

**COMPARATIVE EVALUATION OF PROPOFOL KETAMINE AND PROPOFOL FENTANYL IN DAY CARE SURGERIES**Brajesh Kaushal<sup>1</sup>, Yashwant Dhawale<sup>2</sup>, Deepesh Gupta<sup>3</sup>**HOW TO CITE THIS ARTICLE:**

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**ABSTRACT:** To find the ideal drug combinations which can be used during day care surgeries and procedures. **AIMS:** This study was conducted. To evaluate and compare the efficacy, and haemodynamic stability of ketamine and fentanyl combination with propofol. To compare the incidence of side effects. To compare the time of awakening and recovery time. To compare the discharge criteria in both groups. **METHODS:** The study was conducted in 50 patients of age group 18-50 years of either gender belonging to ASA grade I and II, were divided into two groups of 25 each. They underwent elective surgery of approximately 1 hour duration. Group I received Propofol-ketamine while group II received Propofol-fentanyl for induction and maintenance of anaesthesia. Postoperatively, time for awakening, recovery time (by modified Aldrete scoring system) and discharge status (by modified post anaesthetic discharge scoring system) were recorded and compared in two groups. **RESULTS:** Propofol-fentanyl combination produced a significantly greater fall in pulse rate and in both systolic and diastolic blood pressure as compared to Propofol-ketamine during induction and maintenance of anaesthesia. Fall in respiratory rate was greater in Propofol-fentanyl group as compared to Propofol-ketamine group. The recovery time in group I was longer than group II. Discharge criteria is significantly earlier in group II. **CONCLUSION:** Both Propofol-ketamine and Propofol-fentanyl combination reduce rapid, pleasant and safe anesthesia with only a few untoward side effects and propofol-ketamine produces better haemodynamic statistic, during anaesthesia.

**KEYWORDS:** Propofol, Fentanyl, Ketamine, Day care surgery.

**INTRODUCTION:** Success of day care Anesthesia centres around the Four 'A's - Ambulation, Alertness, Analgesia and Alimentation. It is the quality of recovery from anaesthesia which is particularly important and day care surgery should ensure a period of recovery with swift return to "Street fitness". The Patient should be able to regain ability to respond and react to environmental stimuli in a conscious co-ordinated manner. Furthermore, it is paramount to render the patients free of pain after anaesthesia.

The evolution of day care surgery begins with early ambulation reported by Emil Reis, in 1899. The practice of day care surgery was first reported by Nicoll in 1909. The first outpatient clinic was opened by Ralph Waters in Sioux City, Iowa in 1916. Lawrie first uses the term "Day Surgery".

Day care surgery may be defined as elective minor or intermediate surgeries performed with local or general anaesthesia, on patients who are admitted and discharged on the same day.

We should provide quiet and pleasant induction, predictable loss of consciousness, stable operating conditions, minimal adverse effects, rapid and smooth recovery of protective reflexes and psychomotor functions.

## ORIGINAL ARTICLE

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This study was conducted to evaluate and compare two drug combination of TIVA using propofol-ketamine and propofol-fentanyl and to study the induction characteristics, maintenance of anesthesia and recovery characteristics following anaesthesia with these technique.

The major concern is to determine which patients are appropriate to be scheduled for day-care surgery. Criteria used for selecting outpatients depend upon physical status, type of surgery, special anaesthetic or postoperative consideration and attitude of the patient. The aim of pre-operative screening is to identify patients who are appropriate for day-care surgery.

Propofol is relatively newer intravenous anaesthetic agent for an ideal intravenous anesthetic agent in clinical practice, Kay and Rolly introduced propofol in 1977. It is widely used inducing agent of choice for day care anaesthesia. Its greatest attributes are its dual action as an induction and maintenance agent,<sup>2</sup> rapid and clear headed emergence from anaesthesia, lack of cumulative effects even after prolonged administration, low incidence of PONV, no adverse effect on liver and renal functions and not associated with histamine release or anaphylactic reaction, but preservative or solvent may cause adverse reaction.

Propofol acts only as a sedative and hypnotic, and is devoid of analgesic action. Hence, it is necessary to give an analgesic along with Propofol during anaesthesia to take care of pain component of anaesthesia.

