Comparison of epidural oxycodone and epidural morphine for post-caesarean section analgesia: A randomised controlled trial

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ABSTRACT

Background and Aims: Epidural morphine after caesarean section may cause moderate to severe pruritus in women. Epidural oxycodone has been shown in non-obstetric trials to reduce pruritus when compared to morphine. We hypothesised that epidural oxycodone may reduce pruritus after caesarean section. Methods: A randomised controlled trial was conducted in pregnant women at term who underwent caesarean section with combined spinal-epidural technique initiated with intrathecal fentanyl 15 µg. Women received either epidural morphine 3 mg or epidural oxycodone 3 mg via the epidural catheter after delivery. The primary outcome was the incidence of pruritus at 24 h after caesarean section. The secondary outcomes were the pruritus scores. treatment for post-operative nausea and vomiting (PONV), pain scores and maternal satisfaction. **Results:** One hundred women were randomised (group oxycodone O = 50, morphine M = 50). There was no difference between Group O and M in the incidence of pruritus (n [%] 28 [56%] vs. 31 [62%], P = 0.68) and the worst pruritus scores (mean [standard deviation] 2.6 (2.8) vs. 3.3 [3.1], P = 0.23), respectively. Both groups had similar pain scores at rest (2.7 [2.3] vs. 2.0 [2.7], P = 0.16) and sitting up (5.0 [2.3] vs. 4.6 [2.4], P = 0.38) at 24 h. Pruritus scores were lower at 4-8, 8-12 and 12-24 h with oxycodone, but pain scores were higher. Both groups had a similar need for treatment of PONV and maternal satisfaction with analgesia. Conclusion: There was no difference in the incidence of pruritus at 24 h between epidural oxycodone and morphine. However, pruritus scores were lower with oxycodone between 4 and 24 h after surgery with higher pain scores in the same period.

Key words: Caesarean section, morphine, oxycodone, pain

INTRODUCTION

Neuraxial opioids form an integral part of multimodal analgesia during and after caesarean section. Epidural morphine is a popular choice as it provides superior analgesia compared with intravenous (IV) morphine.^[1] However, there is an increased incidence of opioid-related side effects.^[2,3] Morphine-induced pruritus is a significant concern of parturients and the incidence after intrathecal doses of 100–200 μ g is 70–90%^[2,4] and after an epidural dose of 2.5 mg is 44%.^[5] Intrathecal fentanyl administration is also associated with high incidence of pruritus in parturients.^[6-8]

Oxycodone is a semi-synthetic opioid agonist recommended for the treatment of moderate to severe post-operative pain by the World Health Organization.

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Parenteral oxycodone and morphine have been shown to be equipotent.^[9] However little is known about the efficacy and safety of oxycodone as compared to morphine. One rat study has shown that intrathecal oxycodone produces anti-nociceptive effects together with minimal central nervous system depression with no evidence of neurotoxicity.^[10] No human neurotoxicity reports have been published so far.

In humans, epidural oxycodone produced less pruritus than epidural morphine in gynaecological surgery with no serious or unexpected adverse events noted.^[11] In major abdominal surgery, epidural oxycodone had similar analgesic efficacy with similar adverse effects compared to epidural morphine.^[12]

In this study, we compared the incidence of post-caesarean section pruritus caused by the administration of either epidural oxycodone or epidural morphine for post-operative pain relief. We hypothesised that oxycodone would reduce the incidence and severity of pruritus as compared to morphine. The secondary outcomes included the incidence of nausea, vomiting, pain scores, sedation and respiratory depression.

METHODS

This study was approved by the Centralised Institutional Review Board, and informed written consent was obtained from all subjects in the study. The study was registered with the Health Sciences Authority, Singapore Clinical Trials Registry and Clinical Trials.gov. The study design was a randomised, double-blind, single-centre trial conducted between August 2013 and March 2014.

The inclusion criteria were American Society of Anesthesiologists' (ASA) physical status 1-2 parturients, aged 21-50 years undergoing a full-term elective caesarean section who had consented for combined spinal-epidural (CSE) anaesthesia. Parturients with concurrent opioid therapy, contraindications to CSE anaesthesia or any of the study medications, a history of pre-existing nausea and vomiting, failure to identify intrathecal space at the time of anaesthesia, inadvertent dural puncture with the epidural needle and conversion of regional anaesthesia to general anaesthesia were excluded from the study.

