

Dose dependent Effect of Intrathecal Dexmedetomidine with Bupivacaine in Infraumbilical Surgeries

Sapna Singh¹, B L Mathur², Neena Rungta³

¹(Asst Professor, Dept of Anaesthesiology, JNU IMSRC, Jaipur)

²(Corresponding Author - Prof & Head, Dept of Anaesthesiology, JNU IMSRC, Jaipur)

³(Professor, Dept of Anaesthesiology, JNU IMSRC, Jaipur)

Abstract: Various intrathecal adjuvants are being used with local anesthetics for prolongation of intra-operative and postoperative analgesia. Dexmedetomidine (DMT), a highly selective alpha-2 adrenergic agonist is a new neuraxial adjuvant gaining popularity. The study included 60 ASA class I and II patients undergoing infra umbilical surgery under spinal anesthesia. The patients were randomly allocated into three groups (20 patients each). Each group received 4 µgm, 6µgm, and 8 µgm of DMT with 3 ml of bupivacaine respectively. The onset time to reach peak sensory and motor level, duration of sensory and motor block, duration of postoperative analgesia, hemodynamic changes, and side effects were recorded. **Result** -Onset of sensory and motor blocks were similar in all 3 groups. There was a significant and dose-dependent prolongation of duration of sensory block (190.7+/-21.37, 211.05+/-13, 238.15+/-21.53 min (p.00159<0.05) Duration of motor block (319+/-25.25, 350.42+/-16, 390.7+/-33.55 min p.000267<0.05 and duration of analgesia (442.8+/-34.96, 475.25+/-34.44, 611.58+/-35.46 min (p.0000001<0.05) with escalating doses of DMT. **Conclusions:** There is significant prolongation in duration of motor block, sensory block and analgesia without any significant adverse effect, with increasing doses of intrathecal DMT added to 0.5% bupivacaine

Key words: Analgesia, Bupivacaine, Dexmedetomidine

Date of Submission: 12-03-2018

Date of acceptance: 29-03-2018

I. Introduction

Subarachnoid blockade (SAB) is the most commonly used regional anesthetic technique for infraumbilical surgeries. Various adjuvants have been used with local anesthetics for prolongation of intra-operative and postoperative analgesia.¹ However, their use is abandoned either due to the adverse effects of adjuvants or unreliable postoperative analgesia^{2,3,4}

The addition of opioids to local anaesthetic produces good post-operative analgesia but has disadvantages, such as pruritis, post-operative nausea, vomiting and respiratory depression.² Dexmedetomidine (DMT), a highly selective α_2 adrenergic agonist is under evaluation as a neuraxial adjuvant.^{5,6} It provides stable haemodynamic conditions, good quality of intra-operative analgesia and prolonged post-operative analgesia with minimal side effects.^{7,8,9} However, there may be dose-related prolongation of the duration of motor blockade thus delaying discharge from post-anaesthesia care unit in day care surgeries, but there is lack of conclusive evidence for DMT's ideal dose.

II. Method

After obtaining approval from the Institutional Ethics Committee, 60 adult patients of American Society of Anesthesiologists physical Status I and II undergoing elective infraumbilical surgeries were selected. Patients were randomly allocated to 3 groups of 20 patients each. Group A received 4µg, Group B 6µg and group C received 8µg DMT intrathecally along with 3ml of 0.5% Bupivacaine. Patients with following history or diseases were excluded from the study -

- past history of spine surgery
- diabetes and other endocrine disorders,
- hypertension and other cardiac disorders,
- coagulation disorders and infection at site of lumbar puncture
- neurological and psychiatric disturbances,
- those on beta blockers, calcium channel blockers, α_2 agonists
- patients with history of drug allergy

Dose dependent Effect of Intrathecal Dexmedetomidine with Bupivacaine in Infraumbilical Surgeries

A detailed pre-anesthetic checkup was done and written informed consent was obtained from all patients who fulfilled the inclusion criteria.

Drug preparation

A volume of 3 ml of 0.5% hyperbaric bupivacain (15 mg) was taken in 5 ml syringe; dexmedetomidine was drawn in a standard 1 ml insulin syringe (100 parts = 100 µg) with 4 parts for 4 µg, 6 parts for 6 µg and 8 parts for 8 µg. Then added to bupivacain in 5 ml syringe ,

Anesthesia technique

After recording all the parameters the trial drugs were prepared in unlabeled syringes by an independent anesthesiologist not involved further in the trial. The patients and the anesthesiologist performing the intrathecal injection and collecting the trial data were unaware of the group allocation. The intrathecal injection was given in the L3-L4 intervertebral space with a 25 gauge Quincke spinal needle through the mid-line approach in sitting position and after aspiration of CSF the prepared drug was injected. The patients were immediately made supine after the injection.

Data recording

Demographic data such as age, weight, diagnosis, and duration of surgery were noted. The height of sensory block was assessed by pinprick method (24G hypodermic needle) in mid-clavicular line bilaterally, loss of sensation to pin prick was considered as sensory block. Motor block was assessed according to the Bromage scale-

GRADE	CRITERIA	DEGREE OF BLOCK
I	Free movement of legs and feet	Nil (0%)
II	Just able to flex knees with free movement of feet	Partial (33%)
III	Unable to flex knees but with free movement of feet	Almost Complete(66%)
IV	Unable to move legs or feet	Complete (100%)

Onset of block was assessed by noting time to reach T8 dermatome sensory block, peak sensory level and Bromage 3 motor block. All time durations were calculated considering the time of end of spinal injection as time zero. Sensory and motor block level were recorded every 2 min for 20 min.

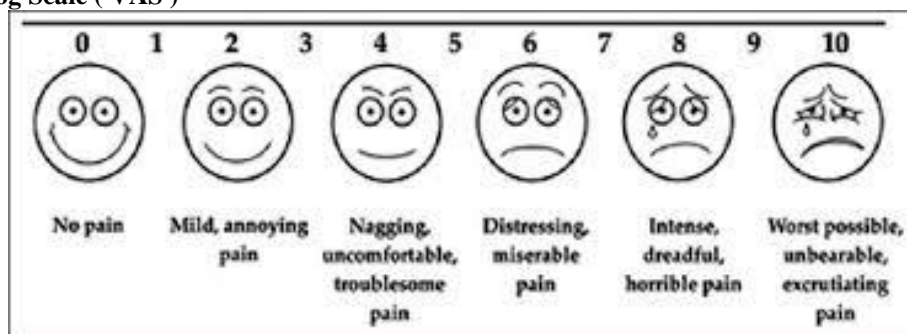
After 15 min of spinal injection, outcome of SAB was assessed. If patient had no sensory or motor block due to some technical reason, it was defined as “technical failure” and the case was excluded from the study. If peak sensory level could not reach toT8, and Bromage score was <3 then it was defined as “failed case” and converted to general anesthesia and further data were not recorded.

If peak sensory level reached to T8 or above with a Bromage score of 3, surgery was allowed to start and the case was defined as “successful.” If surgery could be completed without any supplementation, the case was defined as “completely successful”.

The heart rate (HR), NIBP, and SpO₂ were monitored continuously and recorded at the baseline, 2minute, and subsequently every 5 minutes for the first 15 minutes and then every 15 minutes until the end of surgery. Hypotension was defined as a fall in systolic blood pressure of > 30% below baseline or < 90 mm Hg and was treated with additional IV RL and injection of mephenteramine 6 mg, repeated if necessary. Bradycardia was defined as a fall in HR of > 30% below baseline or < 55/minute and was treated with injection of atropine 0.6 mg IV.

In the intraoperative period sedation and other side effects like nausea, vomiting, bradycardia and requirement of additional analgesics were recorded. In the postoperative period, whenever the patient complained of pain (visual analog scale >3) IV injection of diclofenac 75 mg was given as rescue analgesic and the time was recorded and taken as total duration of post operative analgesia with intrathecal DMT. .

