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Switching from biphasic human insulin to biphasic insulin aspart 30 in type 2 diabetes: Results from the ASEAN subgroup of the A_1chieve study

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ABSTRACT

Aim: To evaluate the safety and effectiveness of biphasic insulin aspart 30 (BIAsp 30) in ASEAN type 2 diabetes (T2D) patients switched from biphasic human insulin (BHI) in the non-interventional 24-week A_1chieve study.

Methods: Indonesian, Malaysian, Filipino and Singaporean patients switched from BHI to BIAsp 30 at their physicians' discretion were included. The incidence of serious adverse drug reactions (SADRs), including major hypoglycaemia was the primary endpoint. Changes in hypoglycaemia, glycated haemoglobin A_{1c} (HbA_{1c}), fasting plasma glucose (FPG), postprandial plasma glucose (PPPG), lipids, body weight and systolic blood pressure were also evaluated. Quality of life (QoL) was measured using the EQ-5D questionnaire.

Results: For the 465 patients included (mean±SD age: 56±10.3 years, diabetes duration: 9.7±7.1 years, baseline HbA_{1c}: 9.4±1.8%), the mean pre-study BHI dose was 0.62±0.28 IU/kg and 63.4% were dosing BHI twice daily (*bid*). The mean baseline BIAsp 30 dose was 0.65±0.27 U/kg, titrated up to 0.71±0.28 U/kg over 24 weeks, and most patients continued *bid* dosing. No SADRs or major hypoglycaemic episodes were reported. The proportion of patients reporting overall hypoglycaemia decreased significantly from 10.8% at baseline to 3.4% at Week 24 ($p < 0.0001$). Significant improvements in glycaemic control were noted (HbA_{1c}: −1.4±1.7%, FPG: −56.7±72.5 mg/dL, post-breakfast PPPG: −84.8±82.8 mg/dL, $p < 0.001$). Mean QoL improved by +6.6±14.6 points ($p < 0.001$).

Conclusion: BIAsp 30 was well-tolerated and significantly increased glycaemic control in this ASEAN subgroup poorly controlled on BHI.

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1. Introduction

The ASEAN countries, including Indonesia, Malaysia, Philippines and Singapore, have seen an alarming rise in the incidence of type 2 diabetes (T2D) over the recent decades [1]. The current prevalence of diabetes is 5.1% in Indonesia, 12.1% in Malaysia, 9.7% in Philippines and 12.45% in Singapore as estimated by the International

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Diabetes Federation. Moreover, Indonesia, Malaysia and Philippines are ranked among the top ten countries by number of diabetes cases in the Western Pacific region. The escalation in the disease burden is directly linked to decreased physical activity, urbanization, dietary transition and increased obesity [2].

With the progressive deterioration of beta-cell function over time, regular testing of blood glucose levels, timely dose titration and appropriate intensification of therapies are essential to maintain near-normal glycaemia in T2D [3]. In the absence of such precautionary measures, T2D patients are at higher risk of developing long-term vascular complications [4]. However, intensification is often delayed in routine clinical practice due to fears of hypoglycaemia and weight gain that may result from high insulin doses [5].

Premixed insulins or biphasic insulins were developed to provide suitable pre-meal and post-meal insulin levels through a combination of fast- and intermediate-acting insulins [6]. However, biphasic human insulin (BHI) is associated with a slow onset of action that necessitates timing injections 30 minutes prior to meals, which may be difficult for patients with varying schedules. In addition, BHI does not adequately control postprandial glucose excursions and patients are at greater risk of hypoglycaemia in case of a delay in the meal timing [7].

Biphasic insulin aspart 30 (BIAsp 30) is a modern premixed analogue that has been found to reach higher serum levels with a shorter time to attain maximum concentration compared to BHI [8]. These enhanced pharmacokinetic properties of BIAsp 30 allow better postprandial glucose (PPPG) control with this formulation compared to BHI. Due to its rapid-acting aspart component, BIAsp 30 can also be injected closer to mealtimes compared to BHI [9]. Transferring patients on BHI therapy to BIAsp 30 is known to be associated with improved PPPG control and decreased nocturnal hypoglycaemia [6].

