ABSTRACT:
A prospective comparative study was carried out to evaluate haemodynamic and recovery status using infusion of propofol-midazolam-nalbuphine and ketamine-diazepam-tramadol in surgical day-cases. Fifty patients of either sex aged within 18-60 years ASA grade I or II requiring routine surgery as day-case basis under GA were selected in Dept of Anaesthesia, CMH, Dhaka during February-May 2006. Cases were randomly divided equally into two groups of 25 each. Group-A received propofol-midazolam-nalbuphine infusion and infusion of ketamine-diazepam-tramadol was used in Group-B for anaesthesia. Haemodynamic parameters, recovery status and home readiness time were monitored and recorded at 10 min intervals. The variations in heart rate, systolic and diastolic BP of both groups were found statistically insignificant (p-values: 0.0524, 0.0513 and 0.0575 respectively). Recovery scores were high in Group-A (p-0.0443) and time for home-readiness were found 242±35 (mean±SD) minutes in Group-A and 367±83 minutes in Group-B (p-0.0329). Drugs used in Group-B were found highly cost effective. It is concluded that by using ketamine, diazepam and tramadol combination (group-B), we can reduce the cost of anaesthesia, which is necessity for majority of patients in our country. On the other hand, propofol, midazolam and nalbuphine combination (group-A), a costlier regime appears suitable for the patients from affluent population. Both the regimes can be practiced with safety.

INTRODUCTION:
One of the most dramatic transformations in health care delivery in the recent past is shift from inpatient to outpatient surgery & associated day-case anaesthesia. The primary impetus for this change is the economic savings afforded by not admitting patients the night before surgery or keeping them in hospital the night after surgery. Other advantages of outpatient surgery include earlier ambulation, patient convenience, and a lessened risk of nosocomial infection. Many operations are performed at one-fifth cost of inpatient surgery if carried out on a day-case basis. Such type of day-case anaesthesia is only economical if it can be carried out safely. Optimum prerequisite for agents of day-case anaesthesia is early discharge & cost effectiveness. Problem is that none of the currently available anaesthetic agents have duration of action short enough to leave the patient with no residual effects within a few hours of surgery.

Comparison of anaesthetic technique to determine which is least likely to impair the patient’s postoperative mental and physical well-being requires the measurement of residual effects. Even when this is established, it is important to realise that each patient is an individual who will have a variable response to anaesthetic drugs. Thus, for each individual patient, it is necessary to assess the degree and quality of recovery from a particular anaesthetic technique. Recovery from intravenous anaesthetic agents is produced usually by the rapid redistribution of the drug from the brain into the other well-perfused tissues, viscera and particularly
muscles. Metabolisms of the drug, which mainly occur in the liver, also contribute to some extent to the recovery. A small proportion of the drug may be excreted unchanged through the kidneys. Aims of this study were to assess and compare haemodynamic and recovery status after infusion of propofol-midazolam-nalbuphine and ketamine-diazepam-tramadol in day-case anaesthesia, to evaluate and compare the speed of home readiness of the groups and to find out the cost effectiveness of two regimes.

MATERIALS AND METHODS:
With approval from the departmental ethical committee and after taking informed consent from patients, this prospective, comparative study was carried out in the Dept of Anaesthesia, CMH Dhaka. In this randomized study 50 patients of either sex of 18-60 years of age and ASA grade I or II were scheduled for routine surgery as day case basis under general anaesthesia. Exclusion criteria were: Obese and epileptic patients, Patients of psychological instability and on CNS depressants, anti-coagulants and steroids. Total 50 patients were divided randomly into 2 (two) equal groups (25 patients in each group): Group-A Patients received infusion of propofol, midazolam and nalbuphine and Group-B Patients received infusion of ketamine, diazepam and tramadol.

In the operating room, after establishment of i.v. line and recording of HR & BP (baseline parameters), patients were pre-oxygenated for 05 minutes before induction. In group-A patient Intubation was done by using propofol 2 mg/kg, vecuronium 0.1 mg/kg and was maintained by propofol10 mg/kg/hr for 1st 10 minutes, 08 mg/ kg/hr for next 10 mins and 06 mg/kg/hr thereafter, midazolam0.2 mg/kg/hr, nalbuphine15mg i.v. stat than 0.25-0.5 mg/kg at 30 minute interval. In group-B patient intubation was done by using ketamine 2 mg/kg, vecuronium 0.1 mg/kg and was maintained by ketamine50ig/kg/min, diazepam0.2 mg/kg i.v. stat, tramadol 100 mg i.v. stat than 20 mg/min up to cumulative dose of 01 mg/kg and thereafter 0.05 mg/kg/min. All patients ventilated with a mixture of 30% O2 in air with Bain circuit.

