**RESULTS**

 One hundred and twenty patients were randomly allocated into three equal groups (each 40 patient); group Ι (propofol TIVA), group ΙΙ (propofol-ketamine TIVA) and group ΙΙΙ (isoflurane inhalational anaesthesia). Each group was divided into two equal subgroups (each 20 patient); subgroups A (ΙA & ΙΙA & ΙΙΙA), where the hypnotic drug concentration (propofol or isoflurane) was adjusted to keep the BIS between 40 and 60 during surgery, and subgroups B (ΙB & ΙΙB & ΙΙΙB), where the hypnotic drug concentration was adjusted according to the standard clinical practice.

***Demographic data:***

There were no significant statistical differences between subgroup IA and subgroup IB as regard age ,sex ,weight and the durations of anaesthesia.

**Table(7-1):** **Demographic characteristics in propofol subgroups (IA&IB )**

|  | **N** | **Mean** | **Std. Deviation** | **t** | **P** |
| --- | --- | --- | --- | --- | --- |
| **Age (**years**)** | ***Subgroup IA*** | **20** | **42.80** | **10.606** | **1.3** | **>0.05** |
| ***Subgroup IB*** | **20** | **37.90** | **12.794** |
| **Wt (**Kg**)** | ***Subgroup IA*** | **20** | **76.75** | **7.656** | **1.2** | **>0.05** |
| ***Subgroup IB*** | **20** | **73.20** | **10.788** |
| **Duration of anaesthesia (**Min**)** | ***Subgroup IA*** | **20** | **60.00** | **18.445** | **0.1** | **>0.05** |
| ***Subgroup IB*** | **20** | **59.50** | **17.695** |
| **Sex (**male **:** female**)** | ***Subgroup IA*** | **11:9** | **X2** | **P** |
| ***Subgroup IB*** | **10:10** | **0.1** | **>0.05** |

There were no significant statistical differences between subgroup ΙΙA and subgroup ΙΙB as regard age ,sex ,weight and the durations of anaesthesia.

**Table(7-2):Demographic characteristics in propofol-ketamine subgroups (IIA &IIB)**

|  | **N** | **Mean** | **Std. Deviation** | **t** | **P** |
| --- | --- | --- | --- | --- | --- |
| **Age**(years) | ***Subgroup IIA*** | **20** | **39.35** | **11.389** | **---** | **----** |
| ***Subgroup IIB*** | **20** | **39.35** | **11.226** |
| **Wt**(Kg) | ***Subgroup IIA*** | **20** | **74.50** | **9.720** | **0.2** | **>0.05** |
| ***Subgroup IIB*** | **20** | **75.00** | **9.177** |
| **Duration of anaesthesia**(Min) | ***Subgroup IIA*** | **20** | **56.75** | **16.667** | **0.1** | **>0.05** |
| ***Subgroup IIB*** | **20** | **56.55** | **17.813** |
| **Sex** (male **:** female) | ***Subgroup IIA*** | **12:8** | **X2** | **P** |
| ***Subgroup IIB*** | **11:9** | **0.1** | **>0.05** |

 Also,there were no significant statistical differences between subgroup ΙΙΙA and subgroup ΙΙΙB as regard age, sex, weight and the durations of anaesthesia.

**Table(7-3):Demographic characteristics in isoflurane subgroups (IIIA &IIIB )**

|  | **N** | **Mean** | **Std. Deviation** | **t** | **P** |
| --- | --- | --- | --- | --- | --- |
| **Age (**years**)** | ***Subgroup IIIA*** | **20** | **39.75** | **11.986** | **0.3** | **>0.05** |
| ***Subgroup IIIB*** | **20** | **40.70** | **10.687** |
| **Wt (**Kg**)** | ***Subgroup IIIA*** | **20** | **73.25** | **9.358** | **0.6** | **>0.05** |
| ***Subgroup IIIB*** | **20** | **71.50** | **10.013** |
| **Duration of anaesthesia(**Min**)** | ***Subgroup IIIA*** | **20** | **59.05** | **18.426** | **0.2** | **>0.05** |
| ***Subgroup IIIB*** | **20** | **57.80** | **17.573** |
| **Sex (**male **:** female**)** | ***Subgroup IIIA*** | **9:11** | **X2** | **P** |
| ***Subgroup IIIB*** | **13:7** | **1.6** | **>0.05** |

