Original Article

Intrathecal Dexmedetomidine and Intrathecal Magnesium Sulphate as Adjuvants with Hyperbaric Bupivacaine for the Prevention of Post Spinal Anaesthesia Shivering in Patients Posted for Uroscopic Procedures - A Comparative Study

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ABSTRACT

Introduction: Hypothermia and chills are common complications of spinal anesthesia (SA) in uroscopic surgery with large volumes of intraluminal irrigation. Shivering tamper with adequate monitoring and is associated with many adverse effects, because it cause increase in the circulating catecholamines, heart rate, cardiac output, minute ventilation, oxygen consumption of patient, intracranial pressure, and postoperative pain due to distension of surgical stitching. Various opioid and non-opioid drugs have been used to prevent shivering, but they have many side effects and the results are inconclusive.

Aims/ objective: To assess and compare the efficacy of intrathecal dexmedetomidine and intrathecal magnesium sulphate for the prevention of shivering after spinal anesthesia.

Materials and Method: Patients were randomly allocated in three equal groups using web generated random numbers. Patients of control Group (n=38) were given 3ml of 0.5% hyperbaric bupivacaine plus 1ml normal saline (NS). Patients of MgSO4 Group (n=38) were given 3ml of 0.5 % hyperbaric bupivacaine plus 20mg of Magnesium sulphate. Patients of dexmedetomidine Group (n=38) were given 3ml of 0.5 % hyperbaric bupivacaine plus 5mcg Dexmedetomidine. Incidence & severity of shivering were evaluated using Crossley and Mahajan scale. The chi-square test was used to analyze categorical data and the unpaired t-test was used for analyzing continuous data.

Results: There was significantly a smaller number of shivering episodes in patients who were given dexmedetomidine as compared to control group ($p<0.05$). But there was no significant difference between dexmedetomidine group and magnesium sulphate group with respect to frequency of shivering episodes ($p>0.05$). There was early sensory and motor block as well greater duration of block in patients who were given dexmedetomidine and there was late sensory and motor block as well lesser duration of block in patients who were given magnesium sulphate.

Conclusion: Both dexmedetomidine and magnesium sulphate were shown to be effective in reducing the occurrence of shivering after spinal anesthesia. Dexmedetomidine was better than magnesium sulphate with respect to onset and duration of sensory and motor block.

Keywords: Spinal Anaesthesia, Shivering, Dexmedetomidine, Magnesium Sulphate.

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INTRODUCTION

Shivering is defined as involuntary repetitive skeletal muscle activity. The mechanisms of shivering in surgical patients are primarily intra-operative heat loss, rise in sympathetic tone, pain, and release of pyrogens in systemic circulation.[1]

Hypothermia and chills are common complications of SAB (Sub-arachnoid block) in Uroscopic surgery in which there is large volumes of intraluminal irrigation.[2] Spinal anaesthesia (SA) is a very reliable and convenient technique for short procedures such as urological surgery, Especially for procedures that require the patient to remain conscious to detect intra-operative complications, like transurethral resection of the prostate (TURP) syndrome.[3]

However, Spinal Anaesthesia act against tonic vasoconstriction and causes a redistribution of core heat from the trunk to the peripheral tissues leading to greater risk of additional hypothermia and shivering in patients.[4] Shivering tamper with adequate monitoring and is associated with many side effects, as it cause rise in the circulating catecholamine, heart rate, cardiac output, minute ventilation, oxygen consumption by patients, CO_2 production from metabolism, rise in lactic acid level, rise in intraocular and intracranial pressure, and rise in postoperative pain from surgical incision stretching.[5]

Various opioid and non-opioid agents, such as meperidine, ketamine, tramadol, and clonidine, have been used to

prevent shivering, but they have many side effects and the results are inconclusive.[6]

Dexmedetomidine is a specific and selective agonist of α2-adrenoceptor in the brain and spinal cord. The effects of activation of these receptors are fall in sympathetic tone with inhibition of the neuro-endocrine and hemodynamic adjustments to anaesthesia and surgery. So, dexmedetomidine can counteract with both beneficial and undesirable effects of hypothermic shivering, including rise in catecholamine levels, increase in oxygen consumption, rise in mean blood pressure, and heart rate. [7-9]