Visual Analog Scale (VAS)



III. Discussion

Local anaesthetic agents have been used for a long time to give subarachnoid block for infraumbilical surgeries. Drugs like opioids, neostigmine and magnesium sulphate which have been added to local anaesthetics to prolong intraoperative and postoperative analgesia¹ have been associated with various side effects hence limiting their use.^{2,3,4}

DMT a highly selective alpha -2 adrenergic agonist has analgesic, sedative and anaesthetic sparing effect when used by parenteral route without any respiratory depression¹⁰. It has been used as an adjuvant to local anaesthetic agents in subarachnoid block to prolong postoperative analgesia with minimal side effects.^{6,7,8,9}

Local anaesthetic like bupivacain acts by blocking sodium channels¹¹. the mechanism by which intrathecal alpha adrenoceptor agonist prolong the motor and sensory block of local anaesthetics is at the best speculative. Dexmedetomidine, owing to its α_2 adrenergic agonistic action may have an additive or a synergistic effect on local anaesthetics as studied by salgado et al.¹² It prolongs the sensory block by depressing neurotransmitter release from C-fibers of the spinal cord and by hyperpolarization of postsynaptic dorsal horn neurons^{13,14} Binding of α_2 adrenergic agonists to motor neuron in the dorsal horn of spinal cord may be the reason for prolongation of the motor block.⁸ Above properties could have contributed to enhanced anesthetic effects with the usage of different doses of Dexmedetomidine.

Intrathecal small dose of dexmedetomidine (4 μ g) used in combination with bupivacaine in human beings for spinal anaesthesia have been shown to produce a prolongation in the duration of motor and sensory block with haemodynamic stability and lack of sedation^{6,7,8,9}.

In our study we have compared 3 different doses (4 μ g, 6 μ g, and 8 μ g) of Dexmedetomidine as an adjuvant to 3 ml of intrathecal bupivacaine for infraumbilical surgeries. Although the postoperative analgesia is more with higher doses (15 μ g which may be beneficial in patient undergoing lengthy surgeries these doses leads to prolonged motor block and higher sedation scores which may be undesirable.¹³ Al ghenem et al has reported hypotension and bradycardia with use of 15 μ g intrathecal DMT in gynecological procedures Eid et al observed higher incidence of bradycardia with higher doses of dexmetomidine.⁷

A similar study was conducted by Mustafa et al⁸ in which 66 patients scheduled for urological procedures were randomly divided into 3 groups and given dexmedetomidine 5 μ g and 10 μ g along with 12.5 mg of bupivacaine. Our results are similar and further confirm the fact that when dexmedetomidine is added as adjuvant to bupivacaine in spinal anaesthesia, the prolongation of motor and sensory block occurs in a dose dependent manner that is as the dose of dexmedetomidine is increased the duration of motor and sensory block increases and duration of analgesia is also prolonged.

Tarbeehet et al and Jamlia RH et al^{16,17} also found that dexmedetomidine has a dose dependent effect on onset and regression of motor and sensory block and time to rescue analgesia with lower VAS scores and minimal side effects when used as an adjuvant to intrathecal bupivacain. However in our study we did not find dose dependent effect on onset of sensory and motor block but effect on prolongation of postoperative analgesia were comparable to our study

Our trial compared 3 doses (4 μ g, 6 μ g and 8 μ g) of DMT The onset time of sensory or motor blockade was comparable in all 3 groups (table 2). Ghanem et al¹⁷ observed relatively shorter time of onset than observed by us which can be attributed their use of isobaric bupivacain and difference in definition of onset time (T8 dermatome versus T- 10 dermatome. Our trial showed that duration of motor blockade (319 \pm 25.25, 329.37 \pm 16, 390.7 \pm 33.55) sensory block (190.7 \pm 21.37, 191.05 \pm 13, 236.15 \pm 21.53) and analgesia (442.8 \pm 34.96, 445.25 \pm 34.44, 611.58 \pm 35.46) increased significantly and congruently with increase in the dosage of intrathecal DMT with comparable hemodynamic and side-effect profile. However there was a greater increase in the duration of analgesia compared with the increase in duration of motor paralysis (table 2). Increasing the dosage of intrathecal DMT from 4 μ g to 8 μ g resulted in a 23.88% (190.7vs. 236.15 minutes), 22.48% (319 vs. 390 minutes) and 26.70% (442.8 vs. 611.58 minutes) increase in the duration of sensory block, motor block and analgesia, respectively. In our study, no sedative was given during premedication and thus most of the patients had a sedation score of 0 at all measured intervals. It has been observed earlier that addition of higher doses of intrathecal DMT to bupivacain cause higher sedation scores.¹⁹