***Anaesthetic drug consumption:***

 A highly significant reduction (**36.1%)** in propofol infusion rate was found in BIS-guided propofol subgroup (ΙA) compared to propofol subgroupΙB (without BIS) [(***8.3*** ± *0****.81***) vs (***11.3*** ± *0****.89***)mg/kg/h, *P < 0.001*].Also there was a high significant reduction (**30.9%)** in propofol infusion rate in BIS- guided propofol-ketamine subgroup ΙΙA compared to propofol-ketamine subgroup ΙΙB (without BIS) [(***7.15*** ± *0****.62***) vs (***9.26*** ± *0****.61***)mg/kg/h, *P < 0.001*].

 There was statistically high significant reduction (**36.8%**) in end tidal isoflurane concentration in BIS-guided subgroup (ΙΙΙA) compared to subgroupΙΙΙB(without BIS) [(*0****.95***± *0****.14***) vs (***1.27***± *0****.25***) **%** , *P < 0.001*].

**Table(8-1): Different subgroups according to the consumption of anaesthetics:**

| **Anaesthetic****drugs** | ***Subgroups*** | **N** | **Mean** | **Std. Deviation** | **t** | **p** | **% change** |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Propofol**(mg/kg/h)  | ***Subgroup IA*** | **20** | **8.2970** | **.80963** | **11.3** | **<0.001** | **36.1%** |
| ***Subgroup IB*** | **20** | **11.3390** | **.88804** |
| ***Subgroup IIA*** | **20** | **7.1470** | **.62294** | **10.9** | **<0.001** | **30.9%** |
| ***Subgroup IIB*** | **20** | **9.2620** | **.60974** |
| **Isoflurane**end-tidal concentration(%)  | ***Subgroup IIIA*** | **20** | **.9525** | **.13969** | **4.9** | **<0.001** | **36.8%** |
| ***Subgroup IIIB*** | **20** | **1.2700** | **.25288** |

 The mean(SD) propofol infusion rate in BIS-guided propofol-ketamine subgroup ΙΙA was lower (**16.9%** ) than in BIS-guided propofol subgroup ΙA [(***7.15*** ± *0****.62***)vs (***8.3*** ± *0****.81***)mg/kg/h, *P < 0.001*] .Also , the mean(SD) propofol infusion rate in propofol-ketamine subgroup ΙΙB(without BIS) was significantly lower (**21.5%**) than in propofol subgroup ΙB(without BIS) [(*9****.26*** ± *0****.61***) vs (***11.3*** ± *0****.89***)mg/kg/h, *P < 0.001*]. So there was a reduction in propofol consumption in group ΙΙ (propofol-ketamine) than in group Ι (propofol), which is statistically highly significant *(P < 0.001)*.

**Table (8-2): Propofol infusion rates in group I &II.**

|  | **N** | **Mean** | **Std. Deviation** | **t** | **p** | **% change** |
| --- | --- | --- | --- | --- | --- | --- |
| **Propofol**(mg/kg/h)  | ***Subgroup IA*** | **20** | **8.2970** | **.80963** | **5.4** | **<0.001** | **16.9%** |
| ***Subgroup IIA*** | **20** | **7.1470** | **.62294** |
| ***Subgroup IB*** | **20** | **11.3390** | **.88804** | **8.3** | **<0.001** | **21.5%** |
| ***Subgroup IIB*** | **20** | **9.2620** | **.60974** |

**Fig. (28):** **Propofol infusion rates in group I&II.**

**Fig. (29): Isoflurane end-tidal concentration in group III.**

***Hemodynamics:***

In propofol group ( Ι ), mean arterial pressure (MAP) in subgroup A (with BIS ) was higher than in subgroup B (without BIS) (***85.61*** vs ***78.09*** mmHg , *P < 0.001*). Also the heart rate (HR) in subgroup A was higher than in subgroup B (***74.32*** vs ***68.85*** bpm, *P* *< 0.001*), which is statistically highly significant *( P < 0.001)*.

