Randomized Trial

A New Look on Adding Dexamethasone as an Adjuvant to Caudal Bupivacaine; Efficacy on Postoperative Pain and Vomiting in Pediatric Patients

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Background: Controlling postoperative pain and vomiting in children remains a great challenge.

Objective: Study the efficacy of adding dexamethasone to caudal bupivacaine on postoperative analgesia and vomiting.

Study Design: Prospective, randomized double blind controlled clinical trial.

Setting: Assiut University Hospital.

Patients: Ninety children ASA I-II, undergoing lower orthopedic surgeries.

Methods: Patients were randomly allocated into 3 equal groups. All received caudal block after induction of anesthesia with 0.5 mL/kg of 0.25% bupivacaine in addition to 5 mL intravenous (IV) normal saline in the control group, IV 0.5 mg/kg dexamethasone in IV dexamethasone group and lastly 0.1 mg/kg dexamethasone in the caudal dexamethasone group. Postoperative pain scores and rescue analgesic consumption were recorded. Blood glucose, postoperative vomiting, and other side effects were evaluated up to 24 hours after extubation.

Results: The time of first analgesia and the number of patients requiring rescue analgesics were significantly decreased with intravenous or caudal dexamethasone. No significant increase in postoperative blood glucose levels were observed. A significant increase in β- Endorphin level at 3 and 24 hours postoperative was found in both dexamethasone groups when compared with the preoperative baseline value. The incidence of postoperative vomiting was significantly decreased in both dexamethasone groups in comparison with the control group. No other side effects were detected.

Limitations: Measurement of serum cortisol.

Conclusion: Analgesic and antiemetic effects of dexamethasone as an adjunct to caudal block with bupivacaine (0.25%) 0.5 mL/kg is similar whether administered intravenously 0.5 mg/kg or caudally 0.1 mg/kg.

Key words: B-Endorphin, bupivacaine, caudal, dexamethasone, pediatric, postoperative analgesia, vomiting

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Postoperative pain morbidities and analgesic dependence continue to adversely affect health care (1). There is good evidence suggesting that untreated pain may have long-term negative effects on pain sensitivity, immune functioning, neurophysiology, attitudes, and health care behavior (2). In the 1970s and 1980s postoperative pain in children to a large extent was either ignored or under treated as

compared with adults. It has been documented that this may have serious implications for the children in the immediate postoperative period as well as in the longer postoperative period. Therefore, the diagnosis, monitoring, and treatment of pain in children are very important (3). Orthopedic procedures tend to have increased pain compared with other procedures, so further research must be done to manage pain more efficiently. However, there appears to be a shift towards multimodal approaches using regional anesthesia to minimize narcotic consumption and to avoid narcotic-related side effects (4). A single shot caudal epidural block is one of the most used techniques for relief of postoperative pain after infraumbilical surgical procedures in pediatric patients. However, in a significant proportion of patients, despite good initial analgesia from a caudal block with local anesthetic, pain develops after the block resolves. In order to decrease postoperative analgesic requirements after a caudal block and to overcome these problems, various drugs have been added to local anesthetic solutions to prolong the duration of the caudal anesthesia provided by a single injection; such as opioids (5), clonidine (6), Ketamine (7), midazolam (8), and neostigmine (9). However, their use has been limited by adverse effects in children (3). Recently, many studies suggested that epidurally administered dexamethasone could reduce the incidence and severity of postoperative pain in adults (10). However, until now there is still some controversy concerning the route of administration, whether regional or systemic and its additive analgesic effects if administrated as an adjuvant (11). The anti-emetic properties of dexamethasone are well established (12-14), but the mechanisms underlying this anti-emetic effect remain largely unknown. A direct inhibition of prostaglandins, serotonin, or endorphin production has been postulated (13).

Methods

Written informed consent was obtained from all parents of the children (ASA physical status I, II) undergoing lower limb orthopedic surgery. The consent was taken after discussing a detailed description of the study with the parents and their children. The study was approved by the research ethics boards of Assiut university hospitals.

Ninety patients (2 – 12 years) were randomly assigned in 3 equal groups (control group, IV dexamethasone group, and caudal dexamethasone group). Randomization was done by using computer generated random numbers contained in opaque sealed envelopes. We excluded cases with parental refusal, diabetes mellitus, failure of caudal block, allergy to the studied drugs used, and children who had any contraindication for regional techniques such as infection near the site of the needle insertion, coagulopathy, anti-coagulation therapy, pilonidal cyst, and congenital anomalies of the lower spine because of unclear or impalpable anatomy. Before induction of anesthesia, one anesthetist who did not follow the patient, opened the closed envelop to know the randomization group, prepared the studied drugs, and performed caudal epidural block and intravenous drug administration. The caudal epidural block was applied to all patients with 0.5 mL/kg of bupivacaine 0.25%. In addition a IV 5 mL syringe was prepared and given in equal volumes of 5 mL so that investigators and observers were blinded to the drug.

- IV dexamethasone group: caudal epidural block (0.5 mL/kg of bupivacaine 0.25% only) and IV dexamethasone (0.5mg/kg with a maximum dose 10 mg) added to 5 mL normal saline.
- Caudal dexamethasone group: caudal epidural block (0.5 mL/kg of bupivacaine 0.25% plus dexamethasone 0.1 mg/kg), and IV 5 mL normal saline.
- Control group: caudal epidural block (0.5 mL/kg of bupivacaine 0.25% only) and IV 5 mL normal saline.

Investigators and observers were blinded to the drug and dose given.

Anesthetic Technique

Anesthesia was induced with sevoflurane plus fentanyl 2 mcg/kg and tracheal intubation was facilitated with cisatracurium 0.1 mg/kg. Anesthesia was maintained with sevoflurane and cisatracurium 0.05 mg/kg/dose was given on the basis of train-of-four neuromuscular monitoring. ECG, noninvasive blood pressure, heart rate, temperature, oxygen saturation, and exhaled CO^2 (end tidal CO^2) were continuously monitored during the procedure.

Caudal Technique

After induction of anesthesia and before skin incision, a caudal epidural block was performed in all patients in the 3 groups. We put our patients in the left lateral decubitus position with knees drawn toward the chest with legs at 90° over the hips and 45° over the knee (the lateral position is efficacious in pediatrics because it permits easy access to the airway when general anesthesia has been administered prior to performing

the caudal block).