Ketamine is a potent analgesic, its anaesthetic and analgesic effects have been suggested to be mediated by different mechanisms. Ketamine in subanaesthetic doses with Propofol has gained attention in TIVA<sup>3</sup> because of its powerful analgesic action in a small dose without causing myocardial and respiratory depression. Ketamine also causes some degree of sympathetic stimulation, which tends to counter balance the cardiovascular effects of Propofol.

Fentanyl is a  $\mu$ -opioid receptor agonist that produces profound dose-dependent analgesia. Fentanyl and its analogue are the most frequently used opioids in clinical balance anaesthesia. It relieves pain, reduces somatic and autonomic response to airway manipulation provides hemodynamic stability and lesser respiratory depression.<sup>4</sup>

Use of modern anaesthetic e.g., Propofol in combination with minimally effective doses of a short-acting opioid analgesic e.g., Fentanyl can facilitate the early recovery process and allow patients to achieve earlier discharge time after ambulatory surgery.

Various doses of Ketamine and Fentanyl have been reported in literature. Therefore present study includes the comparison of combination of Propofol-Ketamine and Propofol-Fentanyl in day care surgeries.

The combination of these drugs provides complete and balanced anesthesia and has advantages such as high potency lower dosages and fewer side effects.

Keeping in consideration the merits of TIVA a case control study was conducted on 50 patients in Department of Anesthesiology, GMC, Bhopal. (M.P.)

**MATERIAL AND METHODS:** 50 adult patients of age group 18-50 years of both Sexes belonging to ASA grade I and II who underwent elective surgery at GMC and Hamidia group of Hospitals, Bhopal were included in the study.

Following patients were excluded from study. The patients having significant history of allergy to egg or fat, pregnant females, patients on MAO inhibitors, history of jaundice, the patients having significant renal, hepatic, cardiac or chronic pulmonary disease, duration of surgery lasting for

## ORIGINAL ARTICLE

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more than 80 minutes. The selected patients were randomly divided into two groups of 25 each. Preanaesthetic checkup and investigations to rule out any systemic involvement other than those indicated for surgical procedures.

Baseline measurement of blood pressure, pulse rate and arterial O<sub>2</sub> saturation were taken before placement of I.V. cannula. After obtaining proper informed consent and confirming 'nil orally' status, during pre oxygenation patients were premeditated with inj. Glycopynolate 0.2 mg I.V. before induction of anaesthesia.

Induction of anaesthesia in patients of group I was done with inj. Ketamine in analgesic dose of 0.5 mg/kg body weight given as IV bolus doses. About 2 minutes after this, inj. Propofol was given in the induction dose of 1.5-2.5 mg/kg body weight till the verbal communication is stopped.

Subsequent doses of 20 mg were given upon the appearance of reaction to painful stimulus and the facemask was applied while in group II were given inj. Fentanyl citrate in the dose of 2 mg/kg body wt. as slow intravenous injection. About 2 minutes after this, inj. Propofol was given in the dose of 1.5-2.5 mg/kg body wt. till the verbal communication is stopped.

Subsequent dose of 20 mg were given upon the appearance of response to painful stimulus and the face mark was applied firmly.

The patients in both the groups were maintained on spontaneous ventilation throughout the procedure. The anaesthesia continued according to the standard practice.

The patients were also assessed for apnea, which was defined as the loss of respiratory efforts for more than 20 seconds or fall of SPO<sub>2</sub> below 95%. Blood pressure and pulse rate were recorded at 1, 5, 10, 15, 20 and 25 minutes intervals of induction of anaesthesia in both the groups, according to standard practice.

Postoperatively, time for awakening, Recovery time (by Modified Aldrete scoring system) and discharge status (by Modified Post Anaesthetic Discharge Scoring System) were recorded and compared in two groups.

Recovery after ambulatory surgery is divided into three distinctive phases:

1. Early phase- patient emerges from anaesthesia and closely monitored. During this patient obeys command.
2. Intermediate phase – During this time psychomotor functions recover and patient assessed for discharge from PACU. Full return of the pre-operative level is not essential.
3. Late recovery phase – Complete recovery from anaesthesia and surgery with resumption of routine work.