In propofol-ketamine group (ΙΙ), MAP in subgroup A (with BIS) was highly significantly lower than in subgroup B (without BIS) (***92.61*** vs ***98.16*** mmHg , *P* *< 0.001*). While HR was insignificantly lower in subgroup A than in subgroup B (***85.82*** vs ***87.44*** bpm,  *P* *> 0.05* ).

In isoflurane group (ΙΙΙ), MAP in subgroup A (with BIS) was significantly higher than in subgroup B (without BIS) (***90.86*** vs ***86.90*** mmHg , *P* *< 0.001*). While HR was significantly lower in subgroup A than subgroup B (***76.38*** vs ***86.44*** bpm , *P* *< 0.001*), which is statistically highly significant *( P < 0.001)*.

Among the BIS subgroups (ΙA , ΙΙA , ΙΙΙA) propofol subgroup ( ΙA ) had the lowest MAP and HR.

 **Fig.(30): Different subgroups according to the mean arterial blood pressure(MAP).**

**Fig.(31): Different subgroups according to the heart rate (HR).**

***Recovery profiles:***

 Spontaneous breathing times were significantly shorter in BIS subgroups (ΙA , ΙΙA , ΙΙΙA) (***2.04 , 4.08 , 1.14*** min.) than in subgroups without aid of BIS information (ΙB , ΙΙB , ΙΙΙB) ( ***4.95 , 6.01, 6.41*** min.) respectively, which is statistically highly significant (*P value < 0.001*) ,with the shortest time being in isoflurane subgroup IIΙA(with BIS ) .

 Extubation times were significantly shorter in BIS subgroups (ΙA, ΙΙA, ΙΙΙA) (***5.05, 6.995 , 2.63*** min.) than in subgroups without aid of BIS (ΙB , ΙΙB , ΙΙΙB) ( ***7.02 , 9.98 , 9.05*** min.) respectively, which is statistically highly significant (*P value < 0.001*),with the shortest time being in isoflurane subgroup IIΙA(with BIS).

 Times to obey commands (eye opening to verbal command) were significantly shorter in BIS subgroups (ΙA , ΙΙA , ΙΙΙA) (***8 , 12.55 , 6.24*** min.) than in subgroups without aid of BIS (ΙB , ΙΙB , ΙΙΙB) ( ***9.93 , 15.65, 16.13*** min.) respectively, which is statistically highly significant (*P value < 0.001*) ,with the shortest time being in isoflurane subgroup IIΙA(with BIS).

 Times to achieve a modified Aldrete score ≥ 9, were significantly shorter in BIS subgroups (ΙA , ΙΙA , ΙΙΙA) (***11.29 , 17.2 , 10.35*** min.) than in subgroups without aid of BIS (ΙB , ΙΙB , ΙΙΙB) ( ***14.41 , 21.35 , 19.90*** min.) respectively, which is statistically highly significant (*P value < 0.001*), with the shortest time being in isoflurane subgroup IIΙA (with BIS ) .

 All recovery times were determined at one-minute intervals from discontinuation of anaesthetics.

**Table(9):Recovery profiles in propofol group I (IA & IB)**

| **Recovery times (min)** | **Subgroup IA** | **Subgroup IB** | **t** | **p** |
| --- | --- | --- | --- | --- |
| Spontaneous breathing | 2.04±0.48 | 4.95±1.26 | 9.6 | <0.001 |
| Extubation | 5.05±0.69 | 7.02±0.76 | 8.6 | <0.001 |
| Obey commands | 8±0.84 | 9.93±1.26 | 5.7 | <0.001 |
| Modified Aldrete**≥**9 | 11.29±1.17 | 14.41±1.28 | 8.1 | <0.001 |