A 23-gauge short-beveled needle less than 4 cm in length was inserted 1 – 2 mm caudally halfway between both cornua, proximal to the vertex of the hiatus, at a 45° angle in relation to the skin. After the loss of resistance (characteristic of passing the sacrococcygeal membrane), the needle was repositioned, decreasing the angle to 20° – 30° and inserted 2 – 3 mm into the vertebral canal under sterile conditions. Two milliliters of the bupivacaine (0.125%) was initially administered with epinephrine 1:200,000 as a test dose and this was followed by the rest of the studied drugs. Aspiration tests should be repeated often during drug administration and should be slow, lasting about 90 seconds, to check for possible presence of cerebro-spinal fluid or blood. If the injection is too slow it may cause leakage of the drugs through the spinal roots; if it is too rapid, it may cause a too high block or, in the case of an inadvertent intravascular injection, toxic plasmatic concentration proportional to infusion speed. Moreover, it was prudent to check if there is a subcutaneous Pompeii (emphysema or bleb) resulting from incorrect placement of the needle.

During surgery, adequate analgesia was defined by hemodynamic stability, as indicated by the absence of an increase in heart rate or systolic blood pressure of more than 15% of the baseline values obtained just before the surgical incision. Anesthesia was discontinued when the wound dressing was applied, and extubation of the patient done. The patient was transferred to the postoperative care unit (POCU). All operations were carried out by the same team of orthopedic surgeons.

We monitored the following data:

1. Demographic data, intraoperative and postoperative variables.
2. Postoperative analgesia was assessed by using the Pediatric Objective Pain Scale (15), where each criterion scores 0 – 2 to give a total score 0 – 10, and a total score of less than 5 mean adequate analgesia, Appendix 1.
3. The duration of analgesia was taken at the time starting from extubation until analgesia was required as evidenced by a pain score > 4.
4. The number of patients who received intravenous paracetamol as a rescue analgesic.
5. The total amount of paracetamol doses (15 mg/kg per dose) as a rescue analgesic needed after the onset of pain.
6. The baseline blood glucose level was checked with routine investigation, rechecked at induction of anesthesia (before caudal block), and 4 hours after injection of caudal block.
7. Postoperative vomiting defined as vomiting and/or retching without expulsion of gastric content were recorded by a nurse who was blinded to study conditions. It was treated if vomiting occurred more than twice in 2 minutes with by granisetron (0.1 mg/kg and repeated if necessary but not in less than 12 hours).
8. B-Endorphin (β-Ep) at baseline before anesthesia, 3 hours, and 24 hours after extubation.
9. Side effects from motor block, paresthesia, and urine retention.

Statistical Analyses

A sample size of 19 cases in each group (completed in 20 cases) was calculated to be sufficient for 80% power to detect a difference of 20% in postoperative pain score (primary outcome variable) and time to first analgesic requirement (secondary outcome variable) to have a 5% significance level. Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS) Windows version 16.0. The normality of the data was assessed by the Kolmogorov-Smirnov test. The 3 groups were compared using analysis of variance (ANOVA) then post hoc (LSD). Paired T-tests were used to compare results within the same group. Pain scores were compared using the Kruskal–Wallis test. Intergroup categorical data were analyzed using the $\chi 2$ test or Fisher exact test when appropriate. P-values were considered significant if < 0.05.

Results

There were no significant differences between the 3 groups regarding preoperative patient's characteristics, Table 1.

The mean blood pressure values showed a significant difference between the 3 groups at 2 and 8 hours postoperatively. In the comparison between the IV dexamethasone group and the caudal dexamethasone group, we found a significant decrease in the mean blood pressure value at 2 hours postoperatively. Also, a significant decrease in mean blood pressure value was found between the IV dexamethasone group compared with the control group at the 8 hours postoperatively. There was no significant difference between the caudal dexamethasone group and the control group. When comparing the baseline mean blood pressure with the other readings within the same group, we found that the IV dexamethasone group showed

Table 1. *Mean ±SD preoperative patient's characteristics among the 3 groups.*

Items	Control group	IV dexamethasone group	Caudal dexamethasone group	*P*-Value
Age (months)	73.8±44.2	70.2±46.8	74.1±40.7	NS
Weight (kg)	18.55±6.4	17.8±7.3	19.45±6.7	NS
Sex: number (%) Male Female	16(53.33%) 14 (46.66%)	17 (56.66%) 13 (43.33%)	15 (50%) 15 (50%)	NS