Dexmedetomidine exerts its binary action by inhibiting vasoconstriction and causing rise in the level of the shivering threshold. Dexmedetomidine has demonstrated its efficacy in the pharmacotherapy and prevention of shivering after spinal anaesthesia when used intrathecally due to its agonistic action on central alpha 2 receptors.[6,10-12]

$MgSO_4$ use can lead to peripheral vasodilatation, that has potential to improve coetaneous circulation, consequently causing fall in frequency of shivering.[4] Beside it, $MgSO_4$ also has inhibitory action to calcium and has non-competitive antagonism on N-methyl-D-aspartate receptors, and its efficacy on analgesia, especially symptoms of neuropathic pain and increase in duration of motor block, has been established in many studies.[2,13,14] This mechanism of action of $MgSO_4$ has also been reflected on its anti-shivering effects, but there is need for further pre-clinical and clinical studies.

Magnesium sulphate ($MgSO_4$), which has been found to inhibit postoperative shivering, showing that the agent reduces the shivering threshold.[15] It has a good safety as there are no adverse effects associated to the use of the drug intrathecally and no significant disturbance in hemodynamic parameters was found.[16] Intravenous (IV) $MgSO_4$ has been successfully examined in many studies in management of post operative shivering, but there are limited number of studies that have investigated on efficacy of intrathecal $MgSO_4$ in reducing shivering.[2,4]

The aim of this study was to assess and compare the efficacy of intrathecal dexmedetomidine and intrathecal magnesium sulphate for the prevention of shivering after spinal anesthesia.

The primary end-points were the frequency and intensity of shivering. The secondary end-points were hemodynamic parameters such as heart rate and blood pressure and frequency of adverse events such as hypotension, bradycardia, and sedation.

MATERIALS AND METHODS

This was a prospective randomised double-blind study with parallel 1:1:1 allocation. The study was done after approval from institutional ethic committee and taking informed written consent from each subject.

Previous studies showed that the frequency of peri-operative shivering in patients undergoing minor lower abdominal surgeries under spinal anaesthesia was nearly 50% and it was 20% in those patients who were given dexmedetomidine. [12] With a power of 80% and an alpha error of 0.05, a minimum sample size of 38 patients was required for each group.

Inclusion criteria:

- Patients aged 20 to 60 years
- American Society of Anaesthesiologists (ASA) Class I or Class II physical status.

Exclusion criteria:

- Patients with coagulopathy
- Patients with a history of hypersensitivity reactions to local anaesthetics
- Patients with cardiac, renal or respiratory diseases.
- Patients with increased liver transaminase levels

Patients were randomly allocated in three equal groups using web generated random numbers.

- **Patients of control Group (n=38)** were given 3ml of 0.5% hyperbaric bupivacaine plus 1ml NS
- **Patients of $MgSO_4$Group (n=38)** were given 3ml of 0.5 % hyperbaric bupivacaine plus 20mg of Magnesium sulphate
- **Patients of dexmedetomidine Group (n=38)** were given of 0.5 % hyperbaric bupivacaine plus 5mcg Dexmedetomidine

Specific intrathecal drug solutions were made and injected by an anaesthesiologist who was not investigator in our study. The patients as well as anaesthesiologists who were responsible for observation of patients and collection of data were unaware about the interventions in groups. Patients were preloaded with pre-warmed fluids. Assessment of ASA standard was done then SAB (sub-arachnoid block) was given to patients of all groups.

Incidence & severity of shivering were evaluated with Crossley and Mahajan scale:[9]

- 0: When no shivering was detected.
- 1: When pilo-erection or peripheral vasoconstriction was present but no shivering was there.
- 2: When patient had muscular activity in only one group of muscle
- 3: When patient had muscular activity in more than one group of muscle but there was no generalized shivering
- 4: When shivering was seen in whole body of patient.

IV tramadol 1mg/kg was given to patients having grade 3 or 4 shivering. Time of onset and duration of sensory and motor block was evaluated by the pinprick test and Bromage scale respectively.

Heart rate and blood pressure were recorded soon after giving spinal anaesthesia then after 5 minutes and then after each 15 minutes till 2 hours. We defined hypotension as blood pressure equal to or less than 20% of the baseline blood pressure. We used IV mephentermine 6mg bolus for management of hypotension. We defined bradycardia as heart rate less than 50beats per minute and IV atropine 0.01-0.02mg/kg bolus was given for its management.