In a sub-analysis of the international, non-interventional A_1chieve study [10], the clinical safety and effectiveness of switching from BHI to BIAsp 30 in patients with T2D was examined [11]. We investigated the safety and effectiveness of BIAsp 30 in T2D patients from Indonesia, Malaysia, Philippines and Singapore, previously treated with BHI. This subgroup analysis also aimed to obtain a perspective on the current standards of T2D care in local outpatient settings in the ASEAN region.

2. Materials and Methods

2.1. Study design

A_1chieve was an open-label, multinational, 24-week, non-interventional study that evaluated the clinical safety and effectiveness of BIAsp 30 (NovoMix® 30, Novo Nordisk A/S, Denmark), insulin detemir (Levemir®, Novo Nordisk A/S, Denmark) and insulin aspart (NovoRapid®, Novo Nordisk A/S, Denmark), in T2D patients in routine clinical practice [10]. Overall study results are available under www.A1chieve.com. Here, we evaluated the clinical safety and effectiveness of BIAsp 30 in patients from Indonesia, Malaysia, Philippines and Singapore, previously treated with BHI.

All decisions related to the dose and administration frequency of BIAsp 30 and concomitant oral glucose-lowering drugs (OGLDs) were left to the attending physicians. Data were collected at each visit from the physicians' notes and the patients' recall and self-monitoring diaries and blood glucose meters. The physicians performed all study assessments.

2.2. Study patients

This ASEAN subgroup consisted of T2D patients enrolled between October 2009 and December 2010 at 359 centers across Indonesia, Malaysia, Philippines and Singapore who were switched from BHI to BIAsp 30 therapy by their physicians. Patients who had received treatment with any of the study insulin analogues (alone or in combination) for over 4 weeks prior to baseline were not eligible for study participation. Women who were pregnant, breast-feeding or intended to become pregnant were also excluded. All patients provided signed informed consent. Ethics committee approval was obtained for the countries involved (Indonesia, Malaysia, Philippines and Singapore).

The investigators were trained in the study protocol, CRF completion, informed consent and safety reporting procedures.

2.3. Assessments and outcome measures

The primary objective was to evaluate the clinical safety of BIAsp 30 based on the number of serious adverse drug reactions (SADRs), including major hypoglycaemic events, recorded from baseline to Week 24. The secondary safety assessments comprised changes in the number of hypoglycaemic events (overall, major, minor and nocturnal), and serious adverse events (SAEs). The effectiveness assessments comprised change from baseline to Week 24 in HbA_{1c}, FPG, PPPG, body weight, blood lipids and systolic blood pressure (SBP). Quality of life (QoL) at baseline and Week 24 was assessed using the EQ-5D questionnaire. Local laboratories performed the laboratory measurements according to local standardization and quality control procedures.

2.4. Statistical methods

Statistical analyses were performed for the ASEAN subgroup of patients switching from BHI to BIAsp 30. Discrete and continuous variables were summarised using frequency tables (n, %) and descriptive statistics, respectively.

Paired t-tests were used to analyze the change from baseline to Week 24 in HbA_{1c}, FPG, PPPG, body weight, blood lipids, SBP and QoL, while McNemar's paired test was used to analyze the change in the proportion of patients reporting at least one hypoglycaemic event from baseline to Week 24. P-values are not presented when the number of patients analysed was less than 100.

Novo Nordisk performed all data analyses using SAS (Version 9.1.3).

3. Results

3.1. General characteristics

A total of 465 patients recruited from the ASEAN region switched treatment from BHI to BIAsp 30. The demographic and baseline characteristics of this subgroup are reported in Table 1.

Table 1 – Demographic and baseline characteristics of patients switching from BHI to BIAsp 30

Characteristic	All patients (N = 465)
Gender (male/female), %	50.5/49.5
Age, years	56.0 (10.3)
Body weight, kg	66.6 (13.6)
Body mass index, kg/m^2	25.6 (4.8)
Duration of diabetes, years	9.7 (7.1)
Time to insulin initiation, years	7.2 (6.1)
Duration on OGLDs, years	8.1 (6.6)
Duration on insulin, years	2.5 (2.7)
HbA_{1c}, %	9.4 (1.8)
HbA_{1c}, mmol/mol	79 (20)
OGLDs at baseline, n (%)	
Metformin	243 (86.8)
Sulfonylureas	45 (16.1)
Alpha-glucosidase inhibitors	29 (10.4)
1 OGLD	216 (77.1)
2 OGLDs	54 (19.3)
>2 OGLDs	10 (3.6)

BHI, biphasic human insulin; BIAsp 30, biphasic insulin aspart 30; OGLD(s), oral glucose-lowering drug(s).
Data are mean (SD) unless specified otherwise.