NS= No Significant

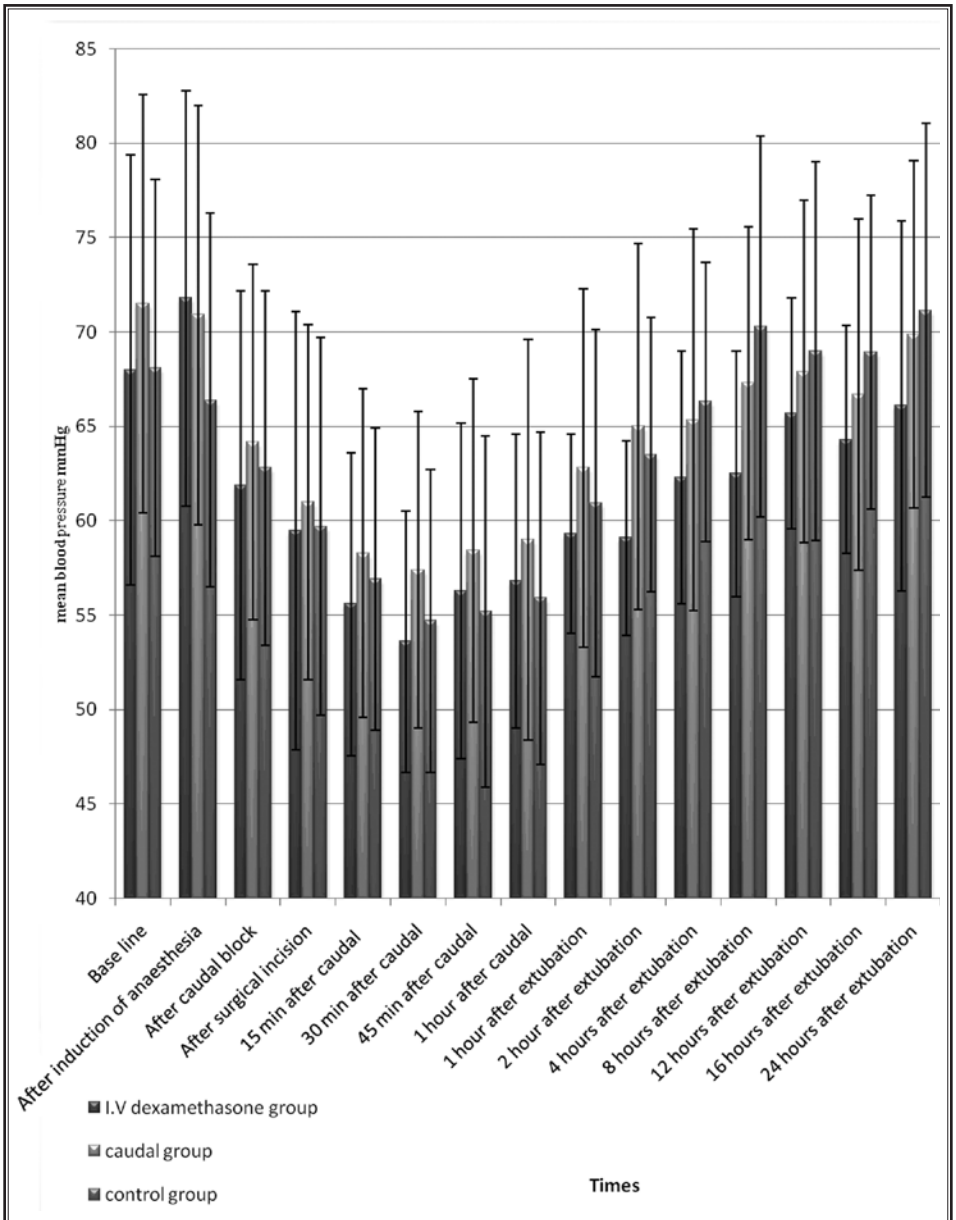

Fig. 1. *The mean blood pressure changes in patients of the three studied groups (mean ±SD) .*

a significant statistical difference except after induction of anesthesia, 12 hours, 16 hours, and 24 hours postoperatively; in the caudal dexamethasone group a significant statistical difference was found except after induction of anesthesia and 24 hours postoperatively; while, in the control group, there was a significant statistical difference except after induction of anesthesia, 2 hours, 4 hours, 8 hours, 12 hours, 16 hours, and 24 hours postoperatively Fig. 1.

The heart rate showed a significant difference between the 3 groups at 1, 2, 4, 8, 12, 16, and 24 hours postoperatively. There were no significant differences between the IV dexamethasone group and the caudal dexamethasone group at all intraoperative and postoperative readings. The IV dexamethasone group showed a significant statistical difference when compared with the control group after caudal analgesia, after surgical incision, 1, 2, 4, 8, 16, and

24 hours postoperatively. The caudal group showed a significant statistical difference when compared with the control group at 1, 2, 4, 8, 12, 16, and 24 hours postoperatively. The results of the 3 groups showed that the baseline heart rate showed a statistical significant decrease with all intraoperative and postoperative readings except after induction of anesthesia and after caudal block in the caudal dexamethasone group, and at 12 hours postoperatively in the control group, Fig. 2.

Regarding the pediatric objective pain score, we found a significant difference between the 3 groups at all times except after 12 hours postoperatively, Fig. 3.

The duration of analgesia and the number of analgesic doses (IV paracetamol 15 mg/kg/dose) in the first 24 hours postoperatively showed a significant difference between the 3 groups. When comparing the control group with the caudal and IV dexamethasone groups, we found a statistical significant difference, while there was no significant difference when comparing the IV dexamethasone group with the caudal dexamethasone group.

We found that none of the patients included in the IV dexamethasone group or caudal dexamethasone group received paracetamol as a rescue analgesic in the early postoperative period (the first 2 hours) versus 7 (11%) in the control group with a significant difference between the 3 groups. The number of patients who didn't need analgesia within the first 24 hours was 1 (1.6%) in both the IV dexamethasone group and caudal dexamethasone group versus none of the patients in

