

7. Jacobsen D.W. Homocysteine and vitamins in cardiovascular disease // Clin. Chemistry. – 1998. – № 44. – P. 1833-1843.
8. Preston R.A., Ledford M., Materson B.J. et al. Effects of severe, uncontrolled hypertension on endothelial activation: soluble vascular cell adhesion molecule-1, soluble intercellular adhesion molecule-1 and von Willebrand factor // J. Hypertens. - 2002. - Vol.20, N5. - P.871-877.
9. Rodrigo R., Passalacqua W., Araya J. et al. Implications of oxidative stress and homocysteine in the pathophysiology of essential hypertension // J. Cardiovasc. Pharmacol.- 2003. - Vol.42, N4. - P.453-461.
10. Saito Y., Kurabayashi M., Nakamura T. et al. Involvement of homocysteine in the pathogenesis of hypertension and hypertensive target-organ damage // Nippon Rinsho.- 2004.- Vol.62.- Suppl 3. - P.211-215.
11. Spencer C.G., Martin S.C., Felmeden D.C. et al. Relationship of homocysteine to markers of platelet and endothelial activation in "high risk" hypertensives: a substudy of the Anglo-Scandinavian Cardiac Outcomes Trial // Int. J. Cardiol.- 2004.- Vol.94, N2-3. - P.293-300.
12. van Guldener C., Nanayakkara P.W., Stehouwer C.D. Homocysteine and blood pressure // Curr. Hypertens, Rep.- 2003.- Vol.5,N1. - P.26-31.

### INTERRELATIONSHIP OF MARKERS OF THE ENDOTHELIUM FUNCTION WITH THE MORPHOFUNCTIONAL CONDITION OF THE CARDIOVASCULAR RISK IN PATIENTS WITH ESSENTIAL HYPERTENSION

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**Abstract.** For the purpose of evaluating the level of the markers of the endothelial function (EF) in patients with essential hypertension (EH), correlations between the indices of diurnal monitoring of blood pressure (DMBP), echocardiography (ECG), the functional condition of the endothelium and the degree of total cardio-vascular risk (CVR) 94 persons with EH of stages II-III aged from 30 to 73 years (the average age – 51.4±7.6 years, 54 men and 40 women) and 30 apparently healthy persons were examined and compared with the sex and age (the control group). The authors disclosed a reliable ( $p<0.05$ ) decline of endothelium-dependent vasodilatation (EDVD) of the brachial artery (BA) (5.15±3.6 versus 12.05±3.8%), a blood rise of the homocysteine (HC) levels (15.75±3.64 versus 10.62±2.02 mkmol/l), soluble vascular cell adhesion molecule-1 (sVCAM-1) (1054±145 vs 799±124 ng/ml), the activity of von Willebrand factor (vWf) (139±25,0 vs 104±9,8%), a correlation of HC content with the indices of DMBP and the association of the circadian pattern of blood pressure of the «nondipper» and «nightpeacker»-status with an elevated blood HC level.

**Key words:** essential hypertension, endothelial dysfunction, homocysteine, von Willebrand factor, soluble vascular cell adhesion molecule-1.

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### IMPULSIVENESS MODIFIES THE EFFECT OF MIDAZOLAM IN PREMEDICATION OF CHILDREN

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**Abstract.** It is assumed that impulsiveness may influence the effect of midazolam. Therefore we compared the level of sedation after premedication with midazolam in children with high and low levels of impulsiveness. To determine the degree of impulsiveness 93 boys were examined one day prior to surgery. Three methods were used: a self-rating scale, a rating scale and a computerized behaviour-reactivity test. Impulsiveness was defined as high scores in each of the three indicators (n=6). The control group consisted of children with low scores in all three indicators (n=30). Indicators for sedation were: a self-rating visual analog scale, a rating scale and the bispectral index. Sedation following the ad-

ministration of midazolam was measured on the day of surgery 25 minutes after the drug administration. After the application of midazolam the bispectral index demonstrated equal levels of the cerebral activity in both groups. Scores from the rating scale and self rating scale showed that children with a high level of impulsiveness became less sedated than children with a low level of impulsiveness. We conclude that the sedating effect of midazolam in premedication depends on the level of impulsiveness and this should be taken into account in preanesthetic preparation.

**Keywords:** impulsiveness, midazolam, premedication, rating scale, bispectral index.

**Introduction.** An important goal of premedication prior to surgery is to provide sedation, anxiolysis and reduction of emotional stress. Midazolam is a

popular agent for this purpose in pediatric patients because of its rapid onset and relatively short duration of action. However, it is reported that effects of

Table

Effects of midazolam in children differing in impulsiveness (M±SD)

Assessment of sedation / scale	Time	High impulsiveness (n=6)	Low impulsiveness (n=30)	P-value (U-test)
Awakeness (self rating scale)	5 minutes before midazolam	83.5±19.5	79.4±28.4	0.73
	25 minutes after midazolam	51.8±35.2	35.6±32.4	0.10
Awakeness (rating scale)	5 minutes before midazolam	0.19±0.17	0.13±0.28	0.10
	25 minutes after midazolam	0.50±0.53	0.10±0.15	0.005
Bispectral index	25 minutes after midazolam	88.4±10.0	87.7±9.4	0.44

Note. p-value is one-tailed for measurements 25 minutes after drug application

psychotropic drugs like midazolam are modified by the personality trait impulsivity [1,5]. In particular this is reported for children, suffering from the attention deficit disorder where impulsiveness is a leading symptom. The prevalence of impulsiveness in large populations may be up to ten percent in boys.

**The aim.** The aim of our study is to compare reactions to midazolam in a normal sample of children prior to surgery who differ in their degree of impulsiveness.

