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APPLICATION OF NONDEPOLARIZING MUSCLE RELAXANTS IN MECHANICALLY VENTILATED CRITICALLY ILL PATIENTS WITH ABDOMINAL HYPERTENSION

K. Dobrev[1], G. Arabadzhiev[1*], P. Taleva[1], V. Ivanov[2], K. Peeva[3]

[1]Department of Anesthesia and Intensive care, Medical Faculty, Trakia University, Stara Zagora, Bulgaria
[2]Department of Chemistry and Biochemistry, Medical Faculty, Trakia University, Stara Zagora, Bulgaria
[3]Department of Social medicine and Health management, Medical Faculty, Trakia University, Stara Zagora, Bulgaria

ABSTRACT
Non-surgical relief of IAP, plays an important role in treating patients developed IAP. The aim of this study was to evaluate the role of NDMR for IAP reduction in mechanically ventilated critically ill patients. For 18 patients hospitalized in intensive care unit of University Hospital in Stara Zagora, a protocol developed by the clinic was used - muscle relaxants were administered and the dynamics of changes in IAP was traced. Patients were divided into three groups according to degree of IAP, as recommended by WSACS. After statistical processing of the data, we found that in patients on mechanical ventilation with intra-abdominal pressure less than 20 mmHg, administration of NDMR leads to significant reductions in IAP and no change in pressure in patients with grade III-intra-abdominal hypertension.

Key words: Intra-abdominal pressure, monitoring, critically ill patients

INTRODUCTION

Intra-abdominal hypertension (IAH) and abdominal compartment syndrome (ACS) are associated with significant morbidity and mortality. The reduction of IAP is a cornerstone of breaking the series of pathophysiological changes that triggered others, and resulting in a poor outcome for the patients.

Nonoperative medical management strategies play an important role in the current treatment of IAH and ACS. There are five medical treatment options to be considered to reduce elevated intra-abdominal pressure (IAP): 1) improvement of abdominal wall compliance; 2) evacuation of intraluminal contents; 3) evacuation of abdominal fluid collections; 4) optimization of systemic and regional perfusion; and 5) correction of positive fluid balance. Nonsurgical management is an important treatment option in critically ill patients with raised IAP (1, 2).

***Correspondence to**: *Georgi Arabadzhiev, Department of Anesthesiology and Intensive Care, UMBAL SZ EAD, Medical Faculty, Trakia University, 11 Armeiska Str, 6003 Stara Zagora, Bulgaria, garabadzhiev@yahoo.com, 00359 42 664 475, 00359 888 228 231*

THE AIM

To determine whether the application of nondepolarizing muscle relaxants (NDMR) is associated with reducing of intra-abdominal pressure in critically ill patients with intra-abdominal hypertension.

Study Design

Prospective observational study in 6 beds mixed ICU – University Hospital, Stara Zagora.

Patients and methods

For the period between August 2010 and April 2012 we followed up 18 critically ill patients on mechanical ventilation, who manifested intra-abdominal hypertension. The application of muscle relaxants is not common practice in our behavior in patients on artificial ventilation,

considering the significant number of adverse effects. Nondepolarising muscle relaxants (NDMR) were applied in certain cases, according to our clinic's protocols for behavior in patients with Acute lung injury (ALI). This explains the longer period of follow-up.

Inclusion criteria: In the study participated all patients on mechanical ventilation with administered muscle relaxants and existing intra-abdominal hypertension. Exclusion criteria: contraindication to the use the transvesical route for IAP monitoring. Demographic data, primary diagnosis, co-morbidities, SOFA score, Dindo-Clavien classification of surgical complication, were collected **(Table 1)**.

For the patients was performed a Normality test and descriptive statistics **(Table 2)**.

