A Comparison of Using Ketamine Versus Combination of Ketamine and Thiopentone in Short Painful Procedures in Pediatrics

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ABSTRACT:

BACKGROUND:

Short painful procedures in pediatric age group like bone marrow aspiration (BMA) and biopsy taking are day case operations which demand rapid recovery and minimal incidence of postoperative complications.

OBJECTIVE:

To compare between intra & postoperative complications & the time of stay in the recovery room for pediatrics undergoing short painful procedures under general anesthesia with either "ketamine and thiopental" or "ketamine alone".

PATIENTS AND METHOD:

THIS IS A PROSPECTIVE RANDOMIZED clinical trial done in Children Welfare Hospital in Medical City, Baghdad, Iraq, from August - November 2010 on 89 children patients who were scheduled for short painful procedures. All patients were allocated randomly into 2 groups: the 1st group (KT) received I.V ketamine 1% (1mg/kg) plus I.V thiopental 1% 3-5 mg/kg (anesthetizing dose) on induction and maintained on intermittent I.V doses of thiopental 1% in case of need. While the 2nd group(K) received I.V ketamine 1% (1.5mg/kg) alone on induction and maintained on intermittent I.V doses of ketamine 1%(0.5mg/kg) in case of need. Any intra or postoperative complications & the duration of recovery for all patients were recorded.

RESULTS:

It was found that the intraoperative complications (temporary & mild decrease in arterial O_2 saturation and its associated breath holding, & cough) occurred more in the KT group, while the occurrence of (mild involuntary movements and verbal responses) occurred more frequently in the K group**.** The postoperative complications (nausea, vomiting, verbal hallucinations and dizziness) occurred only in the K group. The duration of recovery is more prolonged in the (KT) group.

CONCLUSION:

The use of combination of thiopentone and ketamine is associated with more mild and temporary intraoperative decreased arterial oxygen saturation, breath holding, and postoperative cough than using ketamine alone, while the use of ketamine alone is associated with more mild involuntary movements and verbal responses, postoperative nausea &/or vomiting, hallucinations, and dizziness. The duration of recovery is prolonged by the use of thiopental.

KEY WORDS: ketamine, thiopental, TIVA, pediatrics, day case.

INTRODUCTION:

Bone marrow aspiration and biopsy taking are done to investigate the blood cells in the body. Aspiration refers to the removal of fluid by suction. A biopsy is the removal of small piece of marrow tissue by a special biopsy needle. This procedure is done under several approaches of anesthesia [(1)]. In pediatric age group should be done under general anesthesia [(2)].They areregarded as day case surgery which is defined by the Royal College of Surgeons of England as "a patient who is admitted for investigation oroperation on a planned non-resident basis [(3)] . The principles of anesthesia in day case surgery are the same as for in-patient surgery, requires high quality induction, maintenance, and recovery. The recovery should be free from side effects [(4)].The use of continuous infusion techniques has considerable practical advantages, including minimal cardiovascular depression, rapid recovery and the avoidance of hazards of exposure to inhalational agents [(5)].For long time this done using Ketamine alone. The use of acombination of ketamine & thiopental to decrease the doses of both drugs and therefore decreases their side effect. This to evaluate the

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intraoperative and postoperative complications & the time of stay in recovery room for intravenous anesthesia (TIVA) with either a combination of "ketamine plus thiopental" or "ketamine alone".

PATIENTS AND METHOD:

This is a prospective randomised clinical trial done in Children Welfare Hospital in Medical City, Baghdad, Iraq, during 3 months from August - November 2010 on 89 children patients who were scheduled for short painful procedures.Demographic data of name, age & weight of all patients were recorded in an already prepared data collecting sheet.The procedures under GA were performed as day-case surgeries. All children were assessed before the start of procedure by taking history & examination. All children were fasted from solid food & clear fluids for 6 and 2 hours respectively. Any patient with cardiovascular & respiratory diseases, any anomaly of upper airways or history of recent convulsion, allergy or contraindication to drugs used in the study were excluded from the study.All children received intravenous fluid (dextrose saline) to replace fasting and maintenance time and were monitored hemodynamicly and O2 saturation using pulse oxymetry.All patients were allocated randomly into 2 groups: The 1st group (KT) (49 patient) was anaesthetized by giving at first 1 % ketamine (1mg/kg). 1-2 minutes later (during which the positioning of the patient & sterilization of the site of puncture were performed), thiopental 3-5 mg/kg (anesthetizing dose) as 1% (diluted as 10mg/ml) was administered immediately before the start of painful procedure (needle puncture), making the loss of eyelid reflex the sign of reaching the level of surgical anesthesia. In case of movement that disturbing the completion of the procedure, supplemental dose of thiopental was given.9 patients were dropped from this group because when they received an induction dose of ketamine (l mg/kg), showed no need for a dose of thiopental during induction, (all were older than 8 years). The 2nd group (K) (40 patient) was anesthetized by giving 1% ketamine (1.5mg/kg), and in case of movement that disturbing the completion of the procedure, supplemental dose of ketamine (0.5mg/kg) was given.All children were spontaneously breathing with O2 mask, any apnea managed by assisted ventilation using Jacson Ree's breathing system.