**Material and methods.** After ethics committee approval and written informed consent given by the parents, we recruited 93 boys (aged 5-14 years) requiring surgical procedures under general anesthesia. The children were premedicated using midazolam (oral 0.18 mg/kg or rectal 0.36 mg/kg) in the ward one hour prior to the operation. We choose three validated methods to determine impulsiveness on the day prior to surgery [3,6].

1. A self-rating scale using the German version, of Eysenck's impulsivity scale.
2. A rating scale assessing impulsiveness by the parents (Stadler and Janke).
3. A computerized behaviour-reactivity test using a go/no-go task.

Three methods were used to determine sedation:

1. A self-rating visual analog scale with the range 0 (totally tied) to 100 (totally awoken) was taken 5 minutes before and 25 minutes after application of midazolam.
2. A rating scale assessing impulsiveness by the physician (Conners' Teachers Rating Scale) was taken 5 minutes before and 25 after application of midazolam.
3. The bispectral index (BIS) was taken 25 minutes after administration of midazolam. BIS is a well validated electrophysiological method for measuring sedation [2,4].

**Results and discussion.** Impulsiveness was statistically defined as high scores (upper third in each of the three impulsiveness indicators (n=6)). The control group included children with low scores (lower third) in all three impulsiveness indicators (n=30). A classification of impulsiveness was carried out after finishing the study. Therefore during the study the physician did not know the group a child belongs to. The two groups were similar with respect to age (p=0.47), weight (p=0.69), dose of midazolam (p=0.63), drug administration (p=0.43) school level (p=0.61) and school grade (p=0.61).

The hypothesis is that sedation after administration of midazolam is less in children with high impulsiveness. The results concerning the data in the hypothesis are summarized in the table below.

Before the application of midazolam the self-rating scale shows a similar level of sedation. In the rating scale children with a high level of impulsiveness tend to show a higher level of awokeness (p=0.10). 25 minutes after the application of midazolam both groups show a similar level of the cerebral activity. In contrast to these equal cerebral activity levels groups differ in sedation rating at this point of measurement with respect to impulsivity. Children with a high level of impulsiveness were rated more awoken than children with a lower level of impulsiveness (p=0.005) and they described themselves as being less tied (p=0.10).

#### Conclusion

1. Equal doses of midazolam create a similar level of the cerebral activity in both impulsive and non-impulsive children as measured by the bispectral index. These electrophysiological similar groups differ strongly with respect to the rated sedation state.

2. Preoperative sedation with midazolam produces less sedated children with impulsive characteristics than a control group when judged by a parental rating scale. A marginal significant difference was also noted using the self-rating scale. Both of these support our hypothesis. We conclude that the sedative effect of midazolam is modified by impulsiveness and that this modification can even be demonstrated in a sample of normal boys differing in impulsiveness.

#### References

1. Bond A.J. Drug-induced behavioral disinhibition: incidence, mechanisms and therapeutic implications // *CNS-Drugs*. – 1998. – N9. – P. 41-57.
2. Brosius K.K., Bannister C.F. Oral midazolam premedication in preadolescents and adolescents // *Anesth. Analg.* – 2002. – V. 94. – P. 31-36.
3. Fantuzzo J., Grim S., Mordell M. et al. A multivariate analysis of the revised Conners' Teacher Rating Scale with low-income, urban preschool children // *J. Abnorm. Child Psychol.* – 2001. – V.29. – P. 141-152.
4. Kussman B.D., Gruber E.M., Zurakowski D. et al. Bispectral index monitoring during infant cardiac surgery: relationship of BIS to the stress

- response and plasma fentanyl levels // Paediatr. Anaesth. – 2001. - N11. –P. 663-669.
5. Massanari M., Novitsky J., Reinstein L.J. Paradoxical reactions in children associated with midazolam use during endoscopy // Clin. Pediatr. (Phila.). – 1997. – V.36. –P.681-684.
6. Stadler C. Impulsives Verhalten bei Kindern: Entwicklung von Methoden und Ansätze zur Validierung im Feld und im Labor // Marburg: Tectum Verlag, 2000. – 443 p.

## ВПЛИВ ІМПУЛЬСИВНОСТІ НА ДІЮ МІДАЗОЛАМУ ПІД ЧАС ПРЕМЕДИКАЦІЇ У ДІТЕЙ

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**Резюме.** Вважається що імпульсивність дитини може впливати на ефект мідазоламу. У роботі ми порівняли рівень анестезії після премедикації мідазоламом у дітей із високим та низьким рівнем імпульсивності. Обстеження на рівень імпульсивності проводилося в 93 хлопчиків за день до оперативного втручання. Для визначення імпульсивності використовувалися три методики: шкала самооцінки, шкала лікарської оцінки та комп'ютерний тест. У подальшому відібрано 36 пацієнтів: до групи з високою імпульсивністю віднесені діти з високими показниками за кожною із методик (n=6), контрольну групу склали діти з низькими показниками (n=30). Критерії рівня седатції: самооцінка за візуальною аналоговою шкалою, лікарська оцінка та біспектральний індекс. Рівень седатції після введення мідазоламу визначався у день операції через 25 хвилин після введення препарату. Після премедикації біспектральний індекс вказував на однаковий рівень церебральної активності в обох групах. Оцінка за двома шкалами вказувала на менший ступінь седатції в групі дітей із високою імпульсивністю в порівнянні з контрольною. Слід вважати, що седативний ефект мідазоламу в премедикації залежить від рівня імпульсивності і це треба враховувати в переднарковій підготовці.

**Ключові слова:** імпульсивність, мідазолам, премедикація, рейтингова шкала, біспектральний індекс.

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