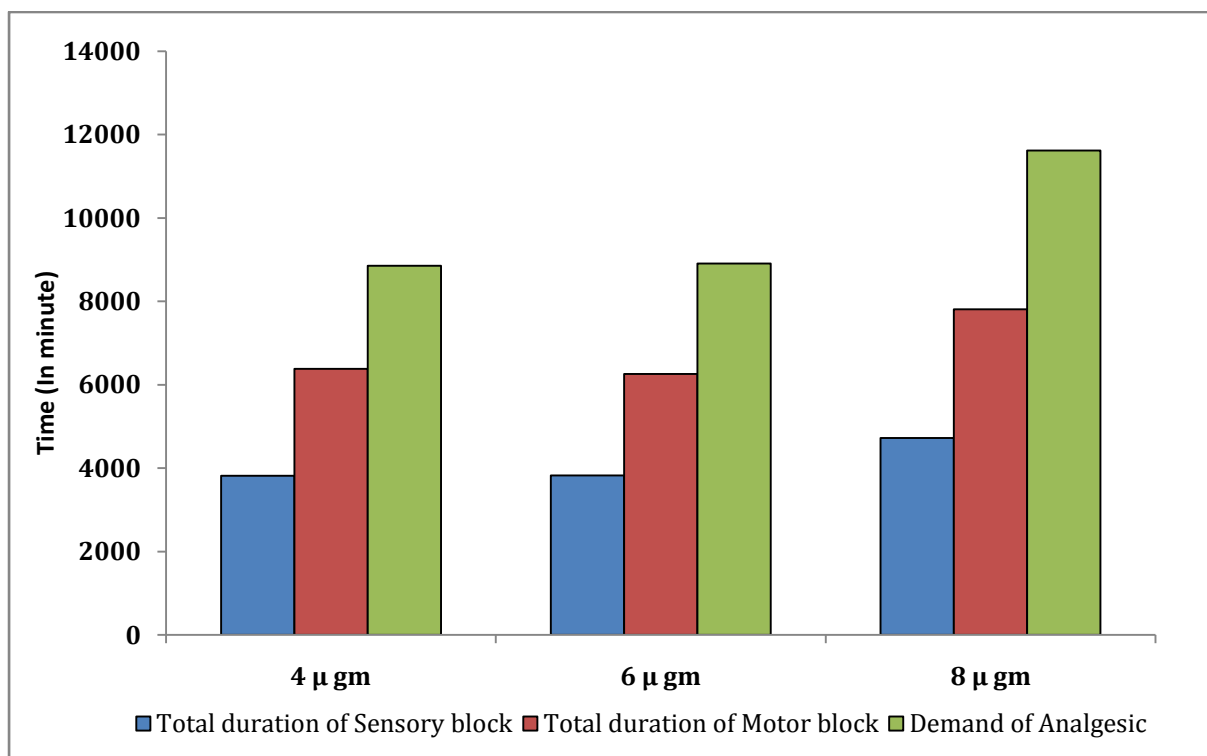
Patients remained haemodynamically stable in all 3 groups at all measured intervals. It is a well known fact that intrathecal local anaesthetics block the sympathetic outflow and cause fall in BP and pulse we observed a similar decrease in haemodynamic parameters in all the patients irrespective of group distribution however Al Mustafa et al⁷ demonstrated a dose dependent but still insignificant decrease in MAP by addition of DMT to bupivacain over a range of 5 μ gm to 10 μ gm though in our study, it was not so. Intrathecal DMT as an adjuvant in low doses does not produce any haemodynamic changes²⁰.

Table no.1: Patients and surgery characteristics

	Group A	Group B	Group C
Variable	(4 μ gm)	(6 μ gm)	(8 μ gm)
Age (Year)	31.25 \pm 5.87	34.9 \pm 4.68	32.9 \pm 6.41
Male (%)	17 (85 %)	12 (60 %)	19 (95 %)
Weight(Kg)	60.03 \pm 6.49	57.20 \pm 9.49	56.49 \pm 7.46
ASA I/II	16/4	13/7	16/4
Pulse rate	83.3 \pm 5.22	86.55 \pm 7.38	80.4 \pm 4.53
Blood pressure	135.5/82 \pm 4.44/3.78	138/85 \pm 5.63/4.98	137/84 \pm 4.62/3.8
Duration of Surgery (in min.)	104.4 \pm 22.09	89.3 \pm 29.67	103.32 \pm 28.28

Table no.2: Block characteristics:

	Group A	Group B	Group C
Variable	4 μ gm	6 μ gm	8 μ gm
Sensory block onset time (min.)	6.85 \pm 1.59	4.75 \pm 1.21	5.5 \pm 0.90
Sensory block duration (min.)	190.7 \pm 21.37	191.05 \pm 13	236.15 \pm 21.53
Motor block onset time (min.)	6.73 \pm 1.22	5.7 \pm 1.60	6.81 \pm 1.17
Motor block duration (min.)	319 \pm 25.25	329.37 \pm 16	390.7 \pm 33.55
Duration of Analgesia (in min.)	442.8 \pm 34.96	445.25 \pm 34.44	611.58 \pm 35.46



For the sensory block p-value is 0.001591 < 0.05 (α) i.e. there is significant difference in the level of doses. For the motor block p-value is 0.000267 < 0.05 (α) i.e. there is significant difference in the level of dose. And for the demand of Analgesic p-value is 0.0000001 < 0.05 (α) i.e. there is highly significant difference between them.

Further studies are required to rule out any short term or long-term adverse effects of intrathecal dexmedetomidine, although in our study 24 hours follow up showed no significant side effects. Patients only in ASA grade I and II were included in our study. Safety of DMT therefore needs to be evaluated in patients with known cardiovascular or other comorbidities or in pregnancy.

IV. Results

A total of 60 patients of ASA grade 1 and 2 were included in this study. All the groups were comparable as regard to age, sex, weight, and ASA grade (Table 1). The number of patients in each group were undergoing different types of infraumbilical surgeries.

The onset of sensory block, The peak sensory block level and the time to attain peak sensory block level were comparable among all the groups (Table 2) However duration of sensory block i.e. time taken to regression

to S-1 was significantly higher in group C(236.15 ± 21.53 min.) as compared to group A(190.7 ± 21.37 min.,) and group B (191.05 ± 13 min.) p- value is $0.001591 < 0.05$ (α) i.e. there is significant difference in the level of sensory block with increasing doses of DMT.

There was no significant difference in onset of motor block between the 3 groups however duration of motor block i.e. motor block regression to Bromage 3 was significantly higher in group C(390.7 ± 33.55 min) as compared to group A (319 ± 25.25 min.) and group B (329.37 ± 16 min). p- value is $0.000267 < 0.05$ (α) i.e. there is significant difference in the duration of motor block with increasing doses of DMT.

The duration of analgesia was significantly prolonged in Group C (611.58 ± 35.46) compared with group A and B ($p < 0.0000001$). Group C required significantly less rescue analgesics in the first 24 hours postoperatively than group B and group A.

The heart rate, blood pressure, and sedation level assessed at various time intervals showed no statistically significant differences. Two patients in group A and one patient in group C had hypotension and bradycardia which were treated with 6mg of mephentermine and 0.6mg of inj atropine.

V. Conclusion

On the basis of our study we conclude that addition of intrathecal dexmedetomidine to hyperbaric Bupivacaine prolongs the sensory and motor block and also prolongs the time of postoperative analgesia in a dose dependent manner with hemodynamic stability and minimal side effects

Dexmedetomidine seems to be an attractive adjuvant to intrathecal bupivacaine especially in long duration surgeries as an alternative to epidural anaesthesia or prolonged general anaesthesia. However, further clinical studies are required to prove the efficacy and safety of varying dosages of DMT for supplementation of spinal local anaesthetics.