Any developed complication intraoperatively like the following was recorded:

1. "Temporary decrease in arterial O_2 saturation" (either associated with breath holding or not) during induction of anesthesia.
2. "Cough" during the procedure.
3. "Mild involuntary movements and /or verbal responses" those didn't disturb the completion of the procedure.

At the end of the procedure, the child was transferred to the recovery room. The discharge from recovery room was made according to modified Aldrete score for children.

Any developed complication postoperatively like the following was recorded:

1. Cough.
2. Nausea +/- vomiting.
3. Hallucinations (verbal, visual).
3. Dizziness.

The data were statistically analyzed and P-value were regarded as significant at 2 levels:

-If P-value ≤ 0.01 = highly accepted (highly significant). if it is ≤ 0.05 = accepted (significant).

RESULTS:

The frequency of each complication mentioned in table (1), and the correlations and regressions (P-values) between each complication and the doses of drugs mentioned in table (2). The mark (-) means the P-value cannot be measured because one of the comparable values is fixed. As the induction dose of ketamine in both groups was fixed, the P-value cannot be measured.The empty space indicates that this complication was not occurring. The need of maintenance dose and it's relation to the duration of procedure were shown in (table 3).While comparing the means of durations of the procedures for those received induction dose only with those received maintenance dose after induction in each group, it is clear that the need of maintenance dose is directly related to duration of the procedure in each group (and in all age groups) i.e. as the duration of the procedure increases, the chance of need of maintenance dose also increases.In (KT) group 7 patients needed a maintenance dose (17.5%) versus only 3 patients (7.5%) in (K) group. It is found that the need of maintenance dose was occurred once only for each one.

Table 1: Intra and Postoperative Complications.

Complications	Group I Ketamine + thiopental					Group II Ketamine only				
	<3y	3-8y	8-12y	>12y	Total	<3y	3-8y	8-12y	>12y	Total
Intraoperatively Temporary decrease in arterial oxygen saturation	16.7%	11.1%	10%	16.7%	12.5%	-	-	11.1%	-	2.5%
Breath holding	16.7%	5.6%	10%	-	7.5%	-	-	11.1%	-	2.5%
Cough	16.5%	-	-	-	2.5%	-	-	-	-	-
Mild involuntary movements +/- verbal responses	33.3%	11.1%	30%	50%	25%	66.7%	42.1%	22.2%	33.3%	42.5%
Postoperatively Cough	33.3%	-	-	-	5%	-	-	-	-	-
Nausea +/- vomiting	-	-	-	-	-	-	10.5%	44.4%	66.7%	20%
Hallucinations	-	-	-	-	-	-	5.26%	11.1%	33.3%	7.5%
Dizziness	-	-	-	-	-	-	5.26%	33.3%	66.6%	15%

Table 2: Correlations and regressions (P-values) between the doses of drugs (induction and maintenance) and the perioperative complications.

GROUP I Total dose of thiopental		Temporary decrease in arterial O_2 saturation	Cough during procedure	Mild involuntary movements +/- verbal responses	Cough during recovery	Nausea +/- vomiting	Hallucination	dizziness
			0.007	0.599	0.516			
Induction dose of thiopental		0.383	0.098	0.660	0.771			
Induction dose of ketamine		-	-	-	-			
Maintenance dose of thiopental			0.319	0.969	0.558			
GROUP II Total dose of ketamine				0.039		0.386	0.623	0.467
Induction dose of ketamine		-		-		-	-	-
Maintenance dose of ketamine				0.000		-	-	-

Table 3: Durations of procedures and recoveries.

DOSES	Duration of procedure		Duration of recovery	
	Range (min)	Mean (min)	Range (min)	Mean (min)
(KT)GROUP Total	00:30-15:50	4:57	2:00-82:00	35:11
Induction only 82.5%	00:30-15:50	4:37	2:00-85:00	31:22
Induction & maintenance 17.5%	4:28-8:00	6:30	18:00-82:00	53:09
(K) GROUP Total	00:46-14:05	4:42	3:00-87:00	28:56
Induction only 92.5%	00:46-10:08	5:03	3:00-87:00	29:42
Induction & maintenance 7.5%	3:30-14:05	7:07	10:25-33:30	19:25

Total: means the all members of the group.
Induction only: means the members who received only induction.
Induction + maintenance: means the members who received induction and maintenance

Table 4: The correlations & regressions (P-values) between the doses of drugs (induction & maintenance) and the durations of recovery.