**FAST TRACKING CONCEPTS:** Ambulatory anaesthesia is administered with the dual goals of rapidly and safely establishing satisfactory conditions for the performance of therapeutic or diagnostic procedures while ensuring rapid, predictable recovery with minimal postoperative sequelae. When the patients are awake and oriented in the operating room, are able to sit up with stable vital signs, minimal pain or bleeding and no nausea, they may be eligible to go directly to the phase 2 recovery (post recovery lounge), bypassing the phase 1 PACU is often called fast tracking.

The criteria used to determine fast-track eligibility have been made. A score over 12 with no individual score less than 1 is required for fast-tracking.

## ORIGINAL ARTICLE

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**POST ANAESTHETIC RECOVERY SCORE:** Standard Modified Aldrete scoring system (PARS) developed to guide the transfer of patients from hospital recovery room to the ward. Five major criteria included in recovery scoring system;

ACTIVITY	SCORE
1) Ability to move	
4 extremities	2
2 extremities	1
No extremity	0
2) Respiration	
Able to breathe deeply and cough freely	2
Dyspnea, shallow or limited breathing	1
Apneic	0
3) Circulation	
Preoperative blood pressure (BP), (mmHg)	
BP $\pm$ 20 mmHg of Pre anaesthesia level	2
BP $\pm$ 20 to 50 mmHg of Pre Anaesth level	1
BP $\pm$ 50 mmHg of pre anaesthesia level	0
4) Consciousness	
Fully awake	2
Arousable on calling	1
Not responding	0
5) Oxygen Saturation	
Able to maintain O <sub>2</sub> saturation >92% on room air	2
Needs O <sub>2</sub> inhalation to maintain O <sub>2</sub> saturation >90%	1
O <sub>2</sub> saturation <90% even with O <sub>2</sub> supplementation	0

A score of >9 required for discharge from acute post anaesthesia care unit.

### OTHER TESTS FOR RECOVERY:

- Digit symbol substitution test.
  - Forward and backward counting test.
  - Coin test.
  - Pair test.
  - The P-deletion test.
- But these tests not included in the study.

**DISCHARGE CRITERIA:** Patient readiness for discharge needs to be addressed in a simple, clear, reproducible manner that meets national standards of medical and anaesthesia care. Nursing staff must be able to evaluate postoperative course in a systemic manner and, when necessary meet guidelines to seek physician consultation.

A simple index has been adapted in most centres:

**Modified Post Anaesthetic Discharge Scoring System (MPADSS):  
(Marshall and Chung):****A) VITAL SIGNS**

- 2 within 20% of preoperative value.
- 1 within 20-40% of preoperative value.
- 0 40% of preoperative value.

**B) AMBULATION**

- 2 Steady gait/ No dizziness.
- 1 With Assistance.
- 0 No ambulation/ dizziness.

**C) NAUSEA AND VOMITING**

- 2 Minimal
- 1 Moderate
- 0 Severe

**D) PAIN**

- 2 Minimal
- 1 Moderate
- 0 Severe

**E) SURGICAL BLEEDING**

- 2 Minimal
- 1 Moderate
- 0 Severe

The total score is 10. With patients scoring >9 are considered fit for discharge home.

**STATISTICAL ANALYSIS:** Data were analyzed using software version SPSS R.O. Demographic data were analyzed using analysis of variance. Unpaired t-test and chi-square tests were used where appropriate. Sample size of 50 with 25 patients in each group was determined with power of study of 80%. Data were expressed as mean+SD. Standard tests of significance were applied to determine the p value  $p < 0.05$  was considered significant.

**RESULTS:** There were no significant difference between the two groups with respect to demographic data. we observed that the loss of consciousness (verbal contact) occurs earlier i.e. 29.60 sec in propofol-ketamine (group-1) as compared to propofol-fentanyl group i.e., 31.32 sec ( $p < 0.05$ ). The abolition of eyelash reflex occurs earlier with propofol-ketamine (group-1) i.e., 34.44 sec.

As compared to propofol-fentanyl (group-2) i.e., 34.84 sec but the difference is not found to be statistically significant ( $P > 0.05$ ) the time of awaking from anaesthesia was (highly significantly ( $P < 0.005$ ) earlier in case of propofol-fentanyl group (633.28 sec) as compared to propofol-ketamine group (847.48 sec).