At baseline, the mean (±SD) age was 56.0±10.3 years and the mean body mass index (BMI) was 25.6±4.8 kg/m^2. The mean diabetes duration was 9.7±7.1 years and the mean HbA_{1c} level was 9.4±1.8% (79±20 mmol/mol). The most common physicians' reasons for switching from BHI to BIAsp 30 were to improve glycaemic control (92.7%), try new insulin (52.5%) and reduce plasma glucose variability (42.2%).

Pre-study, the majority of patients (72.3%) used 1 OGLD and the most common OGLD used was metformin (85.3%). At baseline, the majority of patients (77.1%) continued using 1 OGLD with metformin use (86.8%) predominating.

3.2. SADRs and SAEs

No SADRs were reported during the study. A total of 2 serious adverse events (SAEs) were reported in 1 patient. Both SAEs were considered unlikely to be related to BIAsp 30.

3.3. Hypoglycaemia

After 24 weeks of BIAsp 30 therapy, the event rate of overall hypoglycaemia appeared to decrease from 3.33 to 0.72 events/patient-year (Table 2). Correspondingly, the proportion of patients reporting overall hypoglycaemia decreased from 10.8% at baseline to 3.4% at Week 24 ($p < 0.0001$, Table 2). No major hypoglycaemic events were reported during the study.

Table 2 – Baseline and 24-week data for hypoglycaemia

Hypoglycaemia	Events per patient-year / percent with at least one event		
	Baseline	Week 24	p-value
Overall	3.33 / 10.8	0.72 / 3.4	<0.0001
Nocturnal	1.29 / 5.4	0.19 / 1.0	<0.0001
Major	0.39 / 1.5	0.0 / 0.0	0.0143
Minor	2.94 / 10.3	0.72 / 3.4	<0.0001

p-values are from McNemar's test on paired proportions of patients experiencing hypoglycaemia.

The event rates for nocturnal and minor hypoglycaemia also appeared to reduce with a statistically significant decrease in the proportion of patients reporting these events at Week 24 compared to baseline ($p < 0.0001$, Table 2).

3.4. Insulin dose and blood glucose lowering

Pre-study, the mean BHI dose was 0.62±0.28 IU/kg (Table 3). The mean BIAsp 30 dose was 0.65±0.27 U/kg at baseline,

Table 3 – Insulin dose and dosing frequency pre-study, at baseline and at Week 24

		All patients
Insulin dose, U/day	n	465
	Pre-study[a]	41.3 (19.9)
	Baseline	43.2 (19.1)
	Week 24	47.3 (20.3)
Insulin dose, U/kg	n	453
	Pre-study[b]	0.62 (0.28)
	Baseline	0.65 (0.27)
	Week 24	0.71 (0.28)
Dose frequency, n (%)	Pre-study (n)	462
	Once daily	157 (34.0)
	Twice daily	293 (63.4)
	Thrice daily	12 (2.6)
	>Thrice daily	–
	Baseline (n)	465
	Once daily	7 (1.5)
	Twice daily	290 (62.4)
	Thrice daily	156 (33.5)
	>Thrice daily	12 (2.6)
	Week 24, n	414
	Once daily	12 (2.9)
	Twice daily	361 (87.2)
	Thrice daily	37 (8.9)
	>Thrice daily	4 (1.0)

Pre-study, baseline and Week 24 values are presented as mean (SD) unless specified otherwise.
[a] IU/day pre-study.
[b] IU/kg pre-study.

Table 4 – Baseline and 24-week data for glucose control parameters

	n	Baseline	Week 24	Change	p-value
HbA_{1c}, %	182	9.4 (1.8)	8.0 (1.6)	−1.4 (1.7)	<0.001
HbA_{1c}, mmol/mol	182	79 (20)	64 (17)	−15 (19)	NA
FPG, mg/dL	328	190.9 (70.4)	134.1 (42.6)	−56.7 (72.5)	<0.001
PPPG, mg/dL	202	264.5 (84.2)	179.7 (49.5)	−84.8 (82.8)	<0.001

FPG, fasting plasma glucose; HbA_{1c} glycated haemoglobin A_{1c}; PPPG, postprandial plasma glucose.
Baseline, Week-24 and change values are mean (SD).