One hundred subjects were recruited into the study. Subjects were randomised in a 1:1 allocation ratio using a computer-generated random number sequence and were allocated to one of two groups using serially numbered opaque sealed envelopes after the baby was delivered, just before the study intervention. The research nurses prepared the study drugs. Subjects, the attending anaesthetist, post-operative staff and data collectors were all blinded to group allocation.

Baseline data such as age, ASA status, weight (before caesarean section, pre-pregnancy or 1st visit), height, current body mass index, gravidity, parity, number of previous caesarean sections, pre-operative skin condition and pre-operative itching were recorded. The quality of recovery (QoR) score was administered in the ward before the operation.^[10] An 18-gauge cannula was inserted into a forearm vein, and standard monitoring (pulse oximetry, electrocardiogram and non-invasive blood pressure) were applied. In both groups, CSE anaesthesia (using the needle through needle technique) was established in the L3/L4 interspace using the loss of resistance to saline technique. Hyperbaric bupivacaine 12 mg with fentanyl 15 µg was administered intrathecally after ensuring the free flow of cerebrospinal fluid. If pain was experienced intra-operatively, this was treated using inhalational nitrous oxide, IV ketamine or wound local anaesthetic bupivacaine infiltration followed by small doses of IV fentanyl, as required by the attending blinded anaesthesiologist.

The study intervention occurred after delivery and consisted of an injection of the study drug into the epidural space via the epidural catheter and was either single dose 3 mg morphine (standard epidural dose in our centre) or 3 mg preservative-free oxycodone hydrochloride, each drug in a dilution of 1 mg/ml with a volume of 3 ml after negative aspiration through the epidural catheter. The study drugs were prepared by the research nurses immediately after delivery. Post-operative oral analgesia was provided with regular paracetamol 1 mg time-domain spectroscopy (TDS) and mefenamic acid 500 mg TDS. Breakthrough pain was managed using oral tramadol 50 mg TDS as required as per hospital practice. Anti-emetics were administered as per hospital protocol including ondansetron and/or dexamethasone administered intra-operatively, and as required, post-operatively.

Post-operative monitoring included pain scores, pruritus, nausea, vomiting, sedation scores and respiratory depression (respiratory rate <8 breaths/min) (2 h, 4 h, 8 h, 12 h and 24 h) and maternal satisfaction with analgesia for 24 h after caesarean section and routine vital signs (hourly parameters) were measured for 24 h after neuraxial opioid administration.

At 24 h after surgery, each subject was reviewed by a blinded investigator. The overall incidence of pruritus was determined and whether treatment for the pruritus was required by the subject; maternal satisfaction of pain relief and control of pruritus was recorded (0–100, 0 = totally unsatisfied and 100 = totally satisfied); treatment for post-operative nausea and vomiting (PONV) as requested by the subject; the QoR score;^[13] and the overall benefit of analgesia score (OBAS, range 0–28)^[14] were recorded. Direct questioning was used to assess the presence of side effects, the ability to breastfeed, pass wind, open bowels and presence of a urinary catheter.

The required trial sample size of 100 subjects was calculated by PS Power and Sample Size Calculation Software (Vanderbilt University, Nashville, Tennessee, USA) based on the following assumptions: A decrease in the incidence of pruritus at 24 h from 85% in epidural morphine group to 60% in the epidural oxycodone group; power of 80%; significance level of 0.05; allocation ratio of 1:1 and a 2% dropout rate.^[15]

The incidence of pruritus at 24 h and other categorical variables were summarised using frequency (proportion) and compared between groups using Fisher's exact test. Severity of pruritus and other ordinal variables were summarised using median (interquartile range [IQR]) and compared using Mann–Whitney test, whereas continuous variables were summarised using mean (standard deviation) and compared using two-sample *t*-test. Significance level was set at 5%, and all tests were two-sided. SAS version 9.2 software was used for the analyses.

RESULTS

One hundred and four subjects were screened, 100 subjects were randomised, and 4 subjects were excluded from the study [Figure 1]. The 100 randomised subjects provided complete data and were included in the analysis. The subjects excluded were similar to the subjects who participated in the study with respect to age, weight, height, parity or ASA status. The baseline,



Figure 1: CONSORT diagram of study recruitment

anaesthesia and surgical characteristics of the both groups were similar [Tables 1 and 2]. The incidence and worst score of pruritus were not significantly different between Group O and Group M (56% vs. 62%, P = 0.68; median [IQR; range] 2 [0–5; 0–10] vs. 3 [0–6; 0–9], P = 0.24). However, the pruritus severity scores were worse for Group M at 4–8, 8–12 and 12–24 h [Table 3]. Treatment for pruritus was similar between the two groups [Table 4].

