Clinical Study

Effect of small dose intravenous dexmedetomidine and/or local anaesthetic infiltration on haemodynamic responses to skull pin placement

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Abstract: Fixation of skull pins during craniotomy may cause acute haemodynamic changes. We evaluated, in this randomised double blind placebo controlled trial, the effects of small dose of dexmedetomidine (Dex) infusion in attenuating the haemodynamic profile during skull pin placement.

Twenty-eight patients ASA I and II undergoing elective craniotomy were studied. Anaesthesia induced with sufentanil and sodium thiopentone (STP). Cisatracurium was given to facilitate endotracheal intubation. Patients were randomly allocated to one of four groups (each 7 patients): dex, lidocaine, dex-lidocaine and placebo (groups I, II, III, and IV respectively). Groups I and III received intravenous Dex 0.25 mcg/kg infusion and local infiltration with normal saline (NS) in group I and with 1% lidocaine in group III. Groups II and IV received intravenous NS and local infiltration at each pin insertion site with 1% lidocaine in group II and NS in group IV. The protocol started with intravenous medications to the assigned groups followed (after 8 min) with local infiltration of the scalp. Two minutes later (10 min after intravenous medication), scalp pinning was performed. Variables recorded were heart rate (HR), systolic blood pressure (SBP) and mean blood pressure (MBP) at different times. After opening the dura, brain status was assessed by the surgeon. Repeated measures of variance of HR, SBP, and MBP showed statistically significant interaction between group assignment and assigned time for groups I and III. In conclusion, our results showed that use of small doses of dex has resulted in obtunding the haemodynamic response to skull pin placement.

Keywords: *Craniotomy, head pinning, dexmedetomidine and haemodynamics* (*p29-33*)

Introduction

Skull pins are used to immobilise the head during craniotomy. Fixation of skull pins causes acute haemodynamic changes which may affect cerebral autoregulation and hence cerebral blood flow.[14] Therefore, maintenance of stable haemodynamic parameters during skull pin placement under general anaesthesia is crucial to ensure adequate cerebral perfusion and prevention of acute rise of intracranial pressure.[3]

Many different strategies have been used to minimise the haemodynamic responses to skull pin placement with varying results.[9,11] The use of opioids to obtund haemodynamic responses secondary to skull pin placement for craniotomy was associated, in many reports, with increase in cerebrospinal fluid pressure.[2] Local anaesthetic infiltration at pin application sites has been used but was always unsuccessful in obtunding the haemodynamic responses to skull pin placement.[4] In one study it was found that maximum attenuation of haemodynamic responses to skull pin placement was obtained with the addition of a sub-anaesthetic dose of intravenous ketamine to lidocaine infiltration.[1] In another study, clonidine premedication has improved haemodynamic stability of patients undergoing pin head-holder application during craniotomy.[8] Dex, an alpha-2 adrenoceptor agonist, has been recently introduced as a sedative for patients on mechanical ventilation.[15] In addition to its sedative effect, Dex has significant analgesic qualities and has been

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labelled as "analgesia-sparing" by the FDA.[10] To the best of our knowledge, Dex has never been used to suppress haemodynamic responses to skull pinning. The aim of the current study was to evaluate the efficacy of small dose of Dex in attenuating the haemodynamic responses to skull pin placement for craniotomies.

Patients and methods

After institutional ethics committee approval, and having obtained written informed consent, 28 ASA class I and II patients undergoing elective craniotomy were enrolled in this prospective, randomised, double-blind, placebo controlled study. Inclusion criteria were: patients scheduled for elective craniotomy, aged 16-60 years weighing 52-87 kg. Patients with clinical evidence of raised intracranial pressure (headache, nausea or vomiting) or a history of major systemic illness, hypertension or cardiac diseases were excluded from the study.