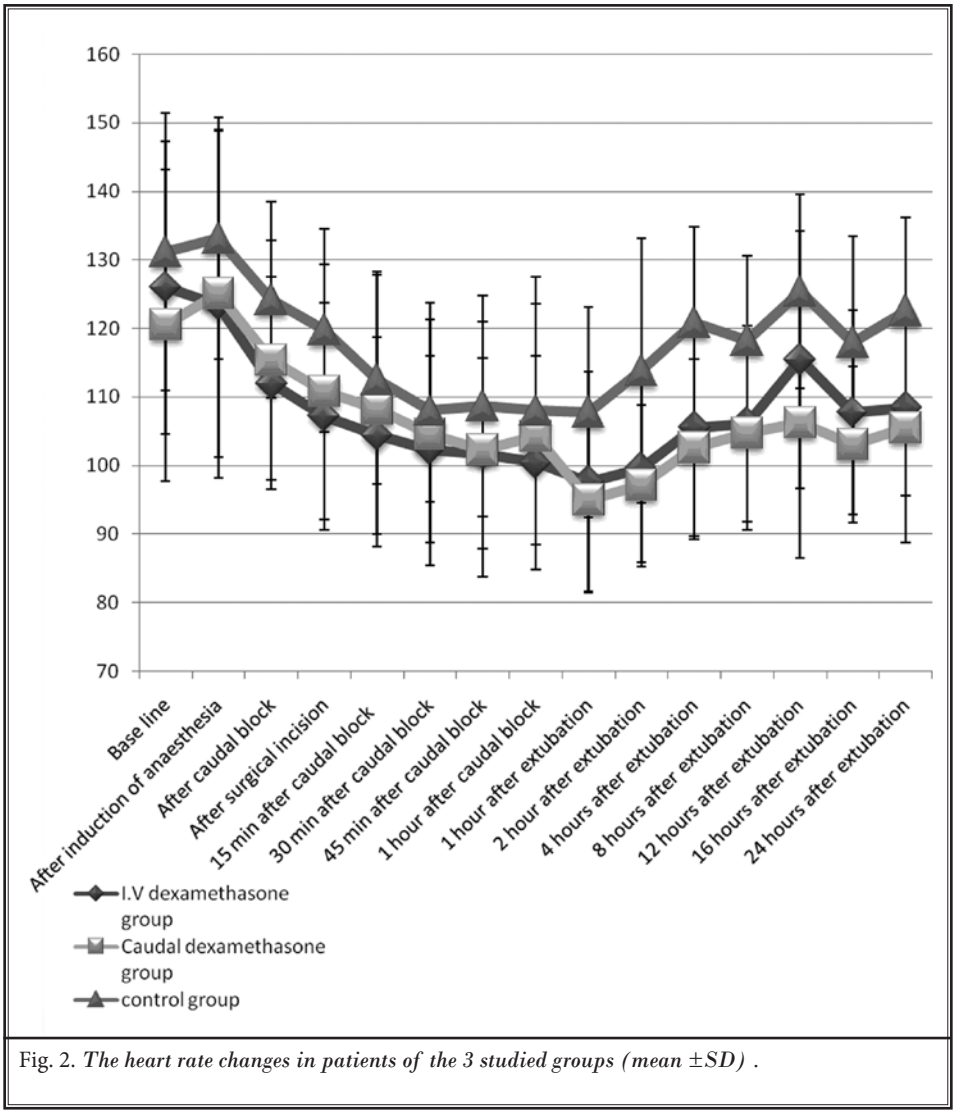

Fig. 2. *The heart rate changes in patients of the 3 studied groups (mean ±SD) .*

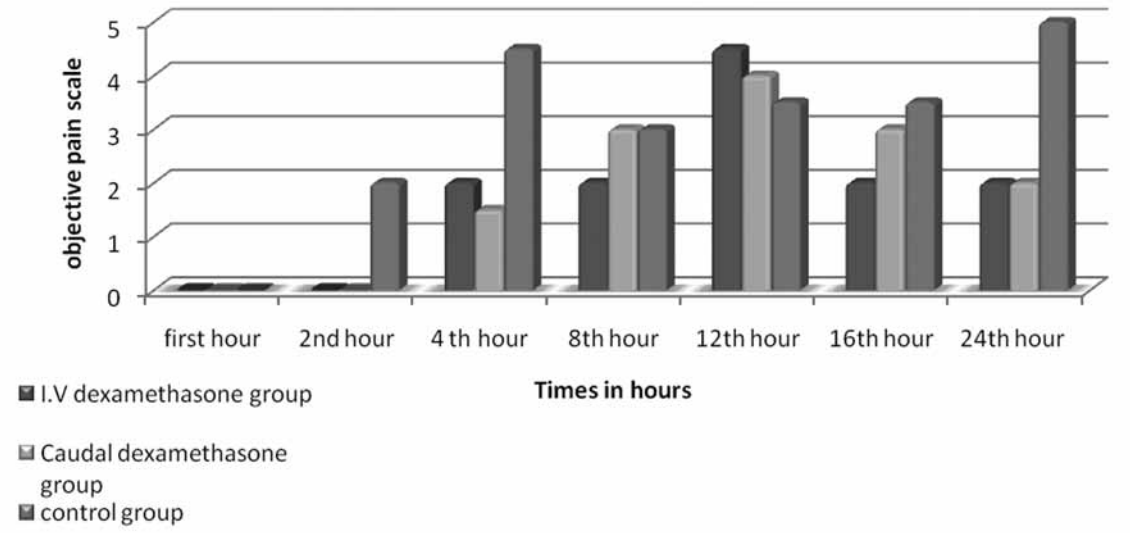

Fig. 3. *Median values for objective pain scale.*

Table 2. *Mean ± SD of duration of analgesia (hours), number of analgesic doses and total amount of paracetamol (mg).*

	Control group	IV dexamethasone group	Caudal dexamethasone group	*P*-value
Duration of analgesia (hours)	4 ± 0.97	12.95 ± 3.66	12.90 ± 3.74	*£&
Number of analgesic doses	3.30 ± 0.65	1.80 ± 0.52	1.80 ± 0.52	*£&
Total amount of paracetamol (mg)	842.5±357.7	440±244.8	458±192	*£&
Number (%) of patients received analgesia in 1st 2 hrs	7 (11%)	0 (0%)	0 (0%)	*
Number (%) of patients did not received analgesia within 24 hrs	0 (0%)	1 (1.6%)	1 (1.6%)	NS

* = significant between the three groups by ANOVA test
£ = significant between IV dexamethasone group and control group by post-hock LSD test
& = significant between caudal dexamethasone group and control group post-hock LSD test
NS = Not Significant

the control group with no significant difference among the 3 groups, Table 2.

Preoperative blood glucose was similar in the 3 studied groups. No significant increase in blood glucose level was recorded at 4 hours after caudal block in any of the 3 studied groups, Table 3.

The β-endorphin showed statistical significant differences between the 3 groups at preoperative and after 24 hours postoperatively. There were no significant statistical differences between the IV dexamethasone group and caudal dexamethasone group at all times. There was a significant difference between the IV dexamethasone group and the control group at the baseline value and 3 hours postoperatively. A significant difference was found between the caudal dexamethasone group and the control group at 24 hours postoperatively.

The β-endorphin levels showed a significant increase at 3 hours and 24 hours postoperatively in the IV dexamethasone group and the caudal dexamethasone group compared to the corresponding preoperative levels in each group. The β-endorphin level in the control group showed a significant increase at 24 hours postoperatively over the preoperative value, Fig. 4.