## ORIGINAL ARTICLE

The analysis indicates the propofol-ketamine produces loss consciousness earlier than propofol-fentanyl when other variable were compared. This indicates that propofol-ketamine and propofol-fentanyl were equally efficacious when used for induction of anaesthesia in short Surgical Day Surgeries.

Pulse rate measured at 1, 5, 10, 15, 20 and 25 min after induction was significantly lower in group-II (propofol-fentanyl) as compared to group-1 (propofol-ketamine). The mean reduction in group-I was 4 beats per minutes in group-II; it was 9 beats per minutes.

Systolic blood pressure measured at 1, 5, 10, 15, 20 and 25 min was significantly lower in group-II (propofol-fentanyl) as compared to group-I (propofol-ketamine). The mean reduction in group-I was by about 9 mm of Hg SBP.SBP was decreased by about 22 mm of Hg in group-II (Table-I)

### SAFETY EVALUATION (Intraoperative period):

Time of Reading (min)	Group	Mean (mm of Hg)	t value	p value
0	I	127.36	1.23	>0.10
	II	130.72		
1	I	119.52	1.56	>0.05
	II	115.68		
5	I	118.32	3.81	<0.005
	II	109.2		
10	I	118.08	3.37	<0.005
	II	110.4		
15	I	121.76	3.66	<0.005
	II	113.92		
20	I	122.33	2.83	<0.01
	II	116.19		
25	I	123.22	1.92	>0.05
	II	118.23		

**Table 1: Systolic Blood Pressure (mm of Hg)**

Diastolic blood pressured measured at 1, 5, 10, 15, 20 and 25 min was significantly lower in group-II (propofol-fentanyl) as compared to group-I (propofol-ketamine). The mean reduction in group-I was by about 5 mm of Hg and by about 11 mm of Hg in group-II (Table-II).

### SAFETY EVALUATION (Intraoperative period):

Time of Reading (min)	Group	Mean (mm of Hg)	p value
0	I	81.6	>>0.10
	II	82.88	
1	I	79.92	<0.05
	II	75.84	
5	I	77.92	<0.0005
	II	71.44	

## ORIGINAL ARTICLE

10	I	78.56	<0.005
	II	72.16	
15	I	79.84	<0.0005
	II	73.52	
20	I	80.33	<0.0005
	II	74.19	
25	I	80.66	<0.0005
	II	75.64	

**Table 2: Diastolic Blood Pressure (mm of Hg):**

Respiratory rate measured at 1, 5, 10, 15, 20 and 25 was also significantly higher in group-I (propofol-ketamine) as compared to group-II (propofol-fentanyl). The mean reduction in group-I was by about 3 beats per minutes and in group-II by about 2 beats per minutes (Table-III).

### **SAFETY EVALUATION (Intraoperative period):**

Time of Reading (min)	Group	Mean (Br./ min)	t value	p value
0	I	19.16	0.903	>>0.10
	II	18.8		
1	I	18.32	3.06	<0.005
	II	17.0		
5	I	18.6	5.72	<0.0005
	II	16.36		
10	I	18.72	4.80	<0.0005
	II	16.72		
15	I	18.2	4.22	<0.0005
	II	16.64		
20	I	18.29	3.57	<0.005
	II	16.66		
25	I	18.44	4.21	<0.0005
	II	16.64		

**TABLE 3: Respiratory Rate (Breathes/ min.)**

About adverse effect 4 patients showed pain on injection in group-I (16%) as compared to 2 patients in group-II (8%). Incidence of Apnea was 16% (4 patients) in group-I and 20% (4 patients) in group-II.

5 patients showed abnormal movements in group-I (20%) as compared to 3 patients (12%) in group-II. This difference is statistically significantly nausea and vomiting was found to be equal in both the group i.e. 4% in each group, no case of hypersensitivity, bronchospasm, tachypnea, upper airway obstruction was reported in any group (Table-IV).