Patients' Heart rate and blood pressure (as recorded by non invasive monitoring) were noted during induction, one minute after intubation and at 10 minutes interval up to the reversal. After reversal recovery score were recorded adapting PADS scoring system (Post Anaesthesia Discharge Scoring system for determining home readiness) at 10 minutes interval until the patients responded to vocal command. After complete recovery, fitness to go home was assessed by adapting the following home readiness (Time in minutes) parameters at 10 minutes interval. The maximum score of home readiness is 10. Patients scoring e” 9 were considered fit for discharge. The time taken for home readiness was recorded. Data were analyzed by Students ‘t’ test and Chi-square test as appropriate. P value < 0.05 (CL-95%) was regarded as significant.

PADS system for determining home readiness parameters were:

Vital signs
Patient’s vital signs being stable and consistent with age and preoperative baseline
- BP and pulse : Within 20% of preoperative baseline - 2
- BP and pulse : 20-40% of preoperative baseline - 1
- BP and pulse : >40% of preoperative baseline - 0

Activity level
Patient’s ability to ambulate at pre operative level
- Steady gait, no dizziness or meets pre operative level - 2
- Requires assistance - 1
- Unable to ambulate - 0

Nausea and vomiting
The patient had minimal nausea and vomiting prior to discharge
- Minimal : Successfully treated with post operative medication - 2
- Moderate : Successfully treated with IM medication - 1
- Severe : Continue after repeated treatment - 0
Results:

Patient’s characteristics were comparable among the groups (Table-I). No significant difference was found in demographic characteristic except Height. Recovery score at different timing were comparable among the groups (Table-II). Significant recovery score was found among the groups. Time taken for fitness to go home was comparable among the groups (Table-V). Significant difference in Time taken for fitness to go home was found among two groups. Cost status of the agents used in different groups was comparable (Figure-2). Significant P<0.05 (among two groups) difference were found for cost of induction agents. Just after induction in group-B there were significant (considering 20% change from base line) increase in heart rate (Figer-1). Arterial pressure was statistically non significant among the groups. The ASA grade was 88% (n=22) : 12% (n=3) in group A and 92% (n=23) : 8% (n=2) in group B. The male female ratio was 76% (n=19):24% (n=6) in group A and 80% (n=20):20% (n=5) in group B.

Pain

The patient had minimal or no pain prior to discharge. The level of pain was acceptable to the patient.

• Acceptability: Yes - 2, No - 1

Surgical bleeding

Post operative bleeding was consistent with expected blood loss for procedure

• Minimal: Does not require dressing change - 2
• Moderate: Up to two dressing changes required - 1
• Severe: More than three dressing changes required - 0

Table-I

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Group A</th>
<th>Group B</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>27.20±3.14</td>
<td>25.95±3.80</td>
<td>0.064 ns</td>
</tr>
<tr>
<td>Body wt (kg)</td>
<td>63.80±4.37</td>
<td>61.50±3.46</td>
<td>0.052 ns</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>156.25±3.49</td>
<td>152.65±4.04</td>
<td>0.013 s</td>
</tr>
</tbody>
</table>

Values are expressed as mean±SD. ns- not significant; s- significant p <0.05, Analysis were done by ‘t’ test.
### Table II

**Recovery score in various timing (adapting SOCA scoring system)**

<table>
<thead>
<tr>
<th>Group</th>
<th>At reversal</th>
<th>Just after reversal</th>
<th>5 min</th>
<th>10 min</th>
<th>After 20 min</th>
<th>After 30 min</th>
<th>After 40 min</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group-A</td>
<td>5.98±2.01</td>
<td>6.00±3.43</td>
<td>7.02±9.72</td>
<td>7.28±6.23</td>
<td>8.86±8.54</td>
<td>9.5±2.89</td>
<td>9.99±4.93</td>
<td>0.0443s</td>
</tr>
<tr>
<td>Group-B</td>
<td>5.26±4.33</td>
<td>5.66±5.11</td>
<td>6.11±4.06</td>
<td>6.46±7.01</td>
<td>6.86±3.59</td>
<td>8.01±9.01</td>
<td>9.00±6.81</td>
<td></td>
</tr>
</tbody>
</table>

Values are expressed as mean±SD s: significant p<0.05 Analysis were done by ANOVA.