Intraoperative monitoring included continuous electrocardiography, intra-arterial blood pressure, end-tidal carbon dioxide (ET CO_2), pulse oximetry, central venous pressure (CVP) and rectal temperature probe. All patients were premedicated with oral lorazepam 2 mg and ranitidine 150 mg 2 hours before surgery. Following preoxygenation, anaesthesia was induced with sufentanil (0.1 mcg/kg) and STP (3-5 mg/kg). Cisatracurium (0.1 mg/kg) was given to facilitate endotracheal intubation. The patient's ventilation was controlled to maintain ET CO_2 between 33 and 38 mmHg. Anaesthesia for all patients was maintained with 60% nitroux oxide in oxygen and IMAC sevoflurane. Patients were randomly allocated to one of four groups (each 7 patients): Dex, lidocaine, Dex-lidocaine and placebo (groups I, II, III and IV respectively). Groups II and IV received intravenous normal saline (NS), then local infiltration at each pin insertion site with NS in group IV and with 1% lidocaine in group II. Groups I and III received intravenous Dex 0.25 mcg/kg by infusion followed by local infiltration at each pin insertion site with NS in group 1 and with 1% lidocaine in group III. Both the anaesthetist who administered i.v medications and the surgeon who performed local infiltration to the scalp were blinded to various treatment groups. The protocol started with i.v medications to the assigned groups followed after 8 min with local infiltration of the scalp at each pin insertion site. After 2 min (10 min after i.v medications), pinning of the scalp was performed. A Mayfield head holder was used for all of the craniotomies in the study. The Mayfield head holder used pointed pins that are inserted simultaneously through the dermis engaging in the periosteum to secure the head in a stable position for surgery. The following variables were recorded, heart rate (HR), systolic blood pressure (SBP) and mean blood pressure (MBP). The variables were recorded at the following time intervals: before i.v Dex/NS (DO), 60 sec after i.v Dex/Ns (D60), at completion of pin insertion (PO), and at 30, 60, 90, 120, 150, 180, 300, 600 and 900 sec after pin insertion. After opening the dura, brain status was assessed by the surgeon as follows: 1= Excellent, 2= Acceptable, and 3= Swollen. At the end of surgery reversal agents of residual muscle relaxants were given and the trachea was extubated. Software SPSS 9.0 was used for data analysis. Two-way analysis of variance (ANOVA) was used for the effects of the treatment groups on different time points. Student's text was used for intergroup differences where $P<0.05$ was considered significant.

Results

The four groups were comparable with regard to the demographic data (Table 1). Repeated measures of variance showed a statistically significant interaction between group assignment and time for the HR from D60-P900 sec (Table 2). Regarding the SBP, repeated measures of variance showed statistically significant interaction between group assignment and time at D60 and P300-900 sec (Table 3). This interaction indicates that neither group assignment alone nor time of data collection alone explained the variability in HR and SBP. Intraoperative HR was greater in the placebo group at pin insertion and continued till 900 sec of the study period. The lowest heart rate recorded intraoperatively was for the Dex-lidocaine group compared to the other groups (Fig. 1). Intergroup comparisons by 2-way ANOVA for all time points revealed statistically significant difference for both the group assignment and time points. Repeated measures of variance for MBP showed statistically interaction between group assignment and time of D60 and P300, 600 and P900 for the MBP (Table 4). Intraoperative SBP and MBP were greater for the placebo group at pin insertion and continued high until P900 sec of the study period. Fig. 2 shows intra-operative trend of the mean SBP. Condition of the brain assessed by the surgeon after opening the dura showed that the best brain condition was achieved with group III patients (Table 5).

Table 1 - Patient and demographic data (values in mean ± SD)

	Group I	Group II	Group III	Group IV
Age (yr)	42 ± 5	46 ± 6	48 ± 3	46 ± 8
Male/ Female	4/3	2/5	4/3	3/4
Weight (kg)	75 ± 7	76 ± 6	74 ± 8	73 ± 9

I: Dex, II: lidocaine, III: Dex/lidocaine, IV: placebo

Table 2 - Results of repeated measures ANOVA of heart rate (HR) for group-time interaction (values in mean ± SD)

	Group I	Group II	Group III	Group IV	F ratio	P value
D0	79±15	86±19	75±17	112±15	1.2	0.3
D60	77±7	75±24	68±17	113±16	9.5	0.0002
P0	78±10	87±21	78±20	114±16	5.6	0.004
P30	79±11	89±19	79±19	117±21	6.5	0.002
P60	75±10	86±20	75±24	124±33	6.3	0.002
P90	73±9	82±19	73±17	121±32	7.5	0.001
P120	72±9	81±20	72±17	117±24	8.6	0.0004
P150	73±9	81±20	70±18	115±24	8.1	0.0007
P180	77±6	79±18	71±18	101±22	4.3	0.01
P300	75±4	80±18	69±20	103±18	5.5	0.004
P600	73±4	78±19	69±14	93±42	5.6	0.004
P900	74±5	78±19	69±13	101±15	6.7	0.001

I: Dex, II: lidocaine, III: Dex/lidocaine, IV: placebo

Table 3 - Results of repeated measures ANOVA of systolic blood pressure (SBP) for group-time interaction (values in mean ± SD)

	Group I	Group II	Group III	Group IV	F ratio	P value
D0	113±18	119±23	118±17	137±10	0.95	0.43
D60	98±14	113±25	98±22	141±9	2.89	0.05
P0	112±32	116±22	112±21	142±19	0.57	0.63
P30	118±26	122±15	111±20	141±16	0.19	0.89
P60	115±27	119±14	107±24	139±12	0.32	0.80
P90	114±23	115±12	105±26	129±17	0.98	0.41
P120	109±22	111±13	103±23	131±30	1.16	0.34
P150	108±18	108±16	100±21	128±33	1.41	0.26
P180	105±19	105±12	102±18	125±24	1.83	0.16
P300	107±17	105±9	99±16	127±22	7.14	0.001
P600	107±18	106±15	94±18	121±24	5.96	0.003
P900	105±14	106±16	95±16	121±27	6.31	0.002

I: Dex, II: lidocaine, III: Dex/lidocaine, IV: placebo

Table 4 - Results of repeated measures ANOVA of mean blood pressure (MBP) for group-time interaction (values in mean ± SD)

	Group I	Group II	Group III	Group IV	F ratio	*P* value
D0	85±12	84±17	84±10	94±5	0.95	0.4
D60	82±16	82±15	78±15	98±7	2.89	0.05
P0	94±19	92±20	89±6	99±9	0.55	0.6
P30	95±14	94±15	91±12	97±12	0.19	0.8
P60	93±15	93±14	91±21	98±1	0.32	0.8
P90	92±13	87±15	87±20	99±5	0.98	0.4
P120	88±11	85±13	85±18	96±4	1.16	0.3
P150	86±12	82±12	82±18	94±4	1.41	0.3
P180	87±13	80±12	83±15	95±4	1.83	0.2
P300	85±13	75±11	79±14	104±10	7.14	0.001
P600	83±11	78±11	76±15	103±15	5.96	0.003
P900	82±12	80±13	73±13	106±20	6.31	0.002

I: Dex, II: lidocaine, III: Dex/lidocaine, IV: placebo

Table 5 - Conditions of the brain as assessed by the surgeon

Group	Excellent	Acceptable	Swollen
I	4	2	1
II	2	4	1
III	6	1	0
IV	2	4	1

I: Dex, II: lidocaine, III: Dex/lidocaine, IV: placebo

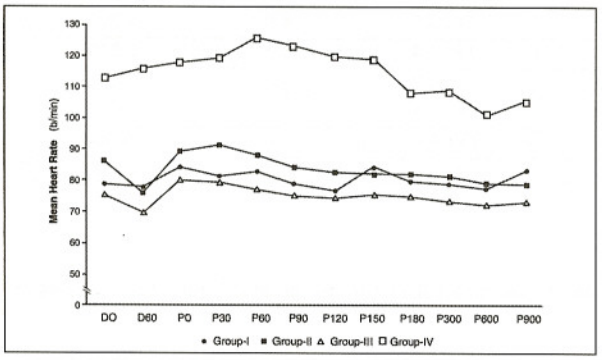

Figure 1 – Changes in the mean values of heart rate (HR) at various time intervals. Closed circle (•) group I; closed square (■) group II; open triangle (Δ) group III and open square (*) group IV

Discussion

In the present study, the Dex-lidocaine group showed the maximum attenuation of haemodynamic responses to skull pin placement versus other groups. However, the trends of HR, SBP and MBP responses were similar in the lidocaine and Dex groups. On the contrary, the placebo group showed the maximum and significantly high haemodynamic responses following skull pin placement. Attenuation of the haemodynamic responses using bupivacaine scalp infiltration has been reported.[7] Scalp infiltration with bupivacaine 0.25% with epinephrine can significantly influence HR and MBP after scalp incision in adult patients undergoing craniotomy.[5] However, the procedure is not always successful in obtunding the haemodynamic changes due to improper local anaesthetic infiltration and movement of the head during pin application. In one study it was shown that a subanaesthetic dose of i.v ketamine (0.5 mg/kg) did not attenuate MBP but attenuated HR after pinning, similar to lidocaine, whereas the combination of lidocaine scalp infiltration to i.v ketamine attenuated both the MBP and HR.[1] Clonidine premedication was reported to attenuate the haemodynamic responses to pin head-holder application during craniotomy.[8] Clonidine, the protypical alpha2-adrenoceptor agonist, has been widely studied in humans. When given by rapid intravenous route

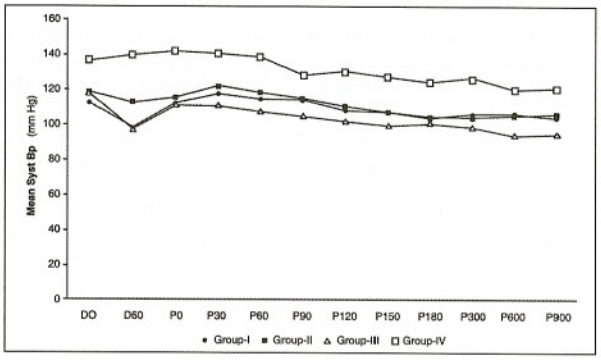

Figure 2 – Changes in the mean values of systolic blood pressure (SBP) at various intervals. Closed circle (•) group I; closed square (■) group II; open triangle (Δ) group III and open square (*) group IV

clonidine exerts a biphasic effect on arterial blood pressure. The haemodynamic profile of Dex was found to be similar to clonidine.[6] Dex is a novel alpha2-agonist with potent anxiolytic and sedative properties. In one study it was shown that Dex appears to produce a significant decrease in both regional and global cerebral blood flow (CBF). Such decrease in CBF might be beneficial while sedating patients with traumatic brain injury or metabolic brain oedema but could be detrimental in the setting of cerebral vasospasm.[13] In addition to its sedative effects, Dex has analgesic properties which is supported by the results of the present study. In the current study Dex-lidocaine group showed significant decrease in the haemodynamic responses to head pinning. However, separately the lidocaine and Dex groups showed similar but non-significant attenuating effect on the haemodynamic profile. The small dose of Dex used in the current study though did result in significant drop of the MBP at P300-900 sec but it was of no clinical significance value. To the best of our knowledge, this is the first study on the use of Dex to attenuate the haemodynamic responses to skull pin placement for neurosurgery.

In conclusion, our results showed that the use of small dose of Dex has resulted in obtunding the haemodynamic responses to skull pin placement similar to lidocaine infiltration. However, the use of intravenous Dex combined with lidocaine infiltration at the sites of pin placement has maximally attenuated the haemodynamic responses to head pinning. We think that further studies are needed to determine the optimal dose and time of Dex administration before head pinning and to evaluate the effectiveness of that technique with special reference to patients with compromised cardiac and cerebral haemodynamics.

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