The numerical rating scale (NRS) pain score at rest was significantly higher at 2–4, 4–8, 8–12 and 12–24 h post-operatively in Group O compared with Group M [Table 3]. The NRS pain score on movement at 4–8 and 8–12 h was also significantly higher in Group O. The NRS pain score at 24 h for cramps and at rest was higher in Group O than Group M [Table 4]. There were no differences in NRS pain scores at 24 h on sitting or use of tramadol for breakthrough pain.

There were no differences in the need for treatment of PONV, OBAS and post-operative QoR score. The incidence of flatulence, open bowels and presence of a urinary catheter were similar. Maternal satisfaction

Table 1: Baseline characteristics data				
Characteristics	Epidural morphine (<i>n</i> =50)	Epidural oxycodone (<i>n</i> =50)		
Age (years)	32.5 (29-37; 21-41)	32.1 (29-36; 24-41)		
Weight pre-pregnancy (kg)	58.0 (54-71; 43-90)	59.0 (52.4-65; 45-90)		
Weight at term (kg)	71.4 (62-80; 57-101)	69 (65-74; 50-99)		
BMI at term (kg)	28.8 (26.1-31.2; 22-40)	28.0 (25.3-30; 21-43)		
Gravida	2 (2-3; 1-7)	2 (2-3; 1-6)		
Parity	1 (1-2; 0-5)	1 (1-2; 0-4)		
Previous caesarean section	1 (0-1; 0-3)	1 (0-1; 0-4)		
Pre-operative QoR score (0-18)	18 (17-18; 13-18)	18 (18-18; 16-18)		

Data represent median (IQR; range). BMI – Body mass index; QoR – Quality of recovery; IQR – Interquartile range

Table 2: Anaesthesia and surgical data					
Parameters	Epidural morphine (<i>n</i> =50) (%)	Epidural oxycodone (<i>n</i> =50) (%)	Р		
Spinal anaesthesia only	50 (100)	50 (100)	1.00		
Pre-delivery nausea	11 (22)	9 (11)	0.80		
Pre-delivery vomiting	0 (0)	1 (2)	1.00		
Pre-drug delivery pruritus	0 (0)	1 (2)	1.00		
Pain at delivery	3 (6)	3 (6)	1.00		
Duration of surgery (min)* 4	7 (35-63; 17-140) 45 (35-63; 18-155)	0.60		
Post-delivery nausea	16 (32)	8 (16)	0.10		
Post-delivery vomiting	3 (6)	3 (6)	1.00		

Data represents median (IQR; range) or n (%). *Duration of surgery calculated from the time of surgical incision to the time surgery ended. IQR – Interquartile range

with analgesia was also similar (Group M 80 [70–90] vs. Group O 80 [70–85], P = 0.54). No patients suffered from respiratory depression in either group.

DISCUSSION

In our study, epidural oxycodone for post-caesarean analgesia did not reduce the incidence of pruritus compared with epidural morphine but did reduce the severity of pruritus score between 4 and 24 h

Table 3: Post-operative pruritus and pain scores				
Pruitus or pain score	Epidural morphine (<i>n</i> =50)	Epidural oxycodone (<i>n</i> =50)	Р	
Pruritus score 0-2 h	0 (0-0; 0-8)	0 (0-3; 0-8)	0.18	
Pruritus score 2-4 h	0 (0-5; 0-8)	0 (0-4; 0-8)	0.43	
Pruritus score 4-8 h	0 (0-5; 0-8)	0 (0-0; 0-7)	0.01*	
Pruritus score 8-12 h	0 (0-5; 0-8)	0 (0-0; 0-10)	0.002*	
Pruritus score 12-24 h	0 (0-4; 0-8)	0 (0-0; 0-7)	0.001*	
Resting pain score 0-2 h	0 (0-1; 0-8)	0 (0-1; 0-10)	0.87	
Resting pain score 2-4 h	0 (0-3; 0-8)	2 (0-5; 0-9)	0.03*	
Resting pain score 4-8 h	2 (0-3; 0-10)	3 (0-5; 0-10)	0.02*	
Resting pain score 8-12 h	2 (0-4; 0-10)	4 (2-6; 0-10)	0.01*	
Resting pain score 12-24 h	2 (0-5; 0-10)	3 (1-5; 0-10)	0.046*	
Pain score on movement 0-2 h	0 (0-1; 0-9)	0 (0-2; 0-10)	0.90	
Pain score on movement 2-4 h	0 (0-3; 0-8)	2 (0-5; 0-9)	0.05	
Pain score on movement 4-8 h	3 (0-4; 0-10)	4.5 (2-6; 0-10)	0.001*	
Pain score on movement 8-12 h	3 (1-5; 0-10)	5 (4-7; 0-10)	0.0003*	
Pain score on movement 12-24 h	5 (3-6; 0-10)	5 (4-7; 0-10)	0.13	