Table 1. *Patients population*

N	Gender	Age	ICU days	SOFA score	Diagnosis
1	Male	72	17	16	Acute respiratory failure; Contusion of thorax; Multiple fractures of ribs; Traumatic haemopneumothorax
2	Male	74	23	20	Abdominal aortic aneurysm, ruptured
3	Male	41	16	22	Acute respiratory failure; Influenza with pneumonia; Adult respiratory distress syndrome
4	Male	63	13	18	Hepatic failure
5	Male	65	15	24	Acute respiratory failure; Pneumonia; Adult respiratory distress syndrome
6	Male	33	13	20	Acute respiratory failure; Pneumonia; Adult respiratory distress syndrome
7	Male	68	14	16	Acute respiratory failure; Pneumonia; Adult respiratory distress syndrome
8	Male	62	31	20	Acute respiratory failure; Pneumonia: Bronchopleural fistula.
9	Female	66	11	22	Hepatic failure; Acute hepatitis B with hepatic coma
10	Male	53	20	22	Acute respiratory failure; Influenza with pneumonia
11	Male	67	20	14	J96.1 Chronic respiratory failure; Chronic obstructive pulmonary disease with acute lower respiratory infection
12	Male	42	25	18	Polytrauma
13	Male	26	20	14	Contusion of thorax; Flail chest; Traumatic haemopneumothorax; Adult respiratory distress syndrome
14	Male	57	22	18	Adult respiratory distress syndrome; Pneumonia; Adult respiratory distress syndrome
15	Male	50	12	16	Polytrauma
16	Female	23	20	22	Adult respiratory distress syndrome; Influenza with pneumonia;
17	Female	28	15	22	Adult respiratory distress syndrome; Influenza with pneumonia;
18	Female	58	13	16	J96.1 Chronic respiratory failure; Chronic obstructive pulmonary disease with acute lower respiratory infection

Study Procedures

The intra-abdominal pressure was measured via a indwelling Foley bladder catheter, according to a standardized technique. The IAP was always measured at end-expiration in the complete supine position and stable conditions. The transduser was zeroed at the level of the mid-axillary line and NaCl 0.9% with room temperature were employed for bladder instillation volume – 20 ml. After each instillation an oscillation test was performed, and 2 minutes period is waited beforewe record the results. We applied standard protocol for neuromuscular relaxation. Tracrium (atracurium besylate) 10 mg/ml (Glaxo Group Ltd), bolus dose 0.5mgper kg and followed by infusion of 12 μg/ kg/ minute. All patients were sedated with Midazolam Torrex 5 mg/ml and Sufentanyl Torrex 5 μg/ml (Torrex Chiesi Pharma Group Gmbh) or Fentanyl-Richter 0.05mg/ml (Gedeon Richter Ltd). Patients were divided into three subgroups according to the values of IAP and WSACS recommendations - Group A (IAP from 12 to 15 mmHg), Group B (IAP from 16 to 20mmHg) and Group C (IAP from 21 to 25 mmHg). In this population of patients, there were none with IAP greater than 25 mmHg.

Table 2. *Normality test and descriptive statistics*

	Data set-A	Data set-B	Data set-C	Data set-D	Data set-E
Number of values	18	18	18	18	18
Minimum	13,00	7,000	6,000	6,000	6,000
25% Percentile	14,75	9,750	8,750	8,000	8,000
Median	17,00	15,00	14,50	14,50	14,50
75% Percentile	20,25	19,25	18,50	18,50	18,50
Maximum	23,00	22,00	22,00	22,00	22,00
10% Percentile	13,00	8,800	7,800	6,900	6,900
90% Percentile	22,10	22,00	21,10	21,10	22,00
Mean	17,44	14,78	13,89	13,67	13,78
Std. Deviation	3,185	4,833	5,040	5,269	5,287
Std. Error	0,7507	1,139	1,188	1,242	1,246
Lower 95% CI of mean	15,86	12,37	11,38	11,05	11,15
Upper 95% CI of mean	19,03	17,18	16,40	16,29	16,41
D'Agostino & Pearson omnibus normality test					
K2	1,834	2,528	2,736	3,464	2,990
P value	0,3998	0,2826	0,2546	0,1769	0,2242
Passed normality test (alpha=0.05)?	Yes	Yes	Yes	Yes	Yes
P value summary	ns	ns	ns	ns	ns
Coefficient of variation	18.26%	32.71%	36.29%	38.56%	38.37%
Skewness	0,2796	0,02634	0,07649	0,05096	0,1133
Kurtosis	-1,038	-1,207	-1,233	-1,323	-1,263
Sum	314,0	266,0	250,0	246,0	248,0

The value of IAP was measured before administering NDMR (Data set –A), 10 minutes after administration (Data set–B), 30 minutes after administration (Data set-C), 60 minutes after the administration (Data set-D), and 180 minutes after the administration (Data set-E). For data processing were used D'Agostino & Pearson omnibus, normality test; Pearson correlation coefficient; Repeated Measures ANOVA & Dunnett's Multiple Comparison Test, Grouped row means with SD analysis, with level of significance P value ($\alpha < 0.05$).

RESULTS

Analyzing the results a significant reduction of IAP was observed in all followed up intervals. **(Tab. 3 and Fig. 1)**. After administrating the bolus dose of NDMR occurs a decrease in IAP in the range of 3-6 mmHg, and this decrease is maintained during the infusion of relaxants at the reported time intervals. It is noteworthy that in Group A and Group B, intra-abdominal pressure lowered at 10 minutes and remained at these values for the entire measurement period **(Fig. 2 and Fig. 3)** In contrast, Group C's results show less effect from the administration of NDMR, and in some of the patients IAP remained unchanged. **(Fig. 4)**.

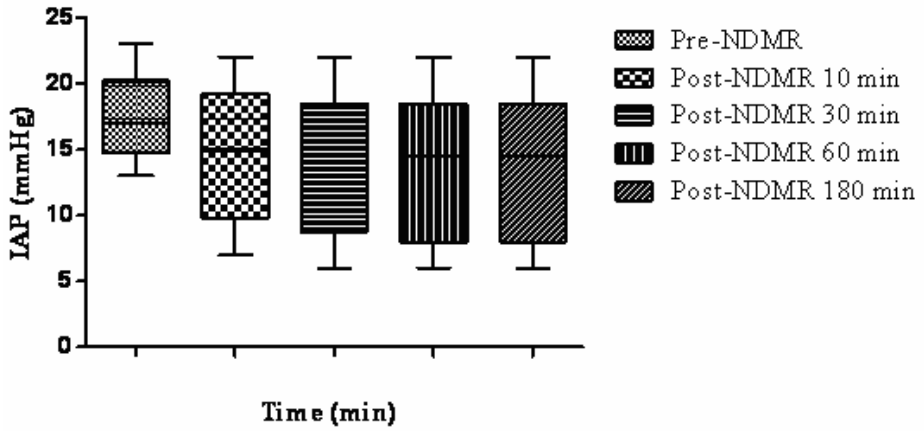

Figure 1. Box and whiskers plot – express mean values and SD of IAP dynamics in this selected time intervals

Table 3. *Showing significant differences in this population before and after NDMR application.*

Repeated Measures ANOVA					
P value	< 0.0001				
P value summary	***				
Are means signif. different? (P < 0.05)	Yes				
Number of groups	5				
F	42,30				
R squared	0,7133				
Was the pairing significantly effective?					
R squared	0,8802				
F	102,5				
P value	< 0.0001				
P value summary	***				
Is there significant matching? (P < 0.05)	Yes				
ANOVA Table	SS	df	MS		
Treatment (between columns)	182,0	4	45,51		
Individual (between rows)	1875	17	110,3		
Residual (random)	73,16	68	1,076		
Total	2130	89			
Dunnett's Multiple Comparison Test	Mean Diff.	q	Significant? P < 0.05?	Summary	95% CI of diff
Column A vs Column B	2,667	7,713	Yes	***	1.802 to 3.531
Column A vs Column C	3,556	10,28	Yes	***	2.691 to 4.420
Column A vs Column D	3,778	10,93	Yes	***	2.913 to 4.642
Column A vs Column E	3,667	10,61	Yes	***	2.802 to 4.531

*** P value–extremely significant (<0.001); ** P value–very significant (0.001-0.01); * P value-significant (>0.05); ns P value not significant (>0.05)

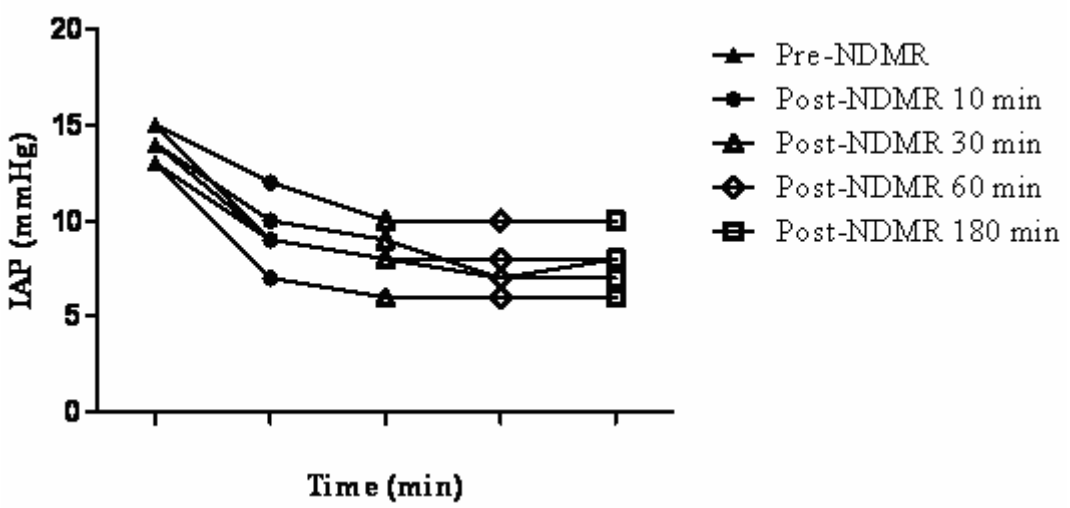

Figure 2. IAP changes in Group-A after NDMR application

CONCLUSION

From our study we can conclude that the administration of NDMR can have beneficial effects on IAP in selected patients and reduce the vicious circle of pathophysiological changes. But in other patients with III grade intra-abdominal hypertension, the application of NDMR did not show a significant change in the values of IAP measured transvesical, which suggested that other non-operative treatment methods should be used for those patients, before a decompressive laparotomy is performed.

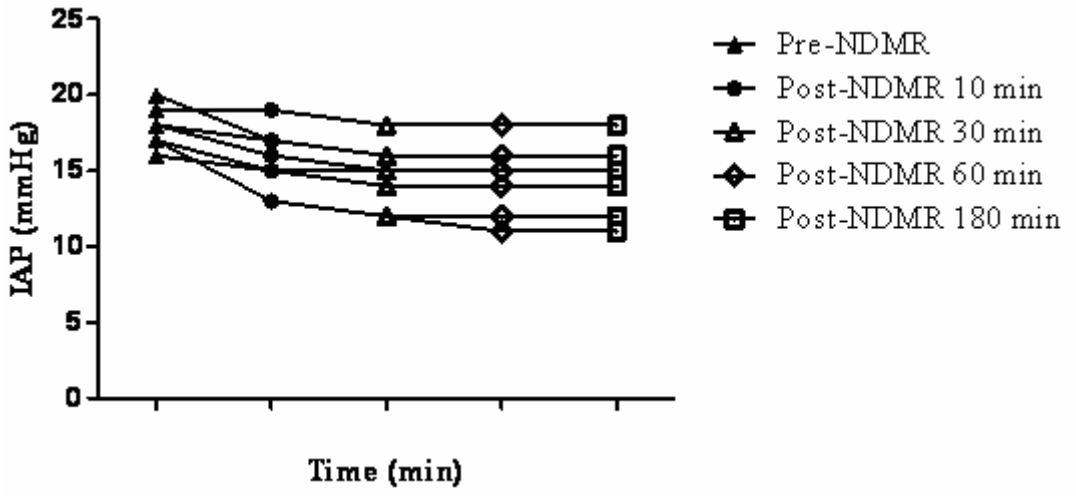

Figure 3. IAP changes in Group -B after NDMR application

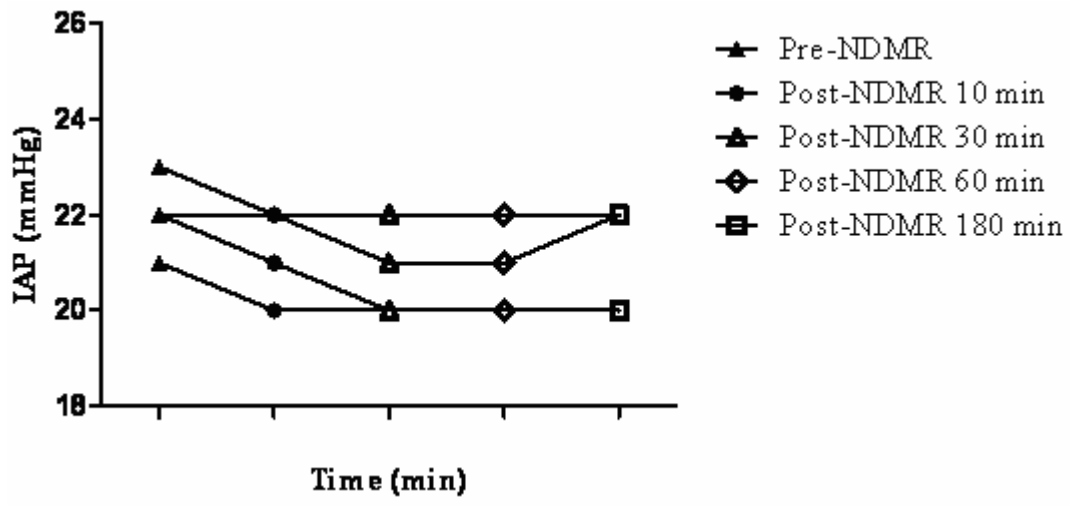

Figure 4. IAP changes in Group -C after NDMR application

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