## ORIGINAL ARTICLE

Adverse effects	Group I (PK) (n=25)		Group II (n=25)	
	Present	Absent	Present	Absent
Pain on Injection	4 (16%)	21	2 (8%)	23
Allergy/ Hypersensitivity	-		-	
Apnea	4 (16%)	21	5 (20%)	20
Nausea/ Vomiting	1 (4%)	24	1 (4%)	24
Abnormal Movements	5 (20%)	20	3 (12%)	22
Bronchospasm	-	25	-	25
Hypoxia	-	25	-	25
Tachypnea	-	25	-	25
Upper Airway Obstruction	-	25	-	25

**TABLE 4: PRESENCE/ ABSENCE OF ADVERSE EFFECTS**

Recovery of the patients judged by modified Aldrete post anesthesia recovery score (MAPARS) system >9 score considered discharge from post anaesthesia care unit. The recovery time (by MAPARS) in group-I was longer than in group-II and the difference was statistically significant (Table-V).

MAPAR score >9 at_min	Group	Mean (min)	Standard Deviation	t value	p value	Inference
Recovery time (min)	I	22.84	2.21	2.67	<0.05	Significant Increase
	II	20.24	4.32			

**TABLE 5: RECOVERY (MIN) BY MAPARS**

Discharge criteria of the patients evaluated by modified post anaesthesia. Discharge scoring system, 4 patients (16%) in group-II (propofol-fentanyl) achieve fast track recovery within 25 minutes and none in group-I (propofol-ketamine), 17 patients in group-I (68%) achieved score > 9 at mean time of 40.52 min, and 18 patients in group-II (72%) achieved score >9 at mean time of 36.27 min.

It is clear from observation table that discharge is significantly earlier in group-II. Remaining 8 patients in group-I (32%) achieved score >9 at mean time of 58.12 min while remaining 3 patients in group-II (12%) achieved score > 9 at mean time of 53.66 min but the difference is insignificant in both groups (Table-VI).

Achievement of MPAD score >9 at_min.	Group	No of patients and %	Mean (min)	Standard Deviation	t value	p value	Inference
Fast track recovery	I II	0 4 (16%)	25				
Score >9 at 30-50 min	I II	17 (68%) 18 (72%)	40.52 36.27	4.82 4.90	2.58	<0.05	Significant Increase
Score >9 at 50-90 min	I II	8 (32%) 3 (12%)	58.12 53.66	5.79 1.15	2.07	>0.05	Insignificant increase

**TABLE 6: Discharge of patients (by MPADSS)**



## ORIGINAL ARTICLE

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**DISCUSSION:** Since last 20 years due to day care surgery. Slowly half of the surgeries are moved out of the hospital indoor setup. The increasing role of ambulatory surgery has emphasized the need for an anaesthetic technique with smooth induction, good intraoperative anaesthesia, rapid recovery with minimal side effects so that on early discharge is possible.

Propofol has an advantage for ambulatory anaesthesia in terms of rapid and reliable return of consciousness with minimal residual central nervous system effects.

Propofol is generally combined with an analgesic being either with fentanyl or propofol with Alfentanil ketamine in subanaesthetic doses with propofol has gained attention in total intravenous anaesthetic technique because of its powerful analgesic action in a small dose without causing myocardial and respiratory depression. Ketamine also causes some degree of sympathetic stimulation, which tends to counter balance, the cardiovascular effects of propofol.

This study titled "Comparative Evaluation of Propofol-Ketamine and Propofol-Fentanyl in Day Care Surgeries". Compared the characteristics of induction, homodynamic changes during induction and maintenance of anaesthesia, time until awakening, the incidence of complication/side effect, recovery and discharge of the patient.

The induction characteristics showed that the time to loss of consciousness (29.60 sec. in group-I vs. 31.32 sec in group-II) was significantly lesser in group-I (Propofol-Ketamine) as compared to group-II (Propofol-Fentanyl) other characteristics viz, time to loss of eyelash reflex showed no significant difference between the two groups. The induction of anaesthesia was smooth in both the groups with occasional instances of pain on injection of propofol (16% in Propofol-Ketamine and 8% in Propofol-Fentanyl group).