Data represents median (IQR; range). h – Hours after caesarean birth. Scores for pruritus, resting pain and pain score on movement are using numerical rating scale (0 – None; 10 – Worst imaginable). IQR – Interquartile range

Table 4: Post-operative re	view at 24 h a	after caesarea	n birth
Parameters	Epidural morphine (<i>n</i> =50)	Epidural oxycodone (<i>n</i> =50)	Р
Treatment for PONV, n (%)	2 (4)	2 (4)	1.00
Pain score at rest (0-10)	0 (0-3; 0-10)	3 (0-4; 0-8)	0.045*
Sitting pain score (0-10)	5 (3-7; 0-10)	5 (4-7; 0-10)	0.35
Cramping pain score (0-10)	0 (0-4; 0-10)	4.0 (0-6; 0-10)	0.002*
Tramadol required, n (%)	2 (4)	9 (18)	0.05
Pruritus, n (%)	31 (62)	28 (56)	0.69
Worst pruritus score	3 (0-6; 0-9)	2 (0-5; 0-10)	0.24
Treatment for pruritus, n (%)	2 (4)	0 (0)	0.49
OBAS (0-28)	5.0 (2-8; 0-15)	4.0 (2-6; 0-8)	0.24
Flatulence, n (%)	37 (74)	31 (62)	0.28
Open bowels, n (%)	3 (6)	4 (8)	1.00
Urinary catheter, n (%)	21 (42)	18 (36)	0.68
Maternal satisfaction with pain relief (0-100)	80 (79-90; 30-100)	80 (70-85; 45-100)	0.23
QoR score (0-18)	13.5 (13-15; 7-18)	13 (12-14; 9-18)	0.29

Scores for pruritus and pain scores are using numerical rating scale (0 - None, 10 - worst imaginable). Data represent median (IQR; range) or n (%). PONV – Post-operative nausea and vomiting; OBAS – Overall benefit of analgesia score; QoR – Quality of recovery; IQR – Interquartile range

post-operatively. Epidural oxycodone group had significantly higher pain scores on movement and cramps although there was the similar maternal satisfaction of analgesia. Aside from a lower nausea score in the immediate post-operative period, there were no significant differences in the incidence and severity of other side effects such as vomiting, sedation and respiratory depression.

To our knowledge, there are only three human clinical studies on the epidural administration of oxycodone. Backlund *et al.* were the first group to compare the efficacy and side effects of epidural morphine and oxycodone for pain following major abdominal surgery. They found that the epidural morphine and oxycodone provided similar analgesia with similar side effects and respiratory depression^[12] Yanagidate and Dohi studied 75 women in a double-blind trial comparing epidural oxycodone with morphine following gynaecological surgery.^[11] Their patients were randomised to receive either an infusion of epidural morphine 6 mg/day, an infusion of epidural oxycodone 6 mg/day or an infusion of epidural oxycodone 12 mg/day. They found higher pain scores at rest in the epidural oxycodone 6 mg group compared with the morphine or oxycodone 12 mg groups. However, comparing the oxycodone 12 mg group with the morphine 6 mg group revealed similarly effective analgesic profiles. There was also significantly less nausea, vomiting and pruritus in both oxycodone groups compared with the morphine group. This contrasts with our study where NRS pain scores on movement and cramps were significantly higher in the epidural oxycodone group compared to the epidural morphine group. This could due to that we used the same dose of oxycodone as morphine. Furthermore, lower doses of both drugs were used. However, caution should be used when comparing the two studies because Yanagidate were investigating the non-obstetric population. Palmer performed a dose comparison study investigating epidural morphine for post-caesarean section analgesia and found an analgesic ceiling at 3.75 mg.^[16] Therefore, a dose of 6 mg epidural morphine would be considered excessive for patients undergoing a caesarean section.

