and other drugs in pediatric patients to improve or enhance the postoperative analgesia but the opioids used as caudal adjuvants were reported to be associated with various side-effects including respiratory depression, pruritus, urinary retention, nausea and vomiting etc.

Hence, other drugs like dexmedetomidine or clonidine became popular to be used as adjuvants with local anesthetics through caudal epidural route to improve postoperative analgesia simultaneously avoiding the opioid related side-effects. Dexmedetomidine is a highly selective α2-adrenoceptor agonist and is more effective analgesic agent than clonidine as the dexmedetomidine has anxiolytic, sedative, analgesic and sympatholytic properties with minimal respiratory depression.

Various studies have undertaken that have used the dexmedetomidine as an adjuvant in caudal epidural block in a various dose range (0.5 µg/kg to 2 µg/kg).8,12-15

In both the groups, most of the children were male (> 90%) and this could be due to inclusion of surgeries like herniotoromy, orchidopexy etc. in our study.

Pain assessment is the most important and critical component of pain management especially in pediatric patients as a wrong concept has been popularized that they neither feel the pain nor remember any painful experience to the same extent like an adult patient.
usually do.

In our study, we have used FLACC pain scale which is a valid, objective and reliable method of pain assessment in children between 2 months to 7 years of age in pediatric population. If the FLACC pain score was ≥ 4, the syrup paracetamol (15 mg/kg) was given as a rescue analgesic. Patients in Group R achieved significantly higher FLACC pain scale as compared with Group RD (p < 0.05). No patient had pain score ≥ 4 till first 4 hours in both the groups.

The mean duration of analgesia was 363.30 ± 31.44 min in group R with a range of 300 to 410 min, while in group RD, the mean duration of analgesia was 797.00 ± 59.20 min with a range of 720 to 940 min, which was significantly longer in Group RD as compared to Group R, (p < 0.05).

The total number of doses of rescue analgesic required were lesser in group RD in comparison to group R, which was statistically significant, (p < 0.05).

The increased mean duration of analgesia and lower FLACC pain scores has been reported by some previous studies where they have used 1 µg/kg of caudal dexmedetomidine in their studies. Neogi et al. compared the efficacy of clonidine (1 µg/kg) and dexmedetomidine (1 µg/kg) used as caudal adjuvants to ropivacaine for postoperative analgesia in pediatric patients and found that mean duration of analgesia was significantly higher in dexmedetomidine group (15.26 ± 0.86 h) as compared to both clonidine (13.17 ± 0.68 h) and control group (6.32 ± 0.46 h) which concurs with our study. Similarly Saadway et al. compared bupivacaine and bupivacaine with dexmedetomidine (1 µg/kg) given caudally and found that 77% of patients did not require any rescue analgesic in 24 hours postoperative period in dexmedetomidine group compared to bupivacaine alone group (10%) which indicates the longer duration of analgesia in patients of dexmedetomidine group. Also the total postoperative rescue analgesic requirement was significantly lower in dexmedetomidine group during the first 24 hours postoperative period. Anand et al. concluded that caudal dexmedetomidine 2 µg/kg with ropivacaine 0.25% 1 ml/kg achieved significant postoperative pain relief. The duration of analgesia was 14.5 hours in RD group in comparison of 5.5 hours in Group R, that was highly significant, (p < 0.001). The patients in Group R achieved a significantly higher FLACC score compared to patients in Group RD. Manoj et al. concluded that addition of dexmedetomidine 2 µg/kg to caudal ropivacaine 0.25% 1 ml/kg significantly prolonged the analgesia in children undergoing lower abdominal surgeries. The duration of analgesia was 750 min in RD group in comparison of 390 min in Group R, that was highly significant, (p < 0.001), patients in Group R achieved a higher FLACC score as compared to patients in Group RD. The total postoperative requirement for oral paracetamol as a rescue analgesic was significantly lesser in RD group during the observation period.

Similarly Bharti N, et al. conducted a study which used caudal dexmedetomidine in three different doses (0.5, 1.0 & 1.5 µg/kg) along with ropivacaine in caudal epidural and found that all of the three doses of dexmedetomidine significantly prolonged the postoperative analgesia (p < 0.001), the patients in the plain ropivacaine group showed higher pain scores and required analgesia within first 6 postoperative hours, while none of the patients required any analgesia in the other three groups. Similar results were observed in the study done by El–Hennaway et al. with caudal dexmedetomidine (2 µg/kg) and bupivacaine. Gupta S et al. compared caudal clonidine (2 µg/kg) and dexmedetomidine (2 µg/kg) along with ropivacaine 0.2% in pediatric patients and found that mean duration of analgesia was significantly prolonged in dexmedetomidine group 17.6 (2.9) h as compared to clonidine group 10.1 (3.2) h, (p < 0.001). The total analgesic consumption was also significantly lesser in the dexmedetomidine group, (p < 0.05). Karupplah et al. compared two different doses of caudal dexmedetomidine (1 & 2 µg/kg ) with 0.25% bupivacaine (1 ml/kg) alone and concluded that mean duration of analgesia was significantly prolonged in both dexmedetomidine groups along with significant reduction in rescue analgesic consumption. All these studies favors the use of caudal dexmedetomidine as an adjuvant to local anesthetics for prolongation of postoperative analgesia along with reduced rescue analgesic consumption which is supported by our study too.