Statistical Analysis

Results were presented in frequencies, percentages and mean ±standard deviation (SD). Chi Square test was used to compare proportion of different gender, ASA categories, type of surgery and grades of shivering between the groups. Unpaired t test was used to compare mean age, time of onset and duration of sensory and motor block between the groups. Results were considered significant when we obtained p-value less than 0.05. We carried out our analysis on SPSS 21.0 version.

RESULTS

Table 1: Baseline demographic and clinical characteristics

Parameters	Control Group (n=38)	Dexmedetomidine Group (n=38)	$MgSO_4$ Group (n=38)	p (C-D)	p (C-M)	p (D-M)
Age in years (mean ± SD)	53.18 ± 9.96	52.12 ± 11.60	52.04 ± 9.92	0.67	0.62	0.97
Gender						
Male (n)	30	31	28	0.77	0.59	0.41
Female (n)	8	7	10			
ASA Classification						
I	20	19	21	0.81	0.82	0.65
II	18	19	17			
Total duration of surgery in minutes (mean ± SD)	111.14 ± 13.68	107.69 ± 11.12	109.28 ± 9.94	0.23	0.50	0.51
Time to reach T10 sensory block (mean ± SD)	4.29 ± 0.72	3.49 ± 0.59	6.78 ± 0.99	**< 0.01**	**< 0.01**	**< 0.01**
Time to reach bromage 4 motor block (mean ± SD)	5.08 ± 0.82	3.91 ± 0.87	8.24 ± 0.90	**< 0.01**	**< 0.01**	**< 0.01**
Duration of sensory block (mean ± SD)	207.03 ± 21.56	321.46 ± 43.33	258.32 ± 26.11	**< 0.01**	**< 0.01**	**< 0.01**
Duration of motor block (mean ± SD)	164.11 ± 15.18	217.68 ± 24.17	204.82 ± 19.74	**< 0.01**	**< 0.01**	**0.01**
Type of Surgery						
TURP	5	7	7			
Urethroscopy	8	8	7	0.87	0.87	0.99
Ureteroscopy	10	11	12			
Cystoscopy	15	12	13			

SD: Standard deviation

p (C-D): p value for comparison between control group and dexmedetomidine group (n=38)

p (C-M): p value for comparison between control group and $MgSO_4$ Group (n=38)

p (D-M): p value for comparison between dexmedetomidine group and $MgSO_4$ Group (n=38)

The groups were comparable with respect to age, sex, ASA classification, and type of surgery. There was early sensory and motor block as well greater duration of block in patients who were given dexmedetomidine and there was late sensory and motor block as well lesser duration of block in patients who were given magnesium sulphate.

Table 2: Comparison of three groups based on frequency of shivering incidence

	Control Group (n=38)	Dexmedetomidine Group (n=38)	$MgSO_4$ Group (n=38)	p (C-D)	p (C-M)	p (D-M)
Number of episodes of shivering	25	15	21	**0.02**	0.35	0.17
Grade of Shivering						
0	13	23	17			
I	1	4	10			
II	3	4	2	**0.02**	**0.01**	0.30
III	11	5	5			
IV	10	2	4			

There was significantly a smaller number of shivering episodes in patients who were given dexmedetomidine as compared to control group ($p<0.05$). But there was no significant difference between dexmedetomidine group and magnesium sulphate group with respect to frequency of shivering episodes ($p>0.05$).