Table 5 – Baseline and 24-week data for blood lipids, body weight and SBP

	n	Baseline	Week 24	Change	p-value
Total cholesterol, mmol/L	121	5.2 (1.5)	4.9 (1.1)	−0.3 (1.5)	0.074
Triglycerides, mmol/L	111	1.8 (0.9)	1.7 (0.9)	−0.1 (0.9)	0.158
HDL cholesterol, mmol/L	99	1.2 (0.4)	1.3 (0.3)	0.1 (0.4)	–[a]
LDL cholesterol, mmol/L	98	3.1 (1.2)	2.9 (0.9)	−0.1 (1.1)	–[a]
Body weight, kg	384	65.8 (12.7)	66.5 (12.4)	0.7 (4.2)	0.002
SBP, mmHg	374	131.3 (16.6)	128.8 (15.4)	−2.6 (16.7)	0.003

HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure.
Baseline, Week-24 and change values are mean (SD).
[a] p-value not reported since n < 100.

titrated up to 0.71±0.28 U/kg at Week 24. In total, 63.4% of patients injected BHI twice daily (*bid*) pre-study, while 62.4% and 87.2% injected BIAsp 30 *bid* at baseline and Week 24, respectively (Table 3).

Statistically significant reductions were noted in the mean HbA_{1c} (−1.4±1.7%/−15±19 mmol/mol), FPG (−56.7±72.5 mg/dL) and post-breakfast PPPG (−84.8±82.8 mg/dL) levels following the therapy switch from BHI to BIAsp 30 ($p < 0.001$, Table 4). The number of patients achieving the HbA_{1c} target of <7.0% (<53 mmol/mol) was 78 (32.6%) at Week 24 compared to 12 (4.6%) at baseline.

3.5. Body weight, lipids and blood pressure control

The mean body weight increased by 0.7±4.2 kg from baseline to Week 24 ($p = 0.002$, Table 5) after switching from BHI to BIAsp 30.

There were no statistically significant changes in the mean total cholesterol and triglyceride levels at the end of the study (Table 5). The mean change from baseline to Week 24 in LDL cholesterol levels was −0.1±1.1 mmol/L, while the mean HDL cholesterol levels appeared to increase by 0.1±0.4 mmol/L.

The mean SBP decreased by −2.6±16.7 mmHg from 131.3±16.6 mmHg at baseline to 128.8±15.4 at the end of the study ($p = 0.003$, Table 5).

3.6. Quality of life

Health-related QoL improved from 73.4±16.1 at baseline to 80.0±11.2 at Week 24 (mean change: +6.6±14.6 points, $p < 0.001$) on the visual analogue scale of the EQ-5D questionnaire.

4. Discussion

This analysis demonstrated the safety and effectiveness of BIAsp 30 therapy in a subgroup of ASEAN patients previously treated with BHI. No SADRs or major hypoglycaemic episodes were reported in this subgroup during the study. Significantly fewer patients reported overall, nocturnal and minor hypoglycaemia at Week 24 compared to baseline showing that the therapy change was well-tolerated and concurring with the results from other non-interventional studies investigating the effects of switching from BHI to BIAsp 30 [11,12].

Poor metabolic and glycaemic control has been observed in the majority of the T2D patients in local clinical practice in the ASEAN region signaling a failure in translating treatment guidelines into real-life practice [1,13–15]. In the DiabCare Asia study conducted in 1998 and 2008, the mean glycated haemoglobin A_{1c} (HbA_{1c}) levels were ⩾8.0% (⩾64 mmol/mol) in Malaysia, Singapore and Indonesia [13–15], although the American Diabetes Association (ADA) recommends intensifying treatment when HbA_{1c} is ⩾7.0% (⩾53 mmol/mol) [16]. In this ASEAN subgroup, marked hyperglycaemia was observed at baseline (mean HbA_{1c}: 9.4±1.8% [79±20 mmol/mol], FPG: 190.9±70.4 mg/dL and PPPG: 264.5±84.2 mg/dL).