The mean recovery time was 4.23 ± 1.04 min in group R compared to 6.20 ± 0.92 min in group RD, which was statistically significant, (p < 0.05). The patients in Group RD achieved higher sedation score than Group R. At the end of first hour, the patients in Group RD had higher sedation scores in comparison to patients in Group R which was highly significant, (p < 0.0001). Although a RSS of ≤ 3 is desirable for the early postoperative period, in Group R, none of the patients had a sedation score of 3, at the end of 2nd and 3rd hours. At the end of 4th hour, none of the patients in both groups had an RSS of 3. An RSS ≤ 3 is associated with arousable sedation which is usually desirable in pediatric patients in early postoperative period and this is characteristic property of dexmedetomidine which is clinically...
acceptable at its particular dose which makes it as a choice of adjuvant along with local anesthetic agents through caudal route.\textsuperscript{5,6,13,19-22}

Anand VG et al.\textsuperscript{5} found that emergence time was 5.4 min in group RD compared to 4.0 min in Group R that was statistically significant, (p < 0.001). The patients in Group RD had significantly higher sedation as compared to patients in Group R, (P <0.05). Similarly Manoj et al.\textsuperscript{4} observed that the patients in dexmedetomidine group had significantly higher sedation as compared to patients in ropivacaine alone group, (p < 0.05). Patients in Group RD were more sedated but easily arousable. Although the sedation scores were comparable in all the three groups in the study done by Neogi et al.\textsuperscript{8}, but the sedation score were higher in more number of patients who received caudal dexmedetomidine as compared to caudal clonidine or ropivacaine alone. Bharti N et al.\textsuperscript{12} showed that patients in the dexmedetomidine groups had higher sedation scores in the postoperative period as compared to ropivacaine alone group. The patients who received dexmedetomidine (1.5 µg/kg) had significantly prolonged sedation as compared to the other groups. However, it was not associated with delayed discharge as all patients had arousable sedation which concurs with our study. El Haanway et al.\textsuperscript{6} Saadway et al.\textsuperscript{13} and Anand VG et al.\textsuperscript{5} also had similar results which are in concordance with findings of our study.

In the present study, heart rate (HR) and blood pressure (SBP, DBP, MAP) of all the patients were monitored at regular intervals. Baseline heart rate was comparable in the two groups, (p > 0.05). There was no significant difference in the heart rate between the two groups at any time interval, (p > 0.05). At all time intervals, the difference in the mean SBP, DBP and MAP between the two groups were insignificant, (p > 0.05) So, all the hemodynamic parameters were comparable and remained stable throughout the whole intraoperative as well as postoperative period which depicted the favorable safety profile of dexmedetomidine. The stable hemodynamics observed in our study may be due to the use of lower doses of dexmedetomidine (1 µg/kg) as compared to other studies where they had used dexmedetomidine in a dose >1 µg/kg (up to 2 µg/kg).\textsuperscript{4,5,14,16} One of the studies found decrease in HR in dexmedetomidine group (1 µg/kg & 1.5 µg/kg) but this was not clinically significant and no therapeutic interventions were required at any stage.\textsuperscript{12} These results concurs with our study. In postoperative complications or adverse events, the postoperative agitation was observed in 2 patients (6.66%), PONV in 1 patient (3.33%) among patients in Group R. Agitation was seen in the immediate postoperative period and it gradually subsided in 10-15 min on its own and no patient required midazolam to resolve it. There was no incidence of bradycardia, hypotension, pruritus and respiratory depression in any of the patients in two groups.\textsuperscript{8,17,23}

Bharti et al.\textsuperscript{12} found that four of twenty patient (20%) in plain ropivacaine group developed agitation while none in the dexmedetomidine group, the agitation was seen in the immediate postoperative period and last for 10-15 min and one patient required midazolam to resolve agitation. PONV and hypotension were noted in both groups in the study done by Manoj et al. but these were clinically not significant.\textsuperscript{4}

\textbf{CONCLUSION}

From our study we conclude that dexmedetomidine 1µg/kg may be used as a useful adjunct to single-shot caudal epidural using 0.25% ropivacaine for effective postoperative analgesia in pediatric patients. It significantly prolongs the duration of analgesia without any significant side effects and provides stable hemodynamics with arousable sedation that has proved its wider margin of safety in the dose 1 µg/kg.

\textbf{Conflicts of interest:} nil
\textbf{Authors’ contribution:}
KJ: Concepts, Design, Data analysis, Supervision
SKS: Design, Literature search, Clinical study, Data acquisition,
Manuscript preparation, Manuscript editing
SLY: Design, Literature search, Clinical study, Data acquisition,
Manuscript preparation, Manuscript editing, S VM, BT, DG:
Conduct of study, Literature search
REFERENCES