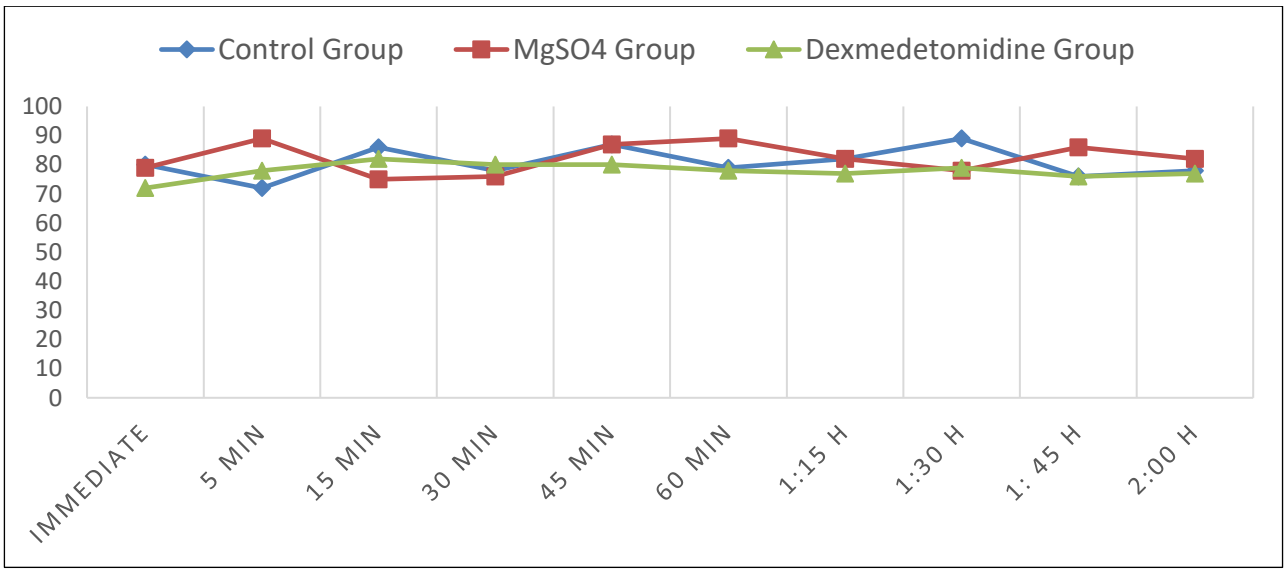

Figure 1: Comparison of heart rate between groups

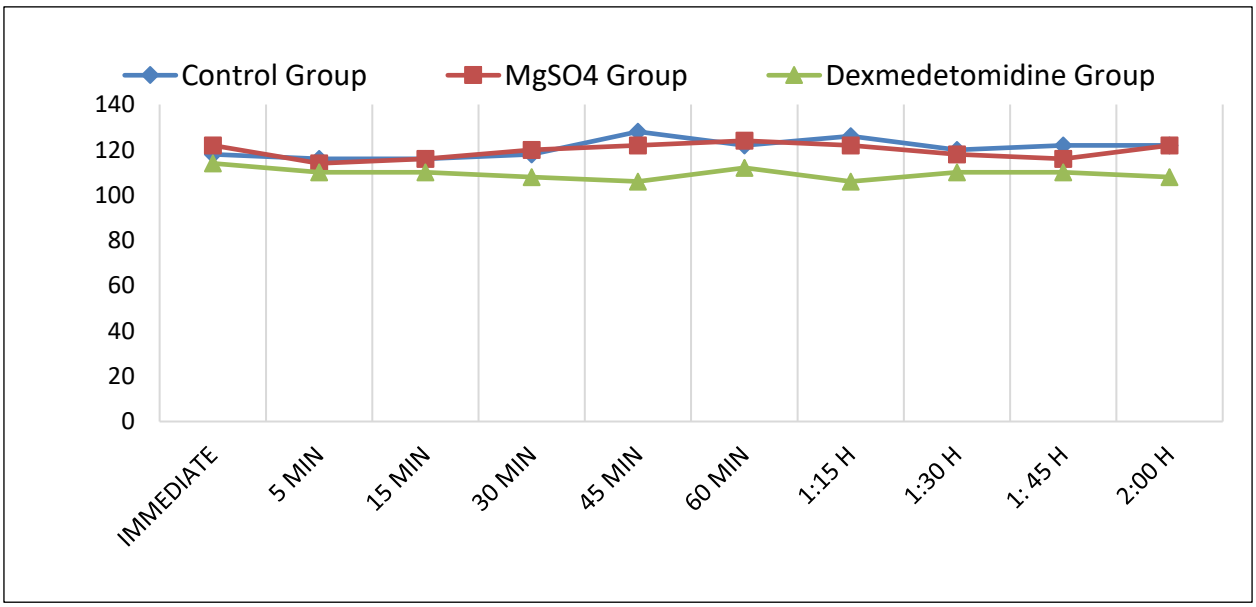

Figure 2: Comparison of systolic blood pressure between groups

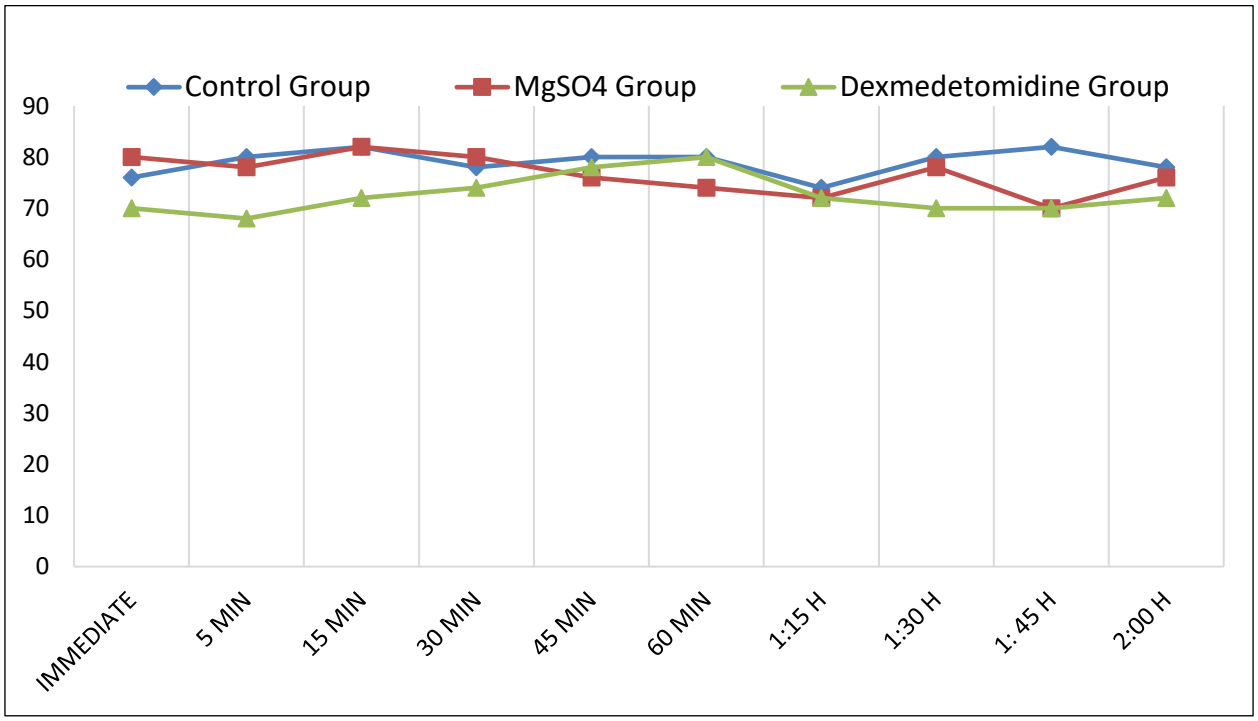

Figure 3: Comparison of diastolic blood pressure between groups

All the groups were comparable with respect to heart rate and blood pressure.

DISCUSSION

Shivering is protective response of body to defend hypothermia but it leads to pain and discomfort to patient and could be a threat to patient with cardiovascular disorders or respiratory diseases because it leads to rise in the level of catecholamine in systemic circulation, heart rate, respiratory rate, cardiac output, requirement of oxygen, formation of $C0_2$ by metabolic processes and lactic acid level. There is also rise in intracranial, intra-ocular pressure and pain after surgery due to stretch on surgical incision. Shivering can also disturb proper monitoring and care of patients by causing disturbance in ECG, blood pressure and reading shown by pulse oximeter.[5] Moreover, shivering in patients under ASA grades III and IV category may add up to challenges to doctor and raise the intra-operative time.