References

- [1]. Buvanendran A, Kroin JS Useful adjuvants for postoperative pain management. *Best Pract Res Clin Anaesthesiol* 2007; 21:31–49.
- [2]. Shende D, Cooper GM, Bowden MI. The influence of intrathecal fentanyl on the characteristics of Subarachnoid block for caesarean section. *Anaesthesia* 1998; 79: 702-710.
- [3]. Chung CJ, Kim JS, Park HS, Chin YJ. The efficacy of intrathecal neostigmine, intrathecal morphine and their combination for post-caesarean section analgesia. *Anesth Analg.* 1998;87:341-6.
- [4]. Fawcett WJ, Haxby EJ, Male DA. Magnesium: physiology and pharmacology. *Br J Anaesth.* 1999;83:302-20
- [5]. Grewal A. Dexmedetomidine: New avenues. *J Anaesthesiol Clin Pharmacol.* 2011;27:297–302. [[PMC free article](#)] [[PubMed](#)]
- [6]. Mantz J, Jossierand J, Hamada S. Dexmedetomidine: New insights. *Eur J Anaesthesiol.* 2011;8:3–6. [[PubMed](#)]
- [7]. Al Ghanem SM, Massad IM, Al-Mustafa MM, Al-Zaben KR, Qudaisat IY, Qatawneh AM, et al. Effect of adding dexmedetomidine versus fentanyl to intrathecal bupivacaine on spinal block characteristics in gynecological procedures: A double blind controlled study. *Am J Appl Sci.* 2009;6:882–7.
- [8]. Al-Mustafa MM, Abu-Halaweh SA, Aloweidi AS, Murshidi MM, Ammari BA, Awwad ZM, et al. Effect of dexmedetomidine added to spinal bupivacaine for urological procedures. *Saudi Med J.* 2009;30:365–70. [[PubMed](#)]
- [9]. Gupta R, Verma R, Bogra J, Kohli M, Raman R, Kushwaha JK. A comparative study of intrathecal dexmedetomidine and fentanyl as adjuvants to Bupivacaine. *J Anaesthesiol Clin Pharmacol.* 2011;27:339–43. [[PMC free article](#)] [[PubMed](#)]
- [10]. Venn RM, Grounds RM. Comparison between dexmedetomidine and propofol for sedation in the intensive care unit: Patient and clinician perceptions. *Br J Anaesth.* 2001;87:684–90. [[PubMed](#)]
- [11]. G.Edward Morgan.Jr Magd.S.Mikhail ;Clinical Anaesthesiology pg 193 chapter 14 2nd Edition A LANGE Medical book
- [12]. Salgado PF, Sabbag AT, Silva PC, Brienze SL, Dalto HP,Módo NS, et al. Synergistic effect between dexmedetomidineand 0.75% ropivacaine in epidural anesthesia. *Rev Assoc Med Bras* 2008;54:110-5.
- [13]. Hala EA, Shafie MA, yousef H. Dose –related prolongation of hyperbaric bupivacaine spinal anesthesia by dexmedetomidine. *AinShams J of Anesthesiol* 2011; 4:83-95. *Anesthesiol.* 2011;4:83–95.
- [14]. Ishii H , Kohno T , Yamakura T , Ikoma M , Baba H. Action of dexmedetomidine on the substantia gelatinosa neurons of the rat spinal cord. *Eur J Neuro sci* 2008; 27:3182-90.
- [15]. Eid HE,Shafie MA,Youssef H. Dose related prolongation of hyperbaric bupivacaine spinal anesthesia by Dexmedetomidine *Ain Shams J Anesthesiol* 2011;4:83-95
- [16]. Tarbeeh GA, Mohamed MA. Effects of intrathecal bupivacaine-fentanyl versus bupivacaine–dexmedetomidine in diabetic surgical patients. *Egyptian J of Anaesth.*2013;29 :13-18
- [17]. Jamliya RH , Deshmukh V , Rajesh C ,Maliwad J, Shah BJ , Minaxi H.Effect of adding dexmedetomidine in intrathecalbupivacaine versus intrathecal bupivacaine alone on spinal block charecteristics inorthopaedic lower limb procedures. *Res J PharmBiol Chem Sci* 2013;4:1340-1346
- [18]. Al-Ghanem SM, Massad IM, Al-Mustafa MM, Al-Zaben KR,Qudaisat IY, Qatawneh AM, et al. Effect of adding dexmedetomidine versus fentanyl to intrathecal bupivacaine on spinal block characteristics in gynecological procedures. *Am JApplSci*2009;6:882-7.
- [19]. Hala EA, Shafie MA, Youssef H. Dose-related prolongation of hyperbaric bupivacaine spinal anesthesia by dexmedetomidine. *Ain Shams J*
- [20]. Kanazi GE, Aouad MT, Jabbour-Khoury SI, Al Jazzar,Alameddine MM, Al-Yaman R, et al. Effect of low dosedexmedetomidine or clonidine on the characteristics of bupivacaine spinal block. *ActaAnesthesiolScand* 2006;50:222-7.

Sapna Singh "Dose dependent Effect of Intrathecal Dexmedetomidine with Bupivacaine in Infraumbilical Surgeries."IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), vol. 17, no. 3, 2018, pp 68-72.