	Duration	Of Recovery	
	For all patients	For those received only induction	For those received induction & maintenance
(KT) GROUP Total dose of thiopental	0.011	0.049	0.255
Induction dose of thiopental	0.016	0.033	0.021
Induction dose of ketamine	-	-	-
Maintenance dose of thiopental	0.071	-	0.271
(K) GROUP Total dose of ketamine	0.428	0.375	0.522
Induction dose of ketamine	-	-	-
Maintenance dose of ketamine	0.428	-	0.768

Total dose: means induction dose + maintenance dose.

By comparing the means of duration of recovery in both groups, patients in (KT) group recovered slower than those in (K) group (35:11 min versus 28:56 min), either the patient received maintenance dose (53:09 min versus 19:25 min) or didn't receive a maintenance dose (31:22 min versus 29:42min), except age group older than 12years (25:40 min in (KT) group versus 42:46 min in (K) group). And as mentioned above, no one older than 12years age in both groups needed a maintenance dose.

Table 5: Doses of thiopental and duration of recovery in (KT) group (Ketamine +thiopental).

Age group	Induction only*			Induction+ Maintenance**				Total	
	%	Dose (mg/kg)	D.R # (min)	%	Dose (mg/kg)		D.R # (min)	%	D.R # (min)
					Induction	Maintenance			
< 3years	7.5%	5.42	53:00	7.5%	6.00	3.30	46:40	15%	49:50
3-8 years	37.5%	4.65	33:00	7.5%	5.44	3.07	58:00	45%	37:10
8-12 years	22.5%	4.48	25.16	2.5%	4.00	2.40	58:00	25%	28:32
>12 years	15%	3.88	25:40	-	-	-	-	15%	25:40
Total	82.5%	4.40	31:22	17.5%	5.47	3.07	53:09	100%	35:11

* Induction only i.e. patients received only induction dose of ketamine and thiopental, didn't need maintenance dose of thiopental.
**Induction + maintenance i.e. patients needed maintenance dose of thiopental.
D.R = duration recovery.
Note: no. of doses and duration of recovery are means.

Table 6: Doses of ketamine and duration of recovery in (K) group (ketamine only).

Age group	Induction only*			Induction+ Maintenance**				Total	
	%	Dose (mg/kg)	D.R# (min)	%	Dose (mg/kg)		D.R# (min)	%	D.R# (min)
					Induction	Maintenance			
< 3years	22.5%	1.5	37:00	-	-	-	-	22.5%	37:00
3-8 years	40%	1.5	23:50	7.5%	1.5	0.5	19:25	47.5%	23:08
8-12 years	22.5%	1.5	28:48	-	-	-	-	22.5%	28:48
>12 years	7.5%	1.5	42:46	-	-	-	-	7.5%	42:46
Total	92.5%	1.5	29:42	7.5%	1.5	0.5	19:25	100%	28:56

*Induction only i.e.: patients received only induction dose of ketamine didn't need maintenance dose of ketamine.
**Induction + maintenance i.e. patients needed maintenance dose of ketamine.
D.R = duration of recovery
Note: no. of doses and durations of recovery are means.

DISCUSSION:

The intraoperative complications "temporary decrease in arterial O2 saturation and the associated breath holding" occurred in the both groups, but they were more frequent in (KT) group (12.5% versus 2.5%), and "cough" occurred only in (KT) group (2.5%). All these mean that thiopental was the causative agent. Some of those cases were associated with breath bolding. It lasted for few seconds and all those cases responded to O2 therapy with or without jaw thrust.

It was mentioned by Joe Mellor in using thiopental "there is generally a short pause in respiration, but this is rarely lasts more than few seconds and respiration then resumes" [(6)] .

While Carl Stevenson mentioned that "with ketamine; apnea is unusual unless ketamine is administered rapidly or another respiratory depressant is given, and airway reflexes are relatively preserved" [(7)] .

Rachael & Raad mentioned that "ketamine in anesthetic dose (1-2 mg/kg) should be given in small increments initially to avoid episodes of apnea" [(8)]. And Joe Miller also mentioned that "with overdosage of ketamine, airway reflexes may be lost and respiration depressed, and oxygen must be available for its safe use" [(6)].

The "mild involuntary movements and verbal responses" that occurred during the procedure seems not disturbing the positioning or the completion of the procedure. In case this movement caused a disturbance of the procedure, indicates that the anesthesia was not adequate and the patient needed a maintenance dose.