**Fig. (32):Recovery profiles in propofol group I (IA & IB).**

**Table(10):Recovery profiles in propofol-ketamine group II(IIA &IIB)**

| **Recovery times** | **Subgroup IIA** | **Subgroup IIB** | **t** | **p** |
| --- | --- | --- | --- | --- |
| Spontaneous breathing | 4.075±1.12 | 6.005±0.69 | 6.6 | <0.001 |
| Extubation | 6.995±0.77 | 9.975±0.9 | 11.2 | <0.001 |
| Obey commands | 12.55±1.77 | 15.65±1.78 | 5.5 | <0.001 |
| Modified Aldrete**≥**9 | 17.2±1.37 | 21.35±1.98 | 7.7 | <0.001 |

**Fig. (33):Recovery profiles in propofol-ketamine group II(IIA &IIB).**

**Table(11):Recovery profiles in isoflurane group ΙΙΙ (ΙΙΙA & ΙΙΙB).**

| **Recovery times** | **Subgroup IIIA** | **Subgroup IIIB** | **t** | **p** |
| --- | --- | --- | --- | --- |
| Spontaneous breathing | 1.14±0.44 | 6.41±0.74 | 27.4 | <0.001 |
| Extubation | 2.63±0.69 | 9.05±1.11 | 22.01 | <0.001 |
| Obey commands | 6.24±0.85 | 16.13±1.7 | 22.9 | <0.001 |
| Modified Aldrete**≥**9 | 10.35±1.06 | 19.9±2.62 | 15.1 | <0.001 |

**Fig. (34):Recovery profiles in isoflurane group ΙΙΙ (ΙΙΙA & ΙΙΙB).**

**Table(12):Recovery profiles in BIS-guided subgroups( ΙA & ΙΙA &ΙΙΙA )**

| **Recovery times** | **Subgroup IA** | **Subgroup IIA** | **Subgroup IIIA** | **f** | **P** |
| --- | --- | --- | --- | --- | --- |
| Spontaneous breathing | 2.04±0.48 | 4.08±1.12 | 1.14±0.44 | 81.3 | <0.001 |
| Extubation | 5.05±0.69 | 6.995±0.77 | 2.63±0.69 | 188.5 | <0.001 |
| Obey commands | 8±0.84 | 1.77±12.6 | 0.85±6.24 | 139.6 | <0.001 |
| Modified Aldrete**≥**9 | 1.17±11.29 | 17.2±1.37 | 10.35±1.06 | 190.2 | <0.001 |

**Fig. (35):Recovery profiles in BIS-guided subgroups( ΙA & ΙΙA &ΙΙΙA ).**

***Awareness:***

 Patients were questioned for recall of events, hearing vague sounds, feeling surgical instruments or dressing application, or dreaming, and we did not encounter any case of operation-related recall (awareness), in either subgroups.

***Postoperative complications:***

The incidence of postoperative nausea and vomiting in the first 24 h postoperatively , was lower in BIS subgroups; ΙA (***n= 1, 5%***) & ΙΙA (***n= 0,* *0%***) & ΙΙΙA (***n= 4, 20%***) than in subgroups without aid of BIS; ΙB (***n= 3,* *15%***) & ΙΙB(***n= 2,* *10%***) &ΙΙΙB (***n= 7,* *35%***) respectively, but these results did not reach a statistically significant value (*P value > 0.05*).The least incidence being in propofol-ketamine subgroup ΙΙA(with BIS) ,and the highest incidence being in isoflurane subgroup ΙΙΙB (without BIS). None of the patients of all six subgroups had experienced any hallucinations.

**Table (13): Different subgroups according to the postoperative data**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | ***IA****(N=20)* | ***IB****(N=20)* | ***IIA****(N=20)* | ***IIB****(N=20)* | ***IIIA****(N=20)* | ***IIIB****(N=20)* |
| ***Awareness*** | **0** | **0** | **0** | **0** | **0** | **0** |
| ***PONV*** | **1 (5%)** | **3 (15%)** | **0 (0%)** | **2 (10%)** | **4 (20%)** | **7 (35%)** |
| ***Hallucination*** | **0** | **0** | **0** | **0** | **0** | **0** |