To the best of our knowledge, there are no published data on epidural oxycodone in the obstetric population. Therefore, it was difficult to ascertain the optimal dose. Care needs to be taken in this group because additional safety issues need to be taken into consideration as oxycodone is not formally approved for epidural administration. It is essential to minimise infant exposure to opioids. Oxycodone is concentrated in human breast milk 72 h post-exposure. This poses a low risk to the breastfeeding infant because low volumes of breast milk are ingested during this period.^[17] Breastfed infants may receive more than 10% of the therapeutic infant dose. Therefore, we decided to use the conservative dose of 3 mg epidural oxycodone to reduce the potential for opioid-related side effects in the infant. Compared to the IV route, epidural oxycodone is able to achieve a higher cerebrospinal fluid concentration resulting in better analgesic efficacy and at the same time, reduce systemic exposure.^[18]

The higher pain scores in the epidural oxycodone group may suggest that our dose of 3 mg epidural oxycodone was inadequate for post-caesarean section analgesia although nausea and pruritus scores were also lower with similar maternal analgesic satisfaction. Parenteral oxycodone has been shown to be equipotent to morphine or even more potent than morphine.^[19] However, Backlund suggested epidural oxycodone may be less potent than morphine when administered after major abdominal surgery.^[12] A possible explanation is the lower affinity of oxycodone for the mu-opioid receptor.^[20] This would also account for the lower severity of pruritus and nausea as their mechanism of actions are thought to be mediated by mu-opioid receptor stimulation at the supraspinal level.^[21,22]

Another explanation could be the distinctly differing anti-nociceptive profiles of oxycodone and morphine found in rat studies.^[9,23] Nielsen suggested that the intrinsic effects of oxycodone are predominantly mediated by kappa-opioid receptors when assessed in rat models of neuropathic pain in contrast with the prototypic mu-opioid agonist. It has been suggested that at least some of oxycodone's analgesic effects are mediated by its active metabolites. Oxycodone is metabolised in humans by hepatic cytochrome P450 isoenzymes, and the main active metabolites include oxymorphone and noroxycodone. In rat studies, Lemberg found oxycodone demonstrated lower efficacy and potency in activating G-proteins particularly in the dorsal horn of the spinal cord and periaqueductal grey.^[10] He also studied oxymorphone and found it had a higher affinity and produced greater anti-nociception. These results suggest that after epidural or intrathecal administration of oxycodone, oxymorphone or some other active metabolite is not formed in the central nervous system thereby explaining the lower potency of epidural oxycodone compared with epidural morphine.

Limitations encountered in our study included the use of CSE anaesthesia. In many centres, clinical practice for elective caesarean section is a single shot spinal technique where post-operative analgesia is provided with intrathecal morphine. The CSE technique was used for the purpose of administering epidural oxycodone in this study. This was necessary as the use of intrathecal oxycodone in humans has not been previously described. Furthermore, we administered the epidural oxycodone and morphine after the delivery of the baby to minimise foetal exposure to opioids. In the aforementioned studies investigating epidural oxycodone, the epidural opioids have either been given at an earlier stage or as an infusion post-operatively. The delayed administration may have reduced the efficacy of both morphine and oxycodone. Another limitation was the conservative dose of epidural oxycodone administered. We felt that due to the paucity of published data on epidural oxycodone in the obstetric population, a low dose of oxycodone would be prudent. However, previous studies suggest that neuraxial oxycodone is less potent than neuraxial morphine.^[11,12] It is difficult to ascertain if a higher dose of oxycodone would have resulted in the similar reduction of opioid side effects.

CONCLUSION

We found no evidence that epidural oxycodone is accompanied with a reduction in the severity of pruritus score when compared to epidural morphine for post-caesarean analgesia. There were no differences in the side effect, quality of recovery and maternal satisfaction with analgesia. Further work is needed to determine the optimal and safe dose of epidural oxycodone as a higher dose may yield higher quality analgesia.

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Conflicts of interest

There are no conflicts of interest.

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Announcement

Conference Calender - 2016

Name of the conference: 64th Annual National Conference of the Indian Society of Anaesthesiologists, ISACON 2016 Date: 25th to 29th November 2016 Venue: Punjab Agricultural University, Ludhiana Organising Secretary: Dr. Sunil Katyal Contact: +91 98140 30552 E-mail: katyalsunilmd@gmail.com Website: www.isacon2016.com

Name of the conference: ISACON SOUTH – 2016 & ISACON Karnataka - 2016 22nd Annual South Zone Conference of ISA Date: 19th to 21st August 2016 Venue: KLE Centenary Convention Center, J N Medical College Campus, Nehru Nagar, Belagavi Organising Secretary: Dr. Manjunath C. Patil Contact: +91 97431 10637 E-mail: isaconsouth2016@gmail.com Website: www.isaconsz2016.in

Name of the conference: ISACON GUJARAT – 2016 & WIZACON 2016 49th Annual State Conference of ISA GUJARAT State Chapter & 12th West Zone Conference

Date: 23rd to 25th September 2016 Venue: Rangoli Hotel & Resorts, Vertej, Bhavnagar Organising Secretary: Dr. Fremiot J. Mascarenhas Contact: +91 94284 01780 E-mail: drfremiot@hotmail.com / isacongujarat2016@gmail.com Website: www.isacongujarat2016.com

Name of the conference: ISACON EAST – 2016 Annual East Zone Conference of ISA Date: 9th to 11th September 2016 Venue: Puri, Odisha

Organising Secretary: Dr. Debaprasad Mohanty Contact: +91 94370 21313 E-mail: drdev07@yahoo.com

Name of the conference: ISACON NORTH EAST 2016 4th North East Zone Conference of ISA

Venue: Assam Medical College, Dibrugarh
Organising Secretary: Dr. Dhrubajyoti Borgohain
Contact: +91 94350 31489
E-mail: dhruba_borgohain@yahoo.co.in

Name of the conference: ISACON KERALA – 2016 40th Annual State Conference of ISA Kerala State Chapter Date: 7th to 9th October 2016 Venue: MAC FAST Auditorium, Tiruvalla Organising Secretary: Dr. Koshy Thomas Contact: +91 94473 98170 E-mail: thomaskoshy59@gmail.com

Name of the conference: ISACON RAJASTHAN – 2016 18th Annual State Conference of ISA RAJASTHAN State Chapter Date: 7th to 9th October 2016 Venue: Government Medical College Auditorium, Kota Organising Secretary: Dr. Mukesh Somvanshi Contact: +91 94142 86314 E-mail: isaconraj2016@gmail.com Website: www.isaconrajasthan2016.com

Name of the conference: ISACON MAHARASHTRA – 2016 (MISACON 2016) Bi Annual State Conference of ISA MAHARASHTRA State Chapter Date: 14th to 16th October 2016 Venue: M G M Medical College Aurangabad Organising Secretary: Dr. Balaji Asegaonkar Contact: +91 93250 78733 E-mail: b_asegaonkar@yahoo.com / misacon2016@yahoo.com Website: www.misacon2016.com

Name of the conference: ISACON TELANGANA – 2016 $2^{\rm nd}$ Annual State Conference of ISA Telangana State Chapter

Date: 27th to 31st July 2016 Venue: Govt. Medical College & Teaching Hospital, Nizamabad Organising Secretary: Dr. Chintala Kishan Contact: +91 98480 71377 & 99490 46637 E-mail: isacontelangana2016@gmail.com, chintala_kishan@yahoo.in Website: www.isatelangana.org

Name of the conference: ISACON MP - 2016 30th Annual State Conference of ISA MP State Chapter Date: 10th September 2016 Venue: Hotel Jabali Palace, Jabalpur Organising Secretary: Dr. Ashish Sethi Contact: +91 98261 68747 E-mail: ashsethi64@yahoo.com Website: http://www.isampchapter.com

Name of the conference: 4th World Congress of Ophthalmic Anaesthesia (WCOA), 2016 Organized by: Sankara Nethralaya and British Ophthalmic Anaesthesia Society Date: 3rd & 4th September, 2016 Venue: ITC Grand Chola, Chennai Organising Secretary: Dr. Jaichandran V V Contact: +91 98840 96860 E-mail: wcoa2016@gmail.com Website: www.sankaranethralaya.org/wcoa2016