As this complication occurred more frequently in (K) group indicates that the use of ketamine alone with increasing dose is the causative factor for this problem.

Carl Stevenson mentioned "it is difficult to assess the depth of anesthesia when using ketamine as there are few obvious signs, as spontaneous movement and eye opening may occur during adequate anesthesia but are more common during subanesthetic doses" [(7)].

Here Carl Stevenson supported the results of this study in that such complication occurs during adequate anesthesia and it is common with ketamine.

The problem of "cough" postoperatively didn't occur at all in (K) group , while it occurred in low frequency, in (KT) group group, which means that thiopental is the causative agent, it was not associated with any change in breathing sounds or appearance of new added sounds.

The other 3 postoperative complications (nausea &/or vomiting, hallucinations, dizziness) occurred only with (K) group, means that the use of ketamine alone is associated with these unpleasant complications, and the use of thiopental offered the patient a smooth recovery. These 3 complications occurred in a pattern of increasing frequency with increasing age, means that as the child get older; he will get benefit from using the combination of ketamine and thiopental versus ketamine alone. It is important to note that these complications occurred only in patients within age group (3-8 years) and all didn't need a maintenance dose, which supports that the induction dose of ketamine by itself was the responsible agent.

Nausea and vomiting are distressing side effects of GA [(9)]. As nausea &/or vomiting were the most frequent complications with ketamine anesthesia in this study,

Only 1 patient had sever hallucinations (versus 2 with mild hallucinations) necessitated the use of

diazepam, which might lead to prolongation of duration of recovery (80:00 min versus 27:37 min as a mean of the other 39 patients in (K) group group who didn't receive diazepam during recovery period). This indicates that the use of a benzodiazepine as a premedication is not necessary in such cases, as the need of it occurred only in small percentage (2.5%) in (K) group as a result of this study.

"Dizziness" in this study was mentioned by one patient as dreaming. By asking all patient aged ≥ 6 years about the recall of intraoperative events, it was found that there is no recall (no awareness) between all these patients in both groups. These results are similar to the those produced by Warwick DNK [(10)]. during their research about postoperative analgesic requirement after cesarean section as a comparison of anesthetic induction with ketamine or thiopental[(10)]. They found that no patient reported recall of intraoperative events, two patients in thiopental group and one in ketamine group reported pleasant intraoperative dreams, no patient reported unpleasant intraoperative dreams [(10)].

It is logical, as the duration of the procedure increases, the chance of need of maintenance dose also increases, and this was happened in this study in both groups. In(K) group, only 3 patients (all were within age group 3-8 years) needed a maintenance dose versus 7 patients in (KT) group (all were younger than 12 years of age). These results may indicate that patients older than 12 years in (KT) group, and older than 8 years in (KT) group already have higher anesthetic requirement, and the use of (1.5 mg/kg) dose of ketamine alone is enough to produce general anesthesia in such procedures versus the use of combination of ketamine (1mg/kg) plus thiopental (anesthetising dose).

These results are theoretically supported by G. Edward Morgan "The volume of distribution for most intravenous drugs is proportionately higher in neonates, infants and young children, and the dose (per kilogram) is usually higher than in older children and adults " [(11)].

In this study the duration of recovery is prolonged by the use of thiopental", and by measuring the P-value it is the induction dose that responsible for this prolongation in time of stay in recovery room, but not the maintenance dose. While in (K) group, the P-value between the doses of ketamine (total and maintenance) and duration of recovery were direct but not significant (not accepted). This result may be related to the longer redistribution half-life and elimination half-life of thiopental than ketamine, as mentioned by G. Edward Morgan "For thiopental; the initial redistribution half-life is of few minutes (20-30 min) and the elimination half-life ranges from (3-12 hours). While for ketamine; the distribution half-life is (10-15 min), and the extensive hepatic uptake for ketamine (hepatic extraction ratio of 0.9) explains relatively short elimination half-life (2 hours)" [(12)].

CONCLUSION:

The use of combination of thiopentone and ketamine is associated with more mild and temporary intraoperative decreased arterial oxygen concentration, breath holding, and postoperative cough than using ketamine alone, while the use of ketamine alone is associated with more mild involuntary movements and verbal responses, postoperative nausea &/or vomiting, hallucinations, and dizziness. The duration of recovery is prolonged by the use of thiopental.

Recommendations

It is safe for the anesthesiologist to use a combination of thiopental 1% and ketamine 1% in short painful procedures in pediatrics, as it causes mild intraoperative complications and offers a smooth recovery but with the cost of longer duration of stay in recovery room.

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