This leads to the conclusion that induction of anaesthesia is comparable with Propofol-Ketamine and Propofol-Fentanyl and both are equally efficacious in inducing general anaesthesia. Our study in contrast with studies done by Cockshott JD et al. (1985)<sup>6</sup> found that induction with propofol occur in 27.1+7.0 sec and another study done by Mackenzie et al. (1985)<sup>7</sup> found that induction with propofol occurs in one arm-brain circulation time, mean induction time of propofol was found 30.6 sec in both the groups, there was a fall in pulse rate.

It may be due to myocardial depressant action of propofol. But the fall in Propofol-Fentanyl group as significant at 1, 5, 10, 15, 20 and 25 min after induction this difference may be due to sympathomimetic activity of ketamine which acts to counter act the myocardial depressant action of propofol.

In both the groups, there was fall in both systolic blood pressure and diastolic blood pressure. But the fall in both SBP and DPB was significant in Propofol-Fentanyl group as compared to Propofol-Ketamine group. The mean reduction in Propofol-Ketamine group was by about 9 mm of Hg of SBP and by about 7 mm of Hg of DBP whereas reduction in Propofol-Fentanyl group was by about 22 mm Hg of SBP and 12 mm Hg of DBP. This difference is statistically significant.

This can be explained by sympathomimetic activity of ketamine, which act to counteract the cardiovascular depressant action of propofol. our study is contrast with studies done by Rolly et al. (1985) and Mc Callan et al. (1986)<sup>8</sup> in their study found that there was a fall in blood pressure initially when propofol was used as an inducing agents.

This was followed by a gradual increases pretreatment values. Hernandez et al. (1999)<sup>9</sup> in their comparative study between propofol-ketamine and propofol-fentanyl found that hemodynamic variables were more stable in propofol-ketamine group than propofol-fentanyl group.

## ORIGINAL ARTICLE

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To recovery characteristics and side effects of our study, the last dose of propofol was administered about 10 to 15 min before the anticipated time of end of surgery. After the last dose, the time of awakening was similar between the two groups.

All patients responded to verbal commands satisfactorily. No patients experienced hallucinations in either group. Although the psychomimetic effects of ketamine are not completely prevented by propofol, these effects were not very severe in the propofol-ketamine group. The incidence of PONV was similar in both the groups (4% in each group).

These finding correlate well with Matsumoto H. et al. (1998)<sup>10</sup> who compared effects of propofol-fentanyl and thiopentone-sevoflurane anesthesia in the recovery phase. They concluded that the propofol-fentanyl group showed significantly shorter time for response to verbal commands (7.5+5.6 min) and orientation (13.1+7.8 min) than thiopentone-sevoflurane group. The incidence of PONV was also significantly lower in propofol-fentanyl group (3.7%).

After injection of propofol, apnea was noted in 16% cases of propofol-ketamine group and 20% cases of propofol-fentanyl group Apnoea may be due to central respiratory depressant action of propofol. This coincides well with the findings of Taylor et al. (1986) and Ground et al. (1987), who found 19.2% incidence of apnea in patients who were administered propofol and Drascovic B. et al. (1998) in his study on TIVA using propofol-fentanyl in children found that the incidence of apnea was 25% after propofol injection. No cases of allergy or hypersensitivity were reported from either groups.

In discharge criteria 68% patients in group-I (17 patients) achieved score > 9 at mean time of 40.52 min, and 72% patients in group-II (18 patients) achieved score > 9 at mean time of 36.27 min, so that discharge is significantly earlier in group-II.

Overall, it may be concluded that propofol-ketamine combination is as safe as and efficacious as propofol-fentanyl combination in both induction and recovery characteristics in short surgical procedures. However, due to haemodynamic stability provided by propofol-ketamine it is on appropriate choice when haemodynamic stability is of great importance. As a recovery points of view the propofol-fentanyl combination is a better choice as a day care intravenous anaesthetics.

**CONCLUSION:** The safe, expeditious conduct of ambulatory surgical care can succeed only by careful selection of patients and procedure, appropriate intra and post-operative anaesthetic management, safe and timely discharge of patients. Discharge of patients should be achieved without compromising the quality of patient care.

It may be concluded from the present study that propofol-ketamine combination is as efficacious as more commonly used propofol-fentanyl combination. Since propofol-ketamine produces better haemodynamic stability during anaesthesia, it is a better choice especially when haemodynamic stability is great importance.

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## ORIGINAL ARTICLE

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