The majority of patients followed BIAsp 30 *bid* dosing at baseline and Week 24. The proportion of patients who reached the ADA target HbA_{1c} level of <7.0% (<53 mmol/mol) was 32.6% at Week 24, comparable to the results from the overall A_1chieve switch cohort (33.6%) [11].

At Week 24, mean HbA_{1c} had improved by −1.4±1.7% (−15±19mmol/mol) and the mean FPG and PPPG also decreased in the ASEAN subgroup. These data support

the results from the overall A_1chieve switch cohort and the IMPROVE and PRESENT observational studies, where switching from BHI to BIAsp 30 also led to significant improvements in blood glucose levels [11,12,17]. However, although the reductions were statistically significant, the mean values at Week 24 for HbA_{1c} and FPG did not meet the ranges recommended jointly by the ADA and the European Association for the Study of Diabetes [3]. This could be due in part to the high baseline levels. Also, the associated mean dose increase over 24 weeks was small in the ASEAN subgroup (0.65 U/kg at baseline to 0.71 U/kg at Week 24). The 24-week study duration was considered adequate to evaluate the response to therapy change; however, with more aggressive titration, continued monitoring of glycaemic levels over a longer period and possible intensification to BIAsp 30 three times daily (*tid*), it is likely that the target HbA_{1c}, FPG and PPPG ranges may be achieved. In fact, in the 1-2-3 study, Garber et al. [18] reported that intensification to BIAsp 30 *tid* after 16 weeks on a *bid* dosing regimen enabled a greater proportion of patients to reach target HbA_{1c} levels.

The mean body weight increased by 0.7 kg in the ASEAN subgroup, similar to the mean increase in the East Asia switch cohort (0.6 kg) of the A_1chieve study [9]. Significant improvements in QoL were noted following the switch to BIAsp 30 from BHI, perhaps related to the more convenient dosing options available with this insulin analogue [7].

This study was observational in nature with no control arm and may have been subject to a recall bias in the recording of hypoglycaemic events owing to retrospective data collection methods. It is also possible that data collection may not have occurred consistently across sites. However, the laboratory measurements were performed following local standardization and quality control procedures. Also importantly, the data obtained from this study could form part of an evidence base, together with the data from randomized clinical trials, which would help inform local clinical practice guidelines.

In conclusion, transferring ASEAN T2D patients from BHI to BIAsp 30 therapy was associated with improved glycaemic control and a decreased risk of hypoglycaemia in this sub-analysis of the non-interventional A_1chieve study. The baseline data obtained from the patients in this ASEAN subgroup corroborated the urgent need to revisit clinical practice guidelines in this region. Greater adherence to the recommended guidelines needs to be ensured so that the quality of diabetes care in local clinical practice can be optimized.

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Conflict of interest statement

Zanariah Hussein received honorarium for conduct of research from Novo Nordisk. Dr. Anand B. Jain is employed by Novo Nordisk Pharma Malaysia. Su Yen Goh received honorarium for conduct of research from Novo Nordisk. Dr. Pradana Soewondo has authored an article sponsored by Novo Nordisk and sanofi aventis, and has served as a consultant (Advisory Board) for Novo Nordisk, sanofi aventis, and Novartis. Dr. Pradana Soewondo has also received research grants from World Diabetes Foundation and grants for lectures from Novo Nordisk, sanofi aventis, Novartis and MSD. Mary Anne Lim-Abrahan received honorarium for conduct of research from Novo Nordisk, and has served as a consultant (Advisory Board) for sanofi aventis, Merck, and Novo Nordisk. This study was sponsored by Novo Nordisk A/S, Denmark. The sponsor took part in the development of the protocol, the process of data collection and analysis, funding of medical writing services, and in reviewing the manuscript, but not in participant selection, choice of therapies (study or otherwise), provision of therapies including insulin or continuing clinical management of the participants.

REFERENCES

[1] Paz-Pacheco E. Diabetes Clinical Practice Guidelines (CPGs) for the ASEAN region: Country initiatives for collectively enhanced diabetes care in the region. JAFES 2011;26(1): 36–7.
[2] Whiting DR, Guariguata L, Weil C, Shaw J. IDF diabetes atlas: global estimates of the prevalence of diabetes for 2011 and 2030. Diabetes Res Clin Pract 2011;94(3):311–21.
[3] Inzucchi SE, Bergenstal RM, Buse JB, Diamant M, Ferrannini E, Nauck M, et al. Management of hyperglycaemia in type 2 diabetes: a patient-centered approach. Position statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetologia 2012;55(6):1577–96.
[4] Stratton IM, Adler AI, Neil HA, Matthews DR, Manley SE, Cull CA, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. BMJ 2000;32:405–12.
[5] Campbell RK. Recommendations for improving adherence to type 2 diabetes mellitus therapy – focus on optimizing insulin-based therapy. Am J Manag Care 2012;18(Suppl 3): S55–61.
[6] Liebl A, Prusty V, Valensi P, Kawamori R, Christiansen JS, Palmer AJ. Ten years of experience with biphasic insulin aspart 30: from drug development to the latest clinical findings. Drugs 2012;72(11):1495–520.
[7] Heller S. Reducing hypoglycaemia with insulin analogues Int J Obes Relat Metab Disord 2002;26(Suppl 3):S31–6.
[8] Heise T, Heinemann L, Hövelmann U, Brauns B, Nosek L, Haahr HL. Biphasic insulin aspart 30/70: pharmacokinetics and pharmacodynamics compared with once-daily biphasic human insulin and basal–bolus therapy. Diabetes Care 2009;32(8):1431–3.

[9] Garber AJ, Ligthelm R, Christiansen JS, Liebl A. Premixed insulin treatment for type 2 diabetes: analogue or human? Diabetes Obes Metab 2007;9(5):630–9.
[10] Home P, Naggar NE, Khamseh M, Gonzalez-Galvez G, Shen C, Chakkarwar P, et al. An observational non-interventional study of patients with diabetes beginning or changed to insulin analogue therapy in non-Western countries: The A_1chieve study. Diabetes Res Clin Pract 2011;94:352–63.
[11] Naggar NK, Soewondo P, Khamseh ME, Chen JW, Haddad J. Switching from biphasic human insulin 30 to biphasic insulin aspart 30 in type 2 diabetes is associated with improved glycaemic control and a positive safety profile: Results from the A_1chieve study. Diabetes Res Clin Pract 2012;98(3):408–13.
[12] Shah S, Benroubi M, Borzi V, Gumprecht J, Kawamori R, Shaban J, et al.; IMPROVE Study Group Expert Panel. Safety and effectiveness of biphasic insulin aspart 30/70 (NovoMix 30) when switching from human premix insulin in patients with type 2 diabetes: subgroup analysis from the 6-month IMPROVE observational study. Int J Clin Pract 2009;63(4):574–82.
[13] Mafauzy M, Hussein Z, Chan SP. The status of diabetes control in Malaysia: results of DiabCare 2008. Med J Malaysia 2011;66(3):175–81.
[14] Lee WR, Lim HS, Thai AC, Chew WL, Emmanuel S, Goh LG, et al.; Diabcare Singapore Local Working Group & Diabetic Society of Singapore. A window on the current status of diabetes mellitus in Singapore – the Diabcare-Singapore 1998 study. Singapore Med J 2001;42(11):501–7.
[15] Soewondo P, Soegondo S, Suastika K, Pranoto A, Soeatmadji DW, Tjokroprawiro A. The DiabCare Asia 2008 study – Outcomes on control and complications of type 2 diabetic patients in Indonesia. Med J Indones 2010;19:235–44.
[16] Nathan DM, Buse JB, Davidson MB, Heine RJ, Holman RR, Sherwin R, et al. Management of hyperglycemia in type 2 diabetes: a consensus algorithm for the initiation and adjustment of therapy: a consensus statement from the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care 2006;29:1963–72.
[17] Shestakova M, Sharma SK, Almustafa M, Min KW, Ayad N, Azar ST, et al. Transferring type 2 diabetes patients with uncontrolled glycaemia from biphasic human insulin to biphasic insulin aspart 30: experiences from the PRESENT study. Curr Med Res Opin 2007;23(12):3209–14.
[18] Garber AJ, Wahlen J, Wahl T, Bressler P, Braceras R, Allen E, et al. Attainment of glycaemic goals in type 2 diabetes with once-, twice-, or thrice-daily dosing with biphasic insulin aspart 70/30 (The 1-2-3 study). Diabetes Obes Metab 2006;8(1):58–66.