Hypothermia is a major inducer of shivering, but no definite linear association has been established between temperature of body and frequency of shivering episodes. Shivering is also associated with age of the patient, level of sensory block, operation theatre temperature, and temperature of intravenous solution.[18] Evidence for explaining the mechanism and association of shivering with major risk factors is weak. Some research has suggested that redistribution of internal heat, loss of body heat to environment and disturbance in central thermoregulation could be the reason. [19] Thermoregulatory centre of the hypothalamus is likely to be affected adversely by administration of general and regional anaesthesia leading to various levels of hypothermia. [20] Under regional anaesthesia, there is vasoconstriction and shivering restricted to part of body above the level of block while there is vasodilatation and redistribution of the core body temperature in the part of body below the level of block because there is block on somatic and sympathetic nerve in lower body.[17]

There is complicated relationship between shivering and the neurotransmitter pathways, and there is involvement of several receptors, such as α-2 adrenergic, cholinergic, opioid, and serotonergic receptors in patients. Various trials have been conducted to study the effect of drug interactions on these receptors on frequency and severity of shivering after spinal anaesthesia.[5] The study has been done on opioids like fentanyl, meperidine, tramadol and other drugs like clonidine and ketamine, and various level of efficacy has been established in those study but occurrence of various adverse effects like instability in haemodynamic, decrease in respiratory rate and power, nausea, and vomiting.[21]

Based on earlier studies, the efficacy of subarachnoid injections of dexmedetomidine and $MgSO_4$ on the prevention of shivering after spinal anaesthesia was compared in the patients who were undergoing Uroscopic surgery. The present study has shown that injection of both dexmedetomidine (5 µg) and $MgSO_4$ (25 mg) after spinal anaesthesia lead to fall in the incidence of shivering after spinal anaesthesia significantly. Five patients (14.3%) in group D, 8 patients (22.8%) in group M, and 21 patients (60%) in group C developed shivering.

Like this study, Ellakany et al. have given the same dose (5 µg) of intrathecal dexmedetomidine and found that both intrathecal dexmedetomidine and meperidine was efficacious in decreasing the frequency of shivering after

spinal anaesthesia in patients who have undergone lower abdominal surgery, but there was higher frequency of adverse effect in the meperidine group than the dexmedetomidine group like itching, nausea and vomiting.[12] In 60 patients who have undergone lower abdominal surgery, Abdel Hamid et al. found that addition of 5 µg of dexmedetomidine to intrathecal bupivacaine lead to improvement in the quality of the spinal block, with decreased analgesic requirements after surgery and a decreased frequency of shivering with no sedation or other adverse effects as compared with the placebo group.[22]

Abdel-Ghaffar et al. have compared the clinical effectiveness and safety of three different doses (0.5, 0.3 and 0.2 µg/kg) of intravenous dexmedetomidine and 0.4 mg/kg dose of intravenous meperidine for the therapy of shivering after spinal anaesthesia in 120 patients. They have reported that 0.3 µg/kg dose of dexmedetomidine was the most effective dose for the optimum therapy of shivering post-spinal anaesthesia, with acceptable effects on hemodynamic properties and sedation.[25]

Gozdemir et al. have reported that, an intravenous administration of 80 kg/mg of $MgSO_4$ over 30 min, followed by intravenous administration at a maintenance dose rate of 2 g/hr after spinal anaesthesia to the end of intraoperative period led to significant reduction in incidence of shivering after spinal anaesthesia in patients who have undergone TURP.[2]

There was no significant difference between the three groups with respect to haemodynamic characteristics during surgery. With respect to the time of onset of sensory and motor block, dexmedetomidine group had the lowest time of onset of sensory and motor blocks, while $MgSO_4$ group had prolonged time of onset of sensory and motor block than dexmedetomidine group. The reason for this could be alteration in the pH and baricity of bupivacaine after adding magnesium sulphate. The patients of dexmedetomidine group have higher durations of both the sensory and motor blocks than the patient of $MgSO_4$ group and patients of $MgSO_4$ group have higher duration of blocks than patients of control group. Our results were consistent with the findings of two earlier studies in which the efficacy of 10 µg of intrathecal dexmedetomidine was compared with the efficacy of 50 mg of intrathecal magnesium sulphate which were added to bupivacaine with respect to quality of the spinal block as primary end-point.[27,28]

CONCLUSION

Dexmedetomidine and magnesium sulphate both proved to be effective in reducing the incidence of post spinal anaesthesia shivering. Dexmedetomidine was better than magnesium sulphate with respect to onset and duration of sensory and motor block. However, use of magnesium sulphate should also be encouraged as it is cheap and available in most operating theatres.

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