### Table III

**Per-operative systolic blood pressure variations**

<table>
<thead>
<tr>
<th>Group</th>
<th>Pre-op</th>
<th>At induction</th>
<th>At intubation</th>
<th>5 min</th>
<th>10 min</th>
<th>20 min</th>
<th>30 min</th>
<th>40 min</th>
<th>50 min</th>
<th>60 min</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group-A</td>
<td>112±10</td>
<td>102±8</td>
<td>121±12</td>
<td>115±9</td>
<td>116±15</td>
<td>114±8</td>
<td>117±20</td>
<td>115±10</td>
<td>116±14</td>
<td>116±4</td>
<td>0.0513ns</td>
</tr>
<tr>
<td>Group-B</td>
<td>118±8</td>
<td>122±9</td>
<td>134±9</td>
<td>128±10</td>
<td>123±13</td>
<td>127±11</td>
<td>132±12</td>
<td>126±5</td>
<td>129±15</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values are expressed as mean±SD ns: not significant p>0.05, Analysis were done by ANOVA test.

### Table IV

**Per-operative diastolic blood pressure variations**

<table>
<thead>
<tr>
<th>Group</th>
<th>Pre-op</th>
<th>At induction</th>
<th>At intubation</th>
<th>5 min</th>
<th>10 min</th>
<th>20 min</th>
<th>30 min</th>
<th>40 min</th>
<th>50 min</th>
<th>60 min</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group-A</td>
<td>74±11</td>
<td>72±3</td>
<td>82±10</td>
<td>78±8</td>
<td>75±2</td>
<td>70±3</td>
<td>75±5</td>
<td>77±11</td>
<td>71±10</td>
<td>74±3</td>
<td>0.0575ns</td>
</tr>
<tr>
<td>Group-B</td>
<td>73±4</td>
<td>91±7</td>
<td>93±9</td>
<td>88±5</td>
<td>89±12</td>
<td>82±10</td>
<td>87±7</td>
<td>90±4</td>
<td>88±5</td>
<td>86±11</td>
<td></td>
</tr>
</tbody>
</table>

Values are expressed as mean±SD ns: significant p>0.05, Analysis were done by ANOVA test.

### Table V

**Time required for Home readiness**

<table>
<thead>
<tr>
<th>Group</th>
<th>Time required for home readiness (min±SD)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group-A(n=25)</td>
<td>242±35</td>
<td></td>
</tr>
<tr>
<td>Group-B(n=25)</td>
<td>367±83</td>
<td>0.0329s</td>
</tr>
</tbody>
</table>

S: significant denotes p<0.05 Analysis were done by using Student’s ‘t’ test.

### DISCUSSION:

The results from the present study show that haemodynamical stability and recovery status (both per- and post-operatively) from group-A population (propofol, midazolam and nalbuphine infusion) were always satisfactory than that from group-B population (ketamine, diazepam and tramadol infusion). However, there was no clinically significant difference in arterial pressure among the groups.

Day-care treatment has come to stay and economic and social pressures dictate that it will expand in the future. Although the importance of patient selection cannot be overemphasized, anaesthetists and their pharmaceutical colleagues must adapt their skills to meet the challenges of providing safe, smooth anaesthesia followed by a rapid, pain free recovery.

At the inception of day-care procedures, a case was considered suitable if it took less than 90 min. Procedures that are commonly selected today are those taking less than 60 min and which do not...
cause severe haemorrhage or produce excessive postoperative pain\textsuperscript{5}.

Many operations are performed at one-fifth cost of inpatient surgery if carried out on a day-case basis\textsuperscript{2}. Such type of day-case anaesthesia is only economical if it can be carried out safely. Problem is that none of the currently available anaesthetic agents have duration of action short enough to leave the patient with no residual effects within a few hours of surgery\textsuperscript{3}. Propofol is having distribution and elimination half-lives of 1.2 minutes and 1-5 hours respectively and providing rapid recovery with minimal residual effects which is suitable for day-case anaesthesia\textsuperscript{20}. But high price of propofol is a hindrance to its use in day-case anaesthesia in our socioeconomic condition. On the other hand, though ketamine is much cheaper than propofol, but its elimination depends on the mixed-function oxidase system associated with the smooth endoplasmic reticulum. Its main metabolite, nor-ketamine has some hypnotic activity with a potency of around 30\% of that of the parent drug and a longer elimination half-life. Both ketamine and nor-ketamine may be metabolised further to hydroxylated derivatives. These are subsequently conjugated and eliminated in the urine as glucuronides. Hence the efficacy of ketamine may be enhanced in patients with renal impairment\textsuperscript{13-14}.

