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The protective effect of magnesium oxide on panitumumab-related hypomagnesemia

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Background

➢Hypomagnesemia, an adverse event for anti-epidermal growth factor receptor (EGFR) antibodies, is caused by a loss of magnesium from kidneys. Anti-EGFR antibodies inhibit EGFRs of renal tubular cells and magnesium reabsorption through TRPM6 (transient receptor potential metastatin 6) is inhibited at the distal tubular site. [1,2)]
➢The incidence rate of panitumumab (Pmab)-related hypomagnesemia is reportedly 16.9% (Gr ≥3:4.0%)[3)] and prophylactic treatment will have significant impacts on the completion rate of treatment and the quality of life (QOL) of patients. [4)]
➢There is a report that magnesium oxide may reduce hypomagnesemia by Cetuximab.[5)]
➢However, the prophylactic effects of magnesium oxide against Pmab-related hypomagnesemia have not been reported.

Objective

This study is to examine the prophylactic effects of magnesium oxide on Pmab-related hypomagnesemia at the Shizuoka Cancer Center.

Methods

➢This study included 86 patients with *KRAS* wild-type unresectable advanced/recurrent colorectal cancer who were treated with either Pmab and concomitant magnesium oxide (concomitant group) or Pmab alone (non-concomitant group) from April 2010 to March 2016.
➢The prophylactic effects of magnesium oxide on Pmab-related hypomagnesemia were retrospectively and comparatively examined regarding age, sex, ECOG performance status (PS), presence or absence of renal and hepatic disorders, treatment regimen, treatment line, number of treatment courses, and dosage of magnesium oxide.
➢Pmab-related hypomagnesemia were assessed using the CTCAE (Common Terminology Criteria for Adverse Events) version 4.0.
➢The study periods were; for 6 weeks from the start of Pmab treatment, and then it went on until the end of overall treatment time, within the period before the end of April 2016.

Results

Patient Characteristics (n = 86)

	Concomitant group (n = 24)	Non-concomitant group (n = 62)	*P* value
Median age (range)	67 (43-84)	67 (40-83)	0.92[a]
Sex (male/female)	17/7	43/19	1.00[b]
PS (0/1/2/3/4)	8/12/4/0/0	25/32/5/0/0	0.28[c]
Renal disorders (present/absent)	3/21	5/57	0.68[b]
Liver disorders (present/absent)	11/13	15/47	0.07[b]
Concomitant regimen (FOLFIRI/FOLFOX/CPT-11/Pmab alone)	6/8/3/7	11/3/13/35	0.19[c]
Treatment line (1/2/3/4)	8/7/9/0	8/20/27/7	0.24[c]
Median number of treatment courses (range)	10 (3-45)	10 (3-58)	0.12[a]
Median dosage of magnesium oxide (range)	990 mg/day (330-2,970 mg/day)		

a) Student's t-test b) Fisher's exact test c) Mann-Whitney's U test

Incidence rate and severity of hypomagnesemia (up to 6 weeks)

	Concomitant group (n = 24)				Non-concomitant group (n = 62)				Univariate analysis *P* value	Multivariate analysis *P* value
Incidence rate (%)	Any Gr			16.7	Any Gr			41.9	0.042*	0.044
Severity grading (%)	Gr1	Gr2	Gr3	Gr4	Gr1	Gr2	Gr3	Gr4	0.043#	
	8.3	8.3	0	0	37.1	4.8	0	0		

*) Fisher's exact test #) Mann-Whitney's U test Multivariate analyses were performed using a logistic regression model

Incidence rate and severity of hypomagnesemia (entire treatment period)

	Concomitant group (n = 24)				Non-concomitant group (n = 62)				Univariate analysis *P* value	Multivariate analysis *P* value
Incidence rate (%)	Any Gr			41.7	Any Gr			51.6	0.475*	0.999
Severity grading (%)	Gr1	Gr2	Gr3	Gr4	Gr1	Gr2	Gr3	Gr4	0.505#	
	29.2	12.5	0	0	40.3	9.7	1.6	0		

*) Fisher's exact test #) Mann-Whitney's U test Multivariate analyses were performed using a logistic regression model

Safety

There were no adverse events due to the concomitant use of magnesium oxide and no cases requiring delay, dose reduction or discontinuation of treatment associated with hypomagnesemia.

Discussion

➢Concomitant use of magnesium oxide may have prophylactic effects against Pmab-related hypomagnesemia during the first 6 weeks. However, no long-term prophylactic effects were observed.
➢It may have been because the constant dosage of magnesium oxide was not maintained but adjusted per patient.
➢The incidence rate of Pmab-related hypomagnesemia in our study was higher than previously reported. [1)] Also, although the frequency is low, serious adverse events such as QT prolongation, tetany, rhabdomyolysis and quadriplegia associated with hypomagnesemia have been reported.[1)] Therefore, we think that further prophylactic treatments need to be considered in the future.

Conclusions

Magnesium oxide has no long-term prophylactic effects against Pmab-related hypomagnesemia.

References

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