Our study showed that only one patient (5%) in IV dexamethasone group and 4 (20%) in the caudal

Table 3. *Mean ±SD of blood glucose levels in the 3 groups.*

Items	Control group	IV dexamethasone group	Caudal dexamethasone group	*P*-Value
Baseline blood glucose (mg/dL)	74.3±13.3	72.2±11.7	73.4±10.4	NS
Blood glucose at induction of anesthesia (mg/dL)	82±14.4	85.7±12.8	83.5±15.3	NS
Blood glucose 4 hours after caudal block (mg/dL)	99.5±15.7	108.8±18.9	105.3±17.1	NS

NS= No Significant

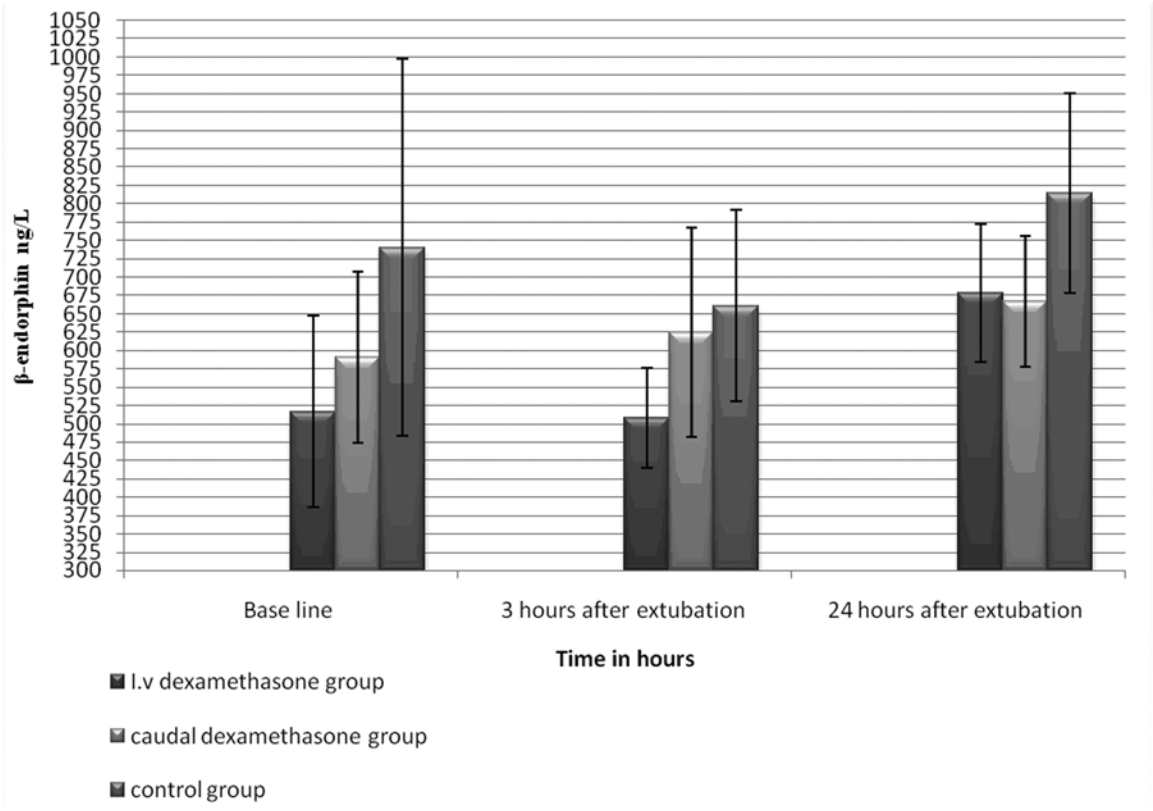

Fig. 4. β-*Endorphin changes in patients of the 3 studied groups (mean ±SD)* .

dexamethasone group complained of postoperative vomiting in comparison to 14 patients (70%) in the control group with a significant statistical difference in comparing the 3 groups, Fig. 5. None of our patients complained of recurrent vomiting in the IV dexamethasone group or the caudal dexamethasone group. While, in the control group 4 patients (20%) had 2 bouts of vomiting, 4 (20%) had 3 bouts, and 2 (10%) had 4 bouts of vomiting.

There were no side effects of dexamethasone usage, such as increased blood glucose, delayed wound healing, and wound infection. No other complications of significant difference were found among the 3 groups from caudal block (motor block, paresthesia, and urine retention).

Discussion

As already known, the usage of steroid in adults for treating chronic pain is well established. Epidural steroids used in the treatment of a compression frac-

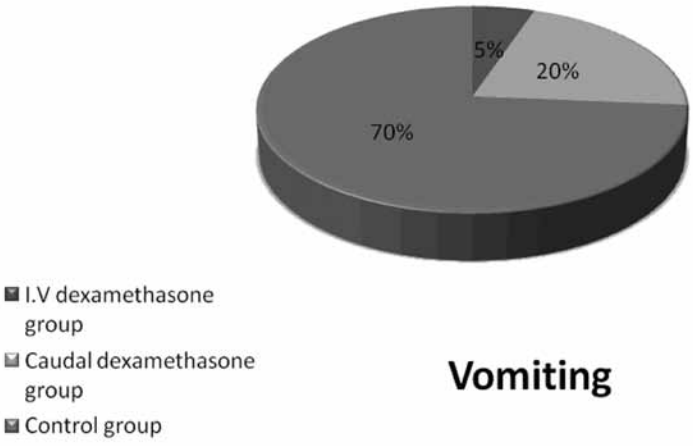

Fig. 5. *Percentage of patients complains of vomiting in the 3 groups.*

ture of the lumbar spine with radicular pain or a facet or nerve root cyst with radicular pain would warrant epidural steroids. The treatment of pain of post-laminectomy syndrome, post-herpetic or post-traumatic (including intercostal) neuralgia, diabetic neuropathy, and muscle contraction headaches (myofascial pain) has also been documented (16). To our knowledge, there are few studies in children and in acute postoperative pain. So, we tried in this study to evaluate the effectiveness of IV dexamethasone versus caudal dexamethasone as an adjuvant to caudal bupivacaine for control of postoperative pain and vomiting after pediatric lower orthopedic surgery. The dose of IV dexamethasone (0.5 mg/Kg) used in this study was based on a study by Hong et al (11) who used IV dexamethasone (0.5 mg/kg) in combination with ropivacaine in caudal block versus caudal ropivacaine alone in children aged 1 – 5 years (< 20 kg) undergoing day-case unilateral orchiopexy. Hong et al (11) showed that IV dexamethasone reduced postoperative pain, decreased rescue analgesic requirements, and prolonged analgesic duration compared to a caudal block alone (10.7 ± 2.4 vs. 7 ± 3.4 hours). Mohamed et al (17) found that pre-operative injection of 0.5 mg/kg dexamethasone IV was as effective as bilateral gloss pharyngeal nerve infiltration with bupivacaine in reducing postoperative pain in electrocautery tonsillectomy in children. These results agreed with our results as we found that IV 0.5 mg/Kg dexamethasone combined with caudal bupivacaine is associated with significant benefits for postoperative analgesia for 12 ± 3.6 hours and reduced analgesic requirements during the first 24 hours postoperatively.

We found that none of our patients included in the IV or caudal dexamethasone groups received paracetamol as a rescue analgesic in the early postoperative period (the first 2 hours as it is the most painful period) which indicated that the analgesic effect of dexamethasone started immediately postoperatively. Abdelmonem and Rizk (18) found that administration of 8 mg dexamethasone intravenously or locally combined with bupivacaine in perianal block in adult patients undergoing hemorrhoidectomy provided faster onset of block and prolonged duration of analgesia (4.78 ± 0.35 hours in the local dexamethasone group and 4.76 ± 0.28 hours in the IV dexamethasone group compared with the control group 2.7 ± 0.28 hours). They reported a lower incidence of vomiting. Our results regarding the onset and duration of analgesia were contrary to Kjetil et al (19) who studied the effect of 16 mg IV dexamethasone when added to non-steroidal anti-inflammatory drugs (NSAIDs) for patients undergoing breast surgery. They demonstrated that there was no effect during the first 6 hours after administration of dexamethasone, while their study showed a significant benefit for postoperative analgesia during the 24 – 72 hours postoperative (19).

The theories of analgesic action of systemic administration of steroids may be related to suppression of tissue levels of bradykinin (20), and the release of neuropeptides from nerve endings (21), both of which can enhance nociception in inflamed tissue. The established reduction in prostaglandin production might further contribute to analgesia by inhibiting the synthesis of the cyclo-oxygenase isoform-2 in peripheral tissues and in the central nervous system (22). Steroids also inhibit other mediators of inflammatory hyperalgesia, for example, tumor necrosis factor α, interleukin-17β, and interleukin-6 (11).

Our study showed that the addition of 0.1 mg/Kg dexamethasone to caudal bupivacaine had a significant postoperative analgesic effect for 12 ± 3.7 hours and significantly decreased the total dose of additional analgesia required (equal to that of the IV dexamethasone group). None of the patients included in the caudal dexamethasone group received paracetamol analgesia in the

first 2 hours postoperatively. This was in agreement with Yousef et al (23), who compared 0.1mg/kg dexamethasone with 50 mg magnesium sulfate combined with caudal ropivacaine and caudal ropivacaine alone in children undergoing inguinal hernia repair. They found that the duration of analgesia without the need for rescue pethidine in the group receiving ropivacaine dexamethasone was 12 ± 4 hours, which was significantly longer than that of the magnesium group (8 ± 3 hours) and that of control group (4 ± 1 hours) (23). El-Feky and Abd El Aziz (24) studied different additives (dexamethasone 0.1 mg /kg, fentanyl 1 mcg/kg, dexmedetomidine 1 mcg/kg) to caudal bupivacaine 0.25% and lidocaine 1% and they found that both caudal dexmedetomidine and caudal dexamethasone provide prolonged postoperative analgesia compared to caudal local anesthetic alone or when caudal fentanyl added. They also showed that dexamethasone had less sedation score than that of fentanyl and dexmedetomidine and fewer side effects (respiratory depression, vomiting, and itching) than that of fentanyl (24). This was in contrast with Blanloeil et al (25) who reported that epidural steroids do not decrease pain after thoracotomy, although in their study the opioid consumption was less in patients who received epidural steroids.

The pathophysiological mechanisms for epidural steroid effects may be related to the anti-inflammatory action, edema reduction, or shrinkage of connective tissue. Local steroid application was found to suppress transmission in thin unmyelinated C-fibers but not in myelinated β-fibers (26). It has also been suggested that steroids may bind directly to the intracellular glucocorticoid receptor, and their effects are predominantly mediated through altered protein synthesis via gene transcription (27). Lastly, epidural dexamethasone may affect intraspinal prostaglandin formation (10).

In our study, we found that there were no significant differences in the analgesic duration or analgesia requirements between the IV dexamethasone group and caudal group which suggests that the analgesic effect of epidurally administered steroids may be due to their systemic absorption. Our study also showed no significant changes in blood glucose in the 3 groups. Maillefert et al (28) found that a single epidural injection of 15 mg dexamethasone acetate is associated with transient adrenal suppression, denoting passage of the steroid into the systemic blood stream (28). Thomas and Beevi (29) revealed that patients receiving epidural dexamethasone either alone or combined with bupivacaine had less postoperative Visual Analogue Scale (VAS) pain scores and analgesic consumption than observed in the control group who received IV dexamethasone and epidural bupivacaine. This indicates that dexamethasone had action at the spinal cord level, in addition to its action on the peripheral tissues, after systemic absorption from the epidural space. They found that postoperative analgesic duration was comparable among the 3 groups which may be due to administration of dexamethasone by either the intravenous or epidural route (29). Also Lansinget al (30) recognized endocrine disorders resulting from prolonged administration of epidural steroids. Systemic absorption of the injected steroids was determined to be the cause of the symptoms and abnormal laboratory findings in each case (30).

Regarding the role of dexamethasone in the prevention and treatment of postoperative nausea and vomiting (PONV), many studies in adults reported the usage of steroid in reducing postoperative nausea and vomiting or even chemotherapy-related nausea and vomiting (31). Multiple theories have been proposed for the mechanism of action of dexamethasone:reduction of 5-hydroxytryptophan (5HT3) in neurons by reduction of tryptophan, decreased serotonin release from the gut, and increasing the response to other antiemetics at a receptor level (32). In addition, there may be decreased 5HT3 turnover in the central nervous system or central inhibition of prostaglandin synthesis (33). In our study, we found that patients who received dexamethasone either intravenously or caudally experienced less incidence and frequency of vomiting during the first 24 hours postoperative than patients who received caudal bupivacaine alone, i.e., dexamethasone either intravenously or caudally prevented postoperative vomiting. This finding was in agreement with Madan et al (34) who evaluated the efficacy and safety of different doses of prophylactic IV dexamethasone for postoperative nausea and vomiting in children (aged 2 – 15 years) scheduled for strabismus surgery. They studied different doses of IV dexamethasone (0.25 mg/kg, 0.5 mg/kg, and 1.0 mg/kg) with normal saline and found that dexamethasone 0.25 mg/kg is more effective than saline and equally effective compared with larger doses for preventing PONV for pediatric strabismus surgery with no statically significant differences in postoperative blood glucose levels and wound healing (34). Our results were in agreement with different studies. Hermans et al (35) found that a single IV injection of dexamethasone either 0.15 mg/kg or 0.5 mg/kg at the induction of anesthesia was effective in reducing the incidence

of early and late PONV and the level of pain on the second postoperative day. Nan Ying et al (36) showed that 1 mg/kg ropivacaine (0.2%) plus dexamethasone 0.5 mg/kg infiltration effectively lowers pain, improves oral intake, lowers postoperative nausea and vomiting, and decreases the time to discharge. Backes et al (37) found that preoperative administration of 10 mg dexamethasone intravenously with 4 mg zofran 15 minutes before skin closure and 10 mg dexamethasone after 24 hours in adult patients undergoing lower limb orthopedic surgeries under general anesthesia without adjuvant neuraxial analgesia reduced the hospital stay and provided better postoperative control on pain and vomiting with less analgesic and antiemetic consumption during the first 24 hours than the use of 4 mg zofran alone 15 minutes before skin closure. They also found that dexamethasone improves the mood and emotional status during the first 24 hours after surgery (37). Khafagy et al (10) used epidural 4 mg dexamethasone versus 50 mcg fentanyl in adult patients undergoing lower abdominal surgeries and found that epidural dexamethasone has the same analgesic potency as epidural fentanyl with antiemetic effect. Hong et al (11) used IV dexamethasone in combination with a caudal block in pediatric patients undergoing orchiopexy and found that the incidences of vomiting were very low in both groups with no statistically significant difference.

The mechanism of dexamethasone as an antiemetic effect is not clear. There are many theories, including prostaglandin antagonism, release of endorphins resulting in mood elevation, a sense of well-being, reduced levels of serotonin in neural tissue, and prevention of release of serotonin in the gut (38). Our finding regarding β-endorphin was in agreement with that theory (release of endorphins resulting in mood elevation) as we found a statistically significant increase in β-endorphin level at 3 and 24 hours postoperatively in patients receiving dexamethasone either intravenously or caudally when compared with the preoperative baseline value. Postoperative vomiting is approximately twice as frequent amongst children as adults with an incidence of 13% – 42% in all pediatric patients (39,40). Postoperative nausea and vomiting remain a significant clinical issue that can detract from patients' quality of life in the hospital as well as in the days immediately after discharge. Severe postoperative vomiting can result in a range of complications including wound dehiscence, dehydration and electrolyte imbalance, and pulmonary aspiration (41); in addition the commonly used antiemetic can produce significant side effects, including sedation, headache, dysphoria, extrapyramidal symptoms, dry mouth, and blurred vision. Although serotonin antagonists are relatively devoid of side effects, high cost limits their use (40).

Conclusion

The addition of dexamethasone either caudally or through the intravenous route to caudal 0.25% bupivacaine significantly prolongs the duration of postoperative analgesia, reduces the need for rescue postoperative analgesia, and improves antiemetic control without an increasing the incidence of side effects, especially blood glucose, in children undergoing lower orthopedic surgery.

We recommend further clinical trials evaluating the efficacy of different doses of dexamethasone either intravenously or caudally on *B*-endorphins and its relation to postoperative vomiting.

Appendices 1. Objective pain scale (15).

Observation	Criteria	Points
Systolic blood pressure	BP ± 10 % Preoperative	0
	BP >20 % Preoperative	1
	BP >30 % Preoperative	2
Crying	Not crying	0
	Crying but responds to tender loving care (TLC)	1
	Crying and does not respond to tender loving care (TLC)	2
Posture	No special posture	0
	Flexing leg and thighs	1
	Holding scrotum or groin	2
Movement	None	0
	Restless	1
	Thrashing	2
Agitation	Patient asleep or calm	0
	Mild	1
	Hysterical	2

References

1. Desai NV, Cheung VE. Postoperative pain associated with orthopedic shoulder and elbow surgery: A prospective study. *J Shoulder Elbow Surg* 2012; 21:441-450.
2. Young KD. Pediatric procedural pain. *Ann Emerg Med* 2005; 45:160- 171.
3. Henneberg WS, Nilsson BL. Acute pediatric pain, review. *Current Anesthesia & Critical Care* 2007; 18:126- 134.
4. Maheshwari VA, Blum CY, Shekhar L, Ranawat AS, Ranawat CS. Multimodal pain management after total hip and knee arthroplasty at the Ranawat Orthopedic Center. *Clin Orthop Relat Res* 2009; 467:1418-1423.
5. Moriarty T, Brown R. Neuraxial blockade in children. *Anaesthesia and Intensive Care Medicine* 2007; 8:194-199.
6. Hansen TG, Henneberg SW, Wlather LS, Lund J, Hansen M. Caudal bupivacaine supplemented with caudal or intravenous clonidine in children undergoing hypospadias repair: Double-blind study. *Br J Anaesth* 2004; 92:223-227.
7. Naguib M, Sharif AM, Seraj M, el Gammal M, Dawlatly AA. Ketamine for caudal analgesia in children: Comparison with caudal bupivacaine. *Br J Anaesth* 1991; 67:559-564.
8. Hong JY, Lee IH, Shin SK, Park EY, Ban SY, Cho JE, Kil HK. Caudal midazolam does not affect sevoflurane requirements and recovery in pediatric day-case hernioplasty. *Acta Anaesthesiol Scand* 2008; 52:1411-1414.
9. Abdulatif M, El-Sanabary M. Caudal neostigmine, bupivacaine, and their combination for postoperative pain management after hypospadias surgery in children. *Anesth Analg* 2002; 95:1215-1218.
10. Khafagy HF, Refaat AI, El-SabaeHH,Youssif MA. Efficacy of epidural dexamethasone versus fentanyl on postoperative analgesia. *J Anesth* 2010; 24:531-536.
11. Hong JY, Han SW, Kim WO, Kim EJ, Kil HK. Effect of dexamethasone in combination with caudal analgesia on postoperative pain control in day case paediatric orchiopexy. *Br J Anaesth* 2010; 105:506-510.
12. Aouad MT, Siddik SS, Rizk LB, Zaytoun GM, Baraka AS. The effect of dexamethasone on postoperative vomiting after tonsillectomy. *Anesth Analg* 2001; 92:636-640.
13. Elhakim M, Ali NM, Rashed I, Riad MK, Refat M. Dexamethasone reduces postoperative vomiting and pain after pediatric tonsillectomy. *Can J Anaesth* 2003; 50:392-397.
14. Karaman M, Ilhan AE, Dereci G, Riad MK, Refat M. Determination of optimum dosage of intraoperative single dose dexamethasone in pediatric tonsillectomy and adenotonsillectomy. *Int J Pediatr Otorhinolaryngol* 2009; 73:1513-1515.
15. Hannallah RS, Broadman LM, Belman AB, Abramowitz MD, Epstein BS. Comparison of caudal and ilioinguinal/iliohypogastric nerve blocks for control of post-orchiopexy pain in pediatric ambulatory surgery. *Anesthesiology*1987; 66:832-834.
16. Neil C, Sanjeeva G. Epidural steroids. *Continuing Education in Anaesthesia, Critical Care & Pain* 2010; 10:1-5.
17. Mohamed SK, Ibraheem AS, and Abdelraheem MG. Preoperative intravenous dexamethasone combined with glossopharyngeal nerve block: Role in paediatric postoperative analgesia following tonsillectomy. *Eur Arch Otorhinolaryngol* 2009; 266:1815-1819.
18. Abdelmonem A, Rizk S. Comparative study between intravenous and local dexamethasone as adjuvant to bupivacaine in perianal block. *Egyptian Journal of Anaesthesia* 2011; 27:163-168.

19. Kjetil H, Sem T, Ellen S, Raeder J. The prolonged postoperative analgesic effect when dexamethasone is added to a nonsteroidal anti- inflammatory drug (Rofecoxib) before breast surgery. *Anesth Analg* 2007; 105:481-486.
20. Hargreaves KM, Costello A. Glucocorticoids suppress levels of immunoreactive bradykinin in inflamed tissue as evaluated by microdialysis probes. *Clin Pharmacol Ther* 1990; 48:168-178.
21. Hong D, Byers MR, Oswald RJ. Dexamethasone treatment reduces sensory neuropeptides and nerve sprouting reactions in injured teeth. *Pain* 1993; 55:171-181.
22. Ferreira SH, Cunha FQ, Lorenzetti BB, Michelin MA, Perretti M, Flower RJ, Poole S. Role of lipocortin-1 in the anti-hyperalgesic actions of dexamethasone. *Br J Pharmacol* 1997; 121:883-888.
23. Yousef G, Ibrahim T, KhderA, Ibrahim M. Enhancement of ropivacaine caudal analgesia using dexamethasone or magnesium in children undergoing inguinal hernia repair. *Anesthesia Essays and Researches* 2014; 8:13-19.
24. El-Feky ME, Abd El Aziz AA. Fentanyl, dexmedetomidine, dexamethasone as adjuvant to local anesthetics in caudal analgesia in pediatrics: A comparative study. *Egypt J Anaesth* 2014; 30:1-6.
25. Blanloeil Y, Bizouarn P, and Le Teurnier Y, Le Roux C, Rigal JC, Sellier E, Nougarède B. Postoperative analgesia by epidural methylprednisolone after posterolateral thoracotomy. *Br J Anaesth* 2001; 87:635-638.
26. Johansson A, Hao J, Sjlund B. Local corticosteroid application blocks transmission in normal nociceptive C-fibers. *Acta Anaesthesiol Scand* 1990; 34:335-338.
27. Barnes P J. Anti-inflammatory actions of glucocorticoids: Molecular mechanisms. *Clin Sci* (*Lond*) 1998; 94:557-572.
28. Maillefert JF, Aho S, and Huguenin MC, Chatard C, Peere T, Marquignon MF, Lucas B, Tavernier C. Systemic effects of epidural dexamethasone injections. *Rev Rhum Engl Ed* 1995; 62:429-432.
29. Thomas S, Beevi S. Epidural dexamethasone reduces postoperative pain and analgesic requirements. *Can J Anesth* 2006; 53:899-905
30. Lansang MC, Farmer T, Kennedy L. Diagnosing the unrecognized systemic absorption of intra-articular and epidural steroid injections. *Endocr Pract* 2009; 15:225-228.
31. Apfel CC, Korttila K, Abdalla M, Kerger H, Turan A, Vedder I, Zernak C, Danner K, Jokela R, Pocock SJ, Trenkler S, Kredel M, Biedler A, Sessler DI, Roewer N; IMPACT Investigators. A factorial trial of six interventions for the prevention of postoperative nausea and vomiting. *New England Journal of Medicine* 2004; 350:2441-2451.
32. Henzi I, Walder B, Tramer MR. Dexamethasone for the prevention of postoperative nausea and vomiting: A quantitative systematic review. *Anesthesia & Analgesia* 2000; 90:186-194.
33. Habib, Ashraf S. Gan, Tong J. Combination antiemetics: What is the evidence? *International Anesthesiology Clinics* 2003; 41:119-144.
34. Madan R, Bhatia A, Chakithandy S. Prophylactic dexamethasone for postoperative nausea and vomiting in paediatric strabismus surgery: A dose ranging and safety evaluation study. *Anesth Analg* 2005; 100:1622-1626.
35. Hermans V, De Pooter F, De Groote F, DeHert S, Van der PL. Effect of dexamethasone on nausea, vomiting, and pain in paediatric tonsillectomy. *British Journal of Anaesthesia* 2012; 109:427-431.
36. Nan YJ, Guang XC, Wei G. Ropivacaine plus dexamethasone infiltration reduces postoperative pain after tonsillectomy and adenoidectomy. *International Journal of Pediatric Otorhinolaryngology* 2013; 77:1881-1885.
37. Backes J, Bentley J, Politi J. Dexamethasone reduces length of hospitalization and improves postoperative pain and nausea after total joint arthroplasty a prospective, pandomized controlled trial. *The Journal of Arthroplasty* 2013; 28:11-17.
38. Harris A. Cytotoxic-therapy-induced vomiting is mediated via enkephalin pathways. *Lancet* 1982; 8274:714-716.
39. Lerman J. Surgical and patient factors involved in postoperative nausea & vomiting. *Br J Anaesth* 1992; 69:24S-32S.
40. Rose JB, Watcha MF. Postoperative nausea & vomiting in paediatric patients. *Br J Anaesth* 1999; 83:04-117.
41. Olutoye O, Watcha MF. Management of postoperative vomiting in paediatric patients. *Int Anaesthesiol Clinics* 2003; 41:99-117.