Nalbuphine is a potent semi-synthetic analgesic. It is equipotent with morphine and three to four times as potent as pentazocine. The opioid antagonist activity of nalbuphine is one-fourth as potent as nalorphine and 10 times that of pentazocine. It is an agonist at \(\epsilon\)-receptors, an antagonist at \(m\)-receptors and has no effects on \(\alpha\)-receptors\textsuperscript{12}. Analgesic tolerance is uncommon and nalbuphine has low abuse potential. Devoid or much less respiratory depression property makes the drug as one of the popular choice for maintaining analgesia in the day-case surgery. On the other hand, good results have been published for cancer pain management with tramadol in several studies. Tramadol can be recommended as a safe and efficient drug for step II according to the World Health Organisation guidelines\textsuperscript{21}.

Optimum prerequisite for agents of day-case anaesthesia is early discharge & cost effectiveness. Extrapolation of our data suggests that there is significant difference (\(p<0.05\)) between the two study groups of observation (propofol-midazolam-nalbuphine and ketamine-diazepam-tramadol) in day-case anaesthesia.

Postoperative complications like airway obstruction, hypoxia, and hypoventilation are quite common in the recovery period\textsuperscript{2}. Many of the death occur in the postoperative ward due to inadequate recovery from anaesthesia\textsuperscript{2}. To reduce mortality and morbidity due to inadequate recovery, various recovery scoring systems are used namely SOCA, modified Steward Coma scale, ABC score, clinical scoring system etc\textsuperscript{23,24,25,19}. Many workers have compared various recovery scoring system. In this study, it is tried to compare the haemodynamic and recovery status in day-case anaesthesia between infusion of propofol, midazolam, nalbuphine and ketamine, diazepam, tramadol. Recovery time and quality varies with the techniques used and the recovery time was recorded as per SOCA\textsuperscript{23} recovery scoring system and home readiness time was recorded as per clinical scoring system\textsuperscript{19}.

The characteristic of the population among the two groups of this study was same. Immediately after reversal, the recovery time is significant (\(p<0.05\)) between the two groups of observation (group-A and group-B). In group-A (propofol, midazolam and nalbuphine) patients, the cardiovascular parameters remained stable and there was no respiratory and cardiovascular depression. Blood pressure and heart rate were not changed remarkably during induction, intubation, maintenance and after recovery on all reading points, i.e. immediately after reversal. The recovery is slightly prolonged in group-B (ketamine, diazepam and tramadol) than group-A and the difference is significant (\(p<0.05\)).

The difference between preoperative and after reversal mean value of SBP, DBP, HR is significant (\(p<0.05\)) in group-A and group-B patients. But the differences between in group-A and group-B patients of same values and at the same point are significant in initial 5-6 reading points. Those were not significant in later half of the study.

Recovery from group-A population is slightly better than that of group-B in terms of cardiovascular stability, its recovery time as expected with clear-headed recovery. The time for home readiness is less in case of group-A (mean time 242±35 minutes) than that with group-B (mean time 367±83 minutes). But if the cost is considered, then the
agents of the later group (group-B) are much more economic than the agents of group-A. The extended time that is required for home readiness in group-B is not that much lengthier.

In the LDC countries like Bangladesh with low economic status, cost of drugs is a matter of consideration during operative procedures. Though, group–A agents are proved to be good for day case anaesthesia regarding its recovery criteria/profile, its cost is very much higher (almost 05 times) than that of group–B agents. In our study, it was found that the price of the agents used for per person in group-A was taka 868.00 and the price of the agents used in group-B was taka 168.00 for each patient i.e. 18.894% of group-A.

CONCLUSION:
In conclusion, it would appear that there could be substantial clinical and financial benefits in developing a day case surgery unit. From this study it may be concluded that haemodynamical stability and recovery status (both per- and post-operatively) from group-A population (propofol, midazolam and nalbuphine infusion) were always satisfactory than that from group-B population (ketamine, diazepam and tramadol infusion). Group-A drug regime ensures clear-headed recovery at a higher cost while recovery score with group-B drug regime is not too far at a much lower cost. Regarding the discharge criteria, it is almost same in two groups. By using ketamine, diazepam and tramadol combination (group-B), we can reduce the cost of anaesthesia, which is necessity for majority of patients in our country. On the other hand, propofol, midazolam and nalbuphine combination (group-A), a costlier regime appears suitable for the patients from affluent population. Both the regimes can be practiced with safety.

REFERENCES:


