Physiologic effects of intraperitoneal vs. subcutaneous insulin delivery in patients with DM1: A systematic review

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Motivation

Aim:

Identify possible different physiologic effects of intraperitoneal (IP) versus subcutaneous (SC) insulin administration in patients with DM1.

Reason for the study:

No systematic review has been performed on this particular topic before.

Challenges:

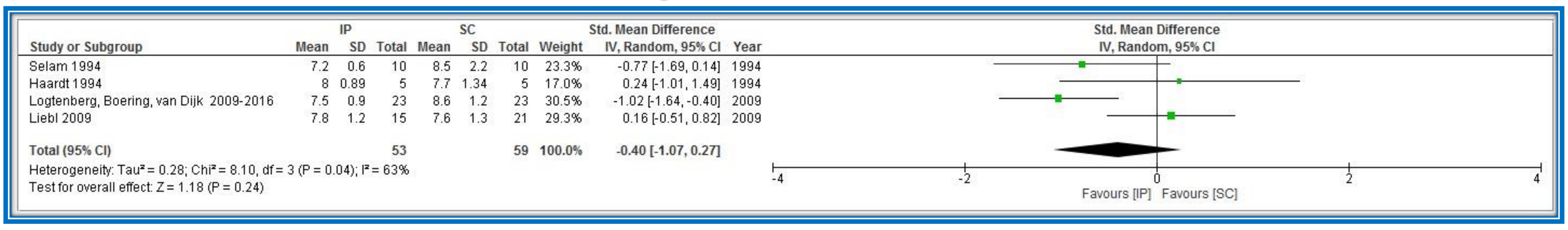
- Differences in reporting
- Different types of insulin used
- Different standards of treatment.

Methods

- Systematic search in PubMed, Scopus, CENTRAL and Embase databases identified 1517 publications. Of these 106 were recognized as relevant for the review.
- Data analyzed using RevMan software.
- Assessment of risk of bias analyzed using Cochrane collaboration tools, STROBE statement checklist and Quality Assessment Tool for Quantitative Studies.

Results

Randomized Controlled Studies: HbA1c changes after 6 months of treatment



Overview over all randomized controlled studies on IP vs SC insulin delivery

Author, date, country	Study type	Participants	Length of follow-up	Reported study objectives	Outcomes	Methodological quality
Selam et al., 1994, USA, California	RCT	10	9 months (3-mo treatment optimization, then 6-mo IPII or SCI	Comparison of cholesterol efflux and cholesterol ester transfer protein activity between IP and SC insulin administration in type 1 diabetic patients.	Mean HbA1c, BG, daily insulin use and plasma free-insulin levels did not change significantly within groups. Triglyceride level did not increase in IP group.	Cochrane risk of bias tool: Unclear risk of bias: random sequence generation, allocation concealment, blinding Low risk of bias:, incomplete outcome data, selective reporting, treatment procedure
Haardt et al., 1994, France, Paris	RCT (crossover)	10	12 months (6-mo per phase)	Comparison of cost-benefits between IPII and MDI in type 1 diabetic patients.	HbA1c, glycemic fluctuation and hypoglycemic events reduced in IP period.	Cochrane risk of bias tool: Unclear risk of bias: random sequence generation, allocation concealment, blinding Low risk of bias: incomplete outcome data, selective reporting, treatment procedure
Logtenberg et al., 2009, Logtenberg et al., 2010[a], Logtenberg et al., 2010[b], van Dijk et al., 2012, van Dijk et al., 2014[c], van Dijk et al., 2014[d], van Dijk et al., 2014[e], van Dijk et al., 2015, Boering et al., 2016, The Netherlands, Sweden	RCT (crossover)	16-24	16 months (3-mo qualification phase, then 6-mo IPII or SCI, crossover phase 4-w)	Comparison of safety, efficacy, QoL and treatment satisfaction, cost of treatment, IGF-1 and IGFBP1 conc. and SHBG conc. between CIPII and intensified SC insulin therapy in patients with inadequately controlled type 1 diabetes.	CIPII treatment decreases hypoglycemic events and reduces time spend in hyperglycemia and significantly reduces HbA1c level. QoL and treatment satisfaction Improves in CIPII group. High costs of the implantable pump and the insulin in CIPII group. Observes significant differences in IGF-1 and IGFBP1 conc. in CIPII but not in CSII group. SHGB conc. decreases significantly during CIPII group.	Cochrane risk of bias tool: Unclear risk of bias: blinding Low risk of bias: random sequence generation, allocation concealment, incomplete outcome data, selective reporting, treatment procedure
Liebl et al., 2009, Germany, The Netherlands, France, Austria, Switzerland	RCT (crossover)	60	18 months (12-mo CIPII and 6-mo SCII)	Comparison of frequency of hypoglycemia, severe hypoglycemia, metabolic control, diabetic QoL and safety between CSII and CIPII in type 1 diabetic patients.	Not observed statistically significant differences of hypoglycemic events, glycemic control or QoL between groups. Similar improvement in HbA1c levels in both groups.	Cochrane risk of bias tool: Unclear risk of bias: random sequence generation, allocation concealment, blinding Low risk of bias: incomplete outcome data, selective reporting, treatment procedure
Selam et al., 1992, USA, California*	RCT	21	9 months (3-mo treatment optimization, then 6-mo IPII or SCI	Comparison between IPII and SC intensive insulin therapy (MDI or CSII).	HbA1c and BG level improves in IPII and SC groups. IPII limits glycemic fluctuations.	Cochrane risk of bias tool: Unclear risk of bias: random sequence generation, allocation concealment, blinding, incomplete outcome data Low risk: selective reporting, treatment procedure

* Cannot make data analysis based on bias in reporting number of patients per group

(C)IPII – (continuous) intraperitoneal insulin infusion
SCI – subcutaneous insulin
CSII – continuous subcutaneous insulin infusion
MDI – multiple daily injections
RCT – randomized controlled trial
QoL – quality of life
IGF-1 – insulin-like growth factor-1
IGFBP1 – insulin-like growth factor-binding protein 1
SHBG – sex hormone binding globulin

Discussion

Overall randomized controlled studies observed a tendency towards improved glucoses control evaluated by HbA1c levels in patients treated with IP insulin delivery. Further continuous IP insulin delivery compared to SC delivery seems to affect IGF-1, IGFBP1 and SHBG concentration in patients with type 1 diabetes (data not shown). Further analyses of all the identified studies